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JOHP

Herbal interventions for enhancing female fertility with a focus on *mangifera indica* bark: A review

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Abstract:

Infertility presents significant difficulties for women and their families, and female fertility is a crucial aspect of human reproductive health. Herbal interventions are gaining popularity as viable treatments for infertility, although there are many contributing factors. This review paper investigates the efficacy of herbal medicines in enhancing female fertility, focusing specifically on the bark of the *Mangifera indica* (mango). We examined the scientific research, conventional wisdom, and action mechanisms about the usage of bark from the *Mangifera Indica* plant as a natural fertility booster. The review emphasizes the possible advantages, safety concerns, and opportunities for further study of herbal remedies for female reproductive health.*Mangifera indica* L. plays a significant role in traditional medical practices. Aqueous *Mangifera indica* bark extract (MIBE) is taken orally. They show the changes inhormonal and estrous cycling patterns in female Rats. MIBE also shows some positive effects regarding the male's hormonal profile and sperm quality.The MIBE significantly raised levels of Luteinizing hormone (LH), Testosterone, and Follicle follicle-stimulating hormone (FSH), according to the results of a hormonal study.This might be due to the extract's capacity to raiselevels of the hormones FSH and LH, which oversee spermatogenesis and estrous cycle pattern. This implies that Mangifera indica stem bark may be used in the creation of female reproductive medications.

Keywords: *Mangifera indica* bark; extract; Infertility; Estrous cycle; Herbal.

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Introduction:

Mango (*Mangifera indica Linn*), often known as Amm or Amba, is a plant that naturally grows in Southeast Asia and India. It is utilized as a sacred plant and in the Hindu religion. Tribal peoples and all Indians use its fruit, root, bark, flower, and leaves to treat a variety of illnesses and problems [1]. It is also used to make furniture and as fuel. It is specifically used to treat conditions like piles, infertility, syphilis, diabetes, kidney stones, sunstroke, TB, urinary disorders, dysentery, eye conditions, diarrhea, syphilis, ulcers, and blood purification [1, 2]. To promote the nutritional use of M. indica as well as its therapeutic usage, it is imperative to extensively research both its good and negative effects, particularly on reproductive functions.Several parts of M. indica, including the leaves, stem bark, fruit peel, flesh, root, and flowers, have anti-inflammatory, anti-bacterial, anti-fungal, antiparasitic, hepatoprotective, and anti-HIV properties [3,4]. They also have antispasmodic, antipyretic, antiviral, anthelminthic, immunomodulatory, anti-diarrhea, and antiviral properties [5]. The results mentioned above served as the foundation for the creation of a new natural product from the MBIE, with the idea being that its antioxidant effects would be more widely applicable than a single medicinal use [6]. Male fertility has been improved and various physiological diseases have been treated using natural plant ingredients. This is due to the abundance of natural antioxidants they contain, including phenols, flavonoids, terpenoids, and xanthones. Additionally, they are quite safe, inexpensive, and accessible [7, 8].

Traditional Knowledge and Ethnopharmacology:

The historical and cultural significance of *Mangifera indica* bark in traditional medicine systems is explored in this section. Indigenous populations have long utilized various parts of the mango tree, including the bark, to address a range of health concerns, including fertility-related issues. These traditional practices provide a foundation for contemporary research.The bark of M. indica is one of the primary organs used in all areas of its distribution; Table 1 lists its therapeutic applications globally. A standardized aqueous extract of *M. indica* L. stem bark with antioxidant, anti-inflammatory, and immunomodulatory effects has recently been developed & based on ethnopharmacological knowledge. It is suggested that this extract be used as an antioxidant nutritional supplement as well as an anti-inflammatory, analgesic, and immunomodulatorytreatment for asthma, AIDS, cancer, and stomach and dermatological disorders, to improve the patient's quality of life and stop the disease from getting worse [9].

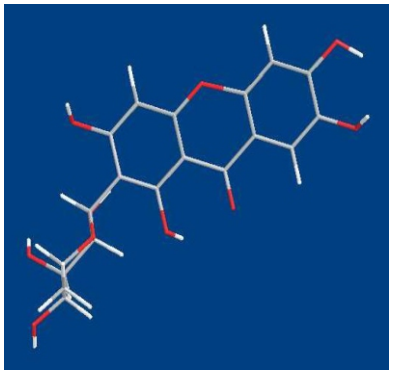
Background:

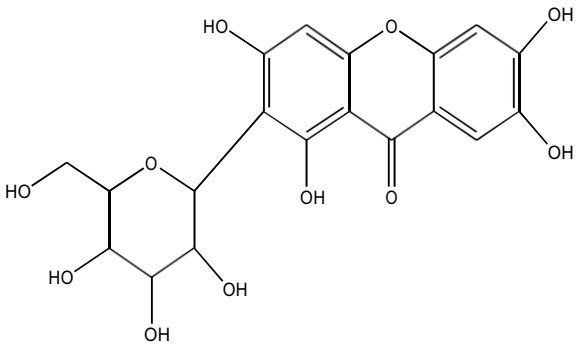
This plant is a substantial tree with deep, robust tap roots. The bark is thick, strong, and rough. It has a dense, spherical crown and is evergreen. Linear leaves are clustered at the ends of branches and are oblong, acute, and acuminate. A small number of white to yellowish blooms are seen in the panicle-like inflorescence. Fruit is a huge, simple drupe that comes in a variety of shapes and colors, from green to yellow or red. The endocarp of the seeds, which are coated in a fibrous sheath, is hairy. The plant can grow up to 1200 mt in the forest, but it is now being grown on a massive scale in India. Plants have been documented in India since prehistoric times.

Taxonomical Classification:

Table 1: Bionomical Classification.

Kingdom	*Plantae*
Class	*Mangoliopsida*
Phylum	*Mangoliophyta*
Order	*Sapindales*
Family	*Anacardiaceae*
Genus	*Mangifera*
Species	*indica*





2-(tetrahydro-3,4,5-trihydroxy-6-(hydroxymethyl)-2*H*-pyran-2-yl)-1,3,6,7 -tetrahydroxy-9*H*-xanthen-9-one

Fig.1: Structure of Mangiferine 3D and 2D

Phytochemical composition:

Mangifera indica bark is rich in bioactive compounds, such as polyphenols, flavonoids, and tannins, which may contribute to its potential efficacy in improving female fertility. This section delves into the phytochemical composition of the bark and its known or potential effects on reproductive health [10, 11].

Table 2: Bio-active chemical compounds present in *Mangifera indica* bark extract (MIBE).

S. No.	Bio-active Compounds
1.	Polyphenols
2.	1 Mangiferin
3.	(+) Catechin
4.	Gallic acid, propyl ester
5.	Benzoic acid, propyl ester
6.	Benzoic Acid
7.	Gallic Acid
8.	Phytosterols
9.	b-Sitosterol
10.	b-Campesterol

Mechanisms of Action:

Numerous possible pathways by which Mangifera Indica bark may affect female fertility have been identified by scientific investigations. These mechanisms include those that control hormones, have antioxidant effects, have anti-inflammatory qualities, and modify the uterine environment. We will provide insights into how the herbal cure may affect reproductive results by the detailed study of these processes that we give [5].

Material & Methods:

Mango stem bark, or *Mangifera indica* L., was gathered from a field under cultivationMango (Mangifera indica L.) The industrial method of MBIE involves the decoction of stem bark using water as a solvent, followed by concentration. No organic solvents are utilized during this process[12]. The samples were then shaken for 24 hours at room temperature in an orbital shaker (Gallenkamp, Loughborough, Leicestershire, UK) under light conditions and a speed of 150 rpm.Using Whatman No. 1 filter paper, the extracts were separated from the residues through filtration. In the same way, the residues were extracted twice, and the extracts were mixed. The mixed extracts were concentrated at 45°C under reduced pressure. After weighing the crude extracts to determine the yield, they were kept at -4°C for additional examination [13].

Clinical and Preclinical Studies:

A comprehensive review of both clinical and preclinical studies related to *Mangifera indica* bark and female fertility is presented. This section examines the existing evidence, highlighting notable findings, limitations, and potential areas for further research [14].

Safety and Considerations:

One major worry is the safety profile of herbal therapies. The safety concerns surrounding the usage of *Mangifera indica* bark are covered in this part, and it is emphasized how crucial it is to carry out thorough safety assessments in future studies.HIV/AIDS, geriatrics, and skin problems have all been the subject of pertinent controlled clinical trials using mango formulations (Vimang), with notable improvements in patient quality of life[4]. Vimang pills per day (2.4 g MIBE daily before meals) were given to HIV patients (seropositive with CD4 levels between 300 and 500) for six months as part of a double-blind randomized and placebo-controlled experiment (82 individuals). In 58% of cases, seven out of nine oxidative stress (OS) indicators improved. Based on scientific evidence ranging from basic to clinical research, MIBE, when utilized as an active principle in various pharmaceutical formulations, has demonstrated efficacy and reproducibility as an antioxidant, anti-inflammatory, and immunomodulator [13]. Mangiferin has been shown to exhibit a wide range of pharmacological properties, including lipolytic, anti- bone resorption, immunomodulatory, antioxidant, radioprotective, anti-allergic, anti- inflammatory, anticancer, antidiabetic, and inhibiting monoamine oxidase. These findings collectively suggest that a significant portion of the actions related to the preparation of *Mangifera indica* bark may be ascribed to this C-glucosyl-xanthone [9].

Future Directions:

The review article's assessment of potential directions for future study emphasizes the necessity of well-planned clinical trials and mechanistic studies to confirm the effectiveness and security of *Mangifera indica* bark and other herbal therapies in boosting female fertility.

Conclusion:

The potential of herbal medicines, especially *Mangifera indica* bark, is highlighted in this review study as a viable approach to enhancing female fertility. It provides important insights into the function of natural

therapies in treating female infertility by fusing conventional knowledge with cutting-edge scientific research. Future investigations have the potential to deepen our understanding of these herbal treatments and give women looking for non-invasive ways to improve their reproductive health hope.

References:

1. Khandare MS. Mango (*Mangifera indica* Linn) A medicinal and holy plant. Journal of Medicinal Plants Studies. 2016;4(4):44-6.
2. Sanusi BM, Garba A, Muhammad A, Mohammed A, David O. Phytochemical screening and antimicrobial efficacy of aqueous and methanolic extract of Mangifera indica (mango stem bark). World Journal Life-Science and Medical Research. 2011;2(2):81.
3. Savant CB, Kulkarni AR, Abdel-Wahab BA, Al-Qahtani AM, Mannasaheb BA, Shaikh IA. Phytochemical characterization and Antibacterial potentials of Mangifera indica L. bark oil. Journal of Applied Pharmaceutical Science. 2017 Apr 30; 7:138-41.
4. Adetuyi FO, Ibrahim TA. Phytochemical Analysis and Antioxidant Activities of Hot and Cold Water Extracts of Mango (Mangifera indica L.) Leaf and Stem Bark. University of Lagos Journal of Basic Medical Sciences. 2022 Aug 31;1(2).
5. Aderonke AA, Ejiofor J, Eniola OW, Akanji MA, Olatunbosun OO. Evaluation of the Safety Profile of Ethanol Stem Bark Extract of Mangifera indica on Reproductive Functions of Male Albino Rats. Nigerian Journal of Pharmaceutical and Applied Science Research. 2019; 8(2):44-8.
6. Aquisman AE, Klutse CK, Droepenu EK. Phytochemical screening for antioxidant activity and elemental analysis of the leaves and cracked-barks of Mangifera indica (Mango). Archives of Pharmacology and Pharmaceutical Sciences. 2019; 1:1-9.
7. Guiekep AJ, Kenfack A, Ngoula F, Vemo BN, Nguemmeugne KS, Tedonkeng EP. Attenuating effects of Mangifera indica leaves ethanolic extract against acetamiprid-induced reproductive toxicity in male guinea pigs. InVeterinary Research Forum 2019 (Vol. 10, No. 3, p. 187).
8. Rasyid R, Mawaddah S, Rivai H. Quantitative determination of mangiferin in methanol extract of Bacang Mango (*Mangifera foetida* L.) leaves by thin-layer chromatography densitometry. World J. Pharm. Pharm. Sci. 2020 Apr 25; 9:1551-60.
9. Wauthoz N, Balde A, Balde ES, Van Damme M, Duez P. Ethnopharmacology of Mangifera indica L. bark and pharmacological studies of its main C-glucosylxanthone, mangiferin. International Journal of Biomedical and Pharmaceutical Sciences. 2007 Aug 15;1(2):112-9.
10. Nwinuka NM, Monanu MO, Nwiloh BI. Effects of aqueous extract of Mangifera indica L.(Mango) stem bark on hematological parameters of normal albino rats. Pakistan Journal of Nutrition. 2008;7(5):663-6.
11. Samrot AV, Rohan B, Kumar D, Sahiti K, Raji P, Samanvitha SK. Detection of antioxidant and antibacterial activity of Mangifera indica using TLC bio-autography. International journal of pharmaceutical sciences and research. 2016 Nov 1;7(11):4467.
12. Núñez-Sellés AJ, Delgado-Hernández R, Garrido-Garrido G, García-Rivera D, Guevara- García M, Pardo-Andreu GL. The paradox of natural products as pharmaceuticals: Experimental evidence of a mango stem bark extract. Pharmacological Research. 2007 May 1; 55(5):351-8.
13. Sultana B, Hussain Z, Asif M, Munir A. Investigation on the antioxidant activity of leaves, peels, stems bark, and kernel of mango (*Mangifera indica* L.). Journal of food science. 2012 Aug; 77(8):C849-52.
14. Kalita P. An overview on *Mangifera indica*: importance and its various pharmacological action. Pharma Tutor. 2014 Dec 1; 2(12):72-6.

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A review and analysis of the steps involved in creating and conducting the assessment study for the anti- aging herbal vanishing cream

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Abstract:

The current review effort set out to create and assess a herbal vanishing cream (HVC). Comparing herbal cream to synthetic cream, there are various advantages. The majority of face creams on the market are made from synthetic medications and provide fairness to the face, but they also have several negative side effects, like irritation or allergic responses. Herbal cream provides skin a fairer appearance and has no negative side effects. Based on the anti-fungal, anti- microbial, anti-inflammatory, skin-soothing, and anti-aging properties of aloe vera, turmeric, and nutmeg, a polyherbal oil-in-water disappearing emulsion cream was created. Using ethanol as a solvent, the maceration process was used to extract all of the herbs. The prepared vanishing cream was assessed using several metrics. Stability tests on the manufactured vanishing cream revealed it was hard and stable.

Keywords: Herbal, Vanishing Cream, Polyherbal, Anti-aging.

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Introduction:

Herbal extracts are used in the cosmetic preparations for augmenting beauty and attractiveness. Creams are semisolid emulsions and intended for application to the skin and mucus membrane. A low fat moisturizer that disappears in to skin is called as vanishing cream [1]. It softens skin, leaving nothing behind. Vanishing cream are oil in water emulsion based preparation containing aqueous phase and oil phase [2]. It form a thin imperceptible and in visible film on the skin, followed by the dissipation of water that gives non - glossy appearance [3] These products are designed to be used topically fir the better site specific delivery of the drug in to the skin for the skin disorder. Creams may be classified as oil in water or water in oil type of emulsion on the basis of phase .The term has been traditionally applied to semisolid formulated as either water in oil (Eg cold cream) or oil in water (Eg vanishing cream) [4]. The current research has been planned to carryout in vitro flavonoid, content of the selected plant species, formulate and evaluate the polyherbal vanishing cream [5].

Advantages and Disadvantages

Advantages and disadvantages of vanishing cream as follows:

Advantages of vanishing cream:-

- They give prolonged contact in their site of application than other doses form formulations
- When applied to skin it gives no irritation and easily water washable.
- More safely drug deliver to specific site.
- Prolonged contact in their site of application can give the other doses form.

Disadvantages of vanishing cream

- Allergy such as skin may occur at site of application due to drug/ excipients.
- Inflammation may occur when applied to skin.
- From the topical doses forms larger particles cannot be absorbed.[6]

Types of skin cream:

1. Oil in water cream which are composed of small droplets of oil dispersed in continuous phase, and an emulsion in which the oil is dispersed as droplets throughout the aqueous phase is termed an oil in water emulsion.
2. Water in oil creams which are composed of small droplets of water dispersed in a continuous oily phase. When water is the dispersed and an oil the dispersion medium, the emulsion is of the water in oil type.[7]

Classification of creams:

Based on function:

1. Make-up cream : Vanishing cream Foundation cream
2. Cleansing cream
3. Winter cream.

Cold cream or moisturizing cream.

4. All purpose cream and general cream.
5. Night cream and massage creams.
6. Skin protective cream.

Materials and Methods:

The fresh plant sample was dried at room temperature for 4 days until the plant was totally dried [8]

Table no.1 Herbal Drug information

S.no.	Herbal extract	Medicinal importance
1.	Neem(*Azadiracta indica*) family - Maliaceae	Neem leaves used to treat skin disease [9] wound, skin ulcers and as a skin softener
2.	Turmeric (*curcuma longa*) Family - Zingiberaceae	Turmeric is claimed to be effective in treating skin-aging induced by sun exposure, increasedthickness and reduction in elasticity of skin, skin injury[10]
3.	Ginger rhizome (*zingiber officinal* Family - Zingiberaceae	Ginger is produced anti- skin aging effect and reduced hyper pigmented spots on the outer most layer of the skin. [11]
4.	Honey (*Apis meliifera*) Family- Apidae	Honey is used in the treatment of wound, eczema, inflammation, burns of the skin.[12]
5.	Aloe vera (*Aloe barbadensis miller*) Family- Liliceae	Aloe vera maintaining moist wounds, increasing collagen production and reduce inflammation[13]
6.	Orange peel (*Citrus limon*) Family - Rutaceae	Cell buildup around the pores enhance the shadow and makes the pore appears larger while dehydration add a cellophane like sheen to the skin, enhancing a rough texture and pore appearance [14]

Method of preparation:

Preparation of alcoholic extract of crude drugs:

All above mentioned powdered crude drugs of 5gms were taken into the conical flask and then 100ml of ethanol was added to it, the conical flask was capped with aluminum foil. Then this mixture was placed for maceration for 5 days. [15]

Classification of extraction based on types of phases: [16]

Liquid liquid extraction
Sample phase (liquid)

Solid phase extraction or Sample phase
(Gas, liquid) Micro- extraction Extract phase
(liquid, solid)

Leaching or solid liquid extraction
Sample phase [solid]
Extract phase [liquid]

Preparation of oil phase:
Supercritical fluids extraction
Sample phase (solid, liquid)
Extract phase (supercritical fluid)

Stearic acid (17%), potassium hydroxide (0.5%), sodium carbonate (0.5%) was taken into the Porcelain dish and this mixture was melted at 70°C. [17]

Preparation of aqueous phase:

Alcoholic extract of crude drugs mentions in step 1(4.5%), glycerin (6%), water (71%) was taken into the Porcelain dish and heated this mixture at 70°C. [18]

Addition of aqueous phase to oil phase:

The aqueous phase was added into the oil phase with continuous stirring at 70°c maintain the temperature of both phases, once the transfer was completed it allowed to stand room temperature if required perfume was added at last just before the finished product were transfer to suitable container**.** [19]

Conclusion:

The best and most nutritious crude medications, known as the "vanishing cream," could be manufactured with minimal equipment and with straightforward techniques. The prepared herbal cream also exhibits antibacterial and antioxidant properties, which help to delay the appearance of wrinkles and pimples on the face. A cream with an oil-in-water emulsion base was created with natural ingredients and assessed. It is possible to conclude that this cream can be used for multiple purposes and that the ingredients when combined can have a synergistic impact on one another. The goal of the current review project was to develop and evaluate a herbal vanishing cream (HVC). When contrasting herbal cream with synthetic cream, there are several benefits. Most face creams available today are derived from synthetic drugs and offer facial fairness, but they also come with a host of unfavorable side effects, such as allergic reactions or discomfort. Herbal cream has no unfavorable side effects and makes skin appear more fair. A polyherbal oil-in-water vanishing emulsion cream was developed based on the antifungal, antimicrobial, anti-inflammatory, skin-soothing, and anti-aging characteristics of nutmeg, turmeric, and aloe vera. All of the plants were extracted through the maceration method, which used ethanol as a solvent. We evaluated the prepared vanishing cream using several measures.

References:

1. Mendhekar Sy, Jori Rr, Shinde Kr, Sl J, Gaikwad Dd. Formulation And Evaluation Of Polyherbal Vanishing Plus Fairness Expert Cream.
2. Prajakta S, Shahu K. Formulation and Evaluation of Vanishing Herbal Cream of Crude Drugs. Asian Journal of Pharmaceutical Research and Development. 2020; 8(3):66-69.
3. Uddin Mf, Ullah Mk, Ahmed Ma, Samreen S, Habeeb H. Preparation And Evaluation Of Polyherbal Vanishing Cream Of Ethanolic Extract Of Crude Drugs. International Journal of Applied Pharmaceutical Sciences and Research. 2019 Oct 1; 4(04):63-67.
4. Krishnan N, Afsal Vi, Jamal F, Rasheed R, Pp Ss. Formulation And Evalution Of Herbal Vanishing Cream. 2022.
5. Mamillapalli V, Katamaneni M, TiyyaguraVm, Kanajam P, Namagiri Ap, Thondepu H, Appikatla B, Devangam B, Khantamneni P. Formulation, Phytochemical, Physical, Biological Evaluation Of Polyherbal Vanishing Cream, and Face wash. Research Journal of Pharmaceutical Dosage Forms and Technology. 2020 Jul 1; 12(3):139-49.
6. https:// brainly.in/question/ 12404815.
7. Krishnan N, Afsal VI, jamal F, Rasheed R, PP SS. " formulation and evaluation of herbal vanishing cream
8. Rai Sk, Maury S. A Review On "Prepartion And Characterization Of Vanishing Cream For Antiaging".

9. Lobo R, Prabhu K, Shirwaikar A, Shirwaikar A, Ballal M. Formulation and Evaluation Of Antiseptic Activity Of The Herbal Cream Containing Curcuma Longa And Tea Tree Oil. Journal of Biologically Active Products from Nature. 2011 Jan 1;1(1):27-32.

10. Chandrasekar R. Sivagami B. "Formulation and evaluation of poly herbal skin care cream containing neem and Tulsi". Research Journal of Topical and Cosmetic Sciences, 2018; 25-32.

11. Zaman SU, Akhta N. "Effect of turmeric Courcuma longa Zingiberaceae) extract cream on human skin sebum secretion". Tropical Journal of pharmaceutical Research. 2013 Oct 29; 12(5):665-9.

12. Asoka Sf, Batubara I, Lestari AR, wahyun PWT, 22 Wahyudi ST. "Compounds in indonesian ginger rhizome extracts and their potential for anti-skin aging band on melecular docking". Cosmetic. 2022 Dec 1;9(6):128.

13. Meloone P, duwradun A. warnoek m, fyfe L. Honey: "a therapeutic agent for disorders of the skin" Central Asiart Journal of global Health. 2016; 5(1).

14. Salum A, Noween I, Nasem m. murad HS. magsoods, Tarlum G. "Aloe vera gel effect on skin and pharmacological properties". Sch Int J Anat. Physiol. 2022; 5(1):1-8.

15. Menthekar SY, JoriRR, shinde KR. SLJ, Gaikwad DD. "formulation and Evaluation of Pelyherbal vanishing plus fairness expert cream"

16. Prajakta S, Shahu K. "Formulation and Evaluation of Vanishing Herbal Cream of Crude Drugs". Asian Journal of Pharmaceutical Research and Development. 2020; 8(3):66-9.

17. Patel k, Panchal N, Ingle P. "Review of extraction techniques". Int J. Adv. Res. Chem. Sci. 2019;6(3): 6-21

18. Rai SK, Maury S. A review on "Preparation. And characterization of vanishing cream for Antiaging".

19. Krishnan N. Afsal VI. 1. Jamalf, Rasheed R. PPSS. "Formulation and Evaluation of Herbal vanishing cream".

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A comprehensive review on exploring Bhringraj (*Eclipta prostrata*) in herbal cares and explores the role of antidandruff shampoo, conditioner, and oral formulations

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Abstract:
The search for herbal and natural hair care solutions has gotten more intense recently, particularly when it comes to anti-dandruff products. Deeply ingrained in ancient Ayurveda medicine for its numerous advantages to hair and scalp health, Bhringraj (*Eclipta prostrata*) has emerged as a promising choice among the wide range of botanical therapies. With an emphasis on antidandruff shampoos, conditioners, and oral dosage forms, this thorough literature review explores the scientific investigation of Bhringraj's potential in the creation of herbal hair care formulations. This provides a basis for understanding its possible efficacy and includes its anti-inflammatory, antifungal, and antibacterial properties on the scalp. The aim is to evaluate the effectiveness of these formulations and discern potential advantages over conventional treatments. Mechanistic insights into Bhringraj's action on dandruff, scalp health, and hair growth are explored, elucidating the molecular underpinnings of its therapeutic effects. Since safety is of the utmost importance, this review aims to evaluate Bhringraj's safety profile in herbal hair care products. Examining possible interactions and adverse effects helps determine whether Bhringraj is suitable for general use. In summary, given the growing popularity of natural hair care products, this literature review summarises what is known about Bhringraj and provides useful information for consumers, researchers, and formulators looking for safe and effective herbal antidandruff remedies.

Keywords: Herbal Extracts, Anti Dandruff, Shikakai, Neem, Bhringraj

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Introduction:

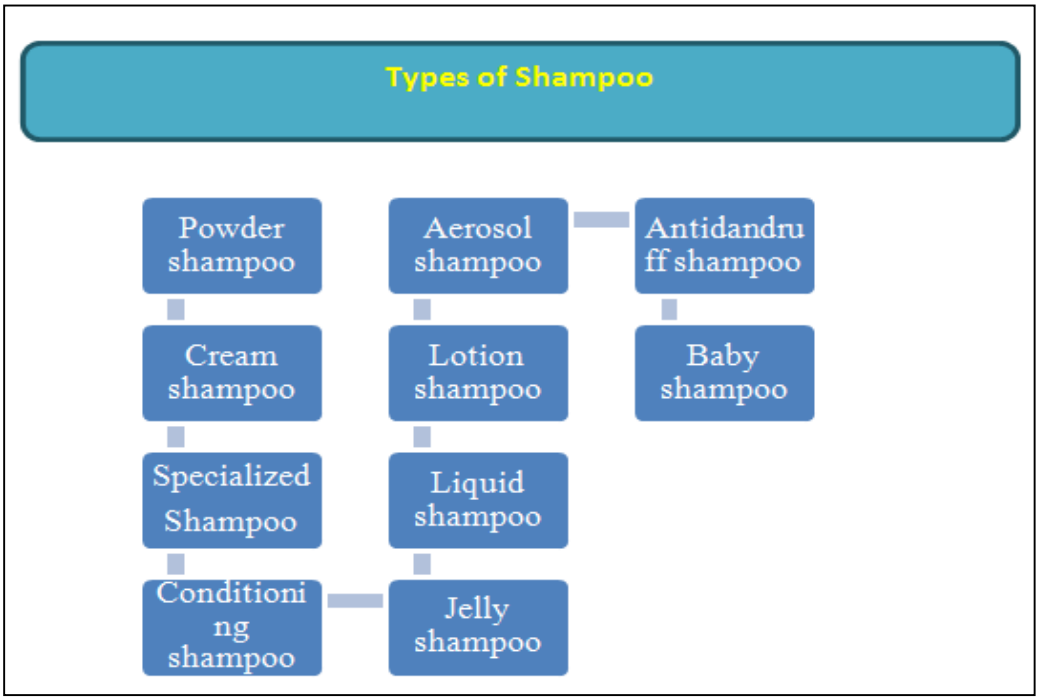
Hair is one of the vital parts of the body derived from ectoderm of the skin and is protective appendages on the body and considered accessory structure of the integument along with sebaceous glands, sweat glands and nails This polyherbal Shampoo was formulated using nature ingredients like *Acacia concinna, Sapindus mukorossi, Aloe barbadensia, Trigonella foencum, Phyllanthus emblica, Azadirachta indica, Hibiscus roseasinesis* and *Lawsonia inermis* [1]. They are also known as epidermal derivatives as they originate from the epidermis during embryological development [2].

Hair is an important part of the overall appeal of the human body. The hair of the head had historically been associated with beauty and social distinction. Innumerable instances from all the art forms can be cited supporting the special prominence accorded to the hair by people of virtually all times and cultures [3]. Whereas the hair has been trimmed, shaped and even colored since the most ancient times, relatively little emphasis has been placed on the process of cleaning it. Only in this century has a real technology in the cleaning of hair and scalp developed. First came the mass distribution of cake soap and sanitary facilities to make bodily cleanliness and personal hygiene practice. Shampoos are probably the most widely used hair products today, based on herbal ingredients as well as synthetic ingredients.

Shampoos are most probably used as cosmetics. It is a hair care product that is used for cleansing scalp and hair in our daily life. Shampoos are most likely utilized as beautifying agents and are a viscous solution of detergents containing suitable additives preservatives and active ingredients [4]. It is usually applied on wet hair, massaging into the hair, and cleansed by rinsing with water. The purpose of using shampoo is to remove dirt that is build up on the hair without stripping out much of the sebum. Many synthetic shampoos are present in the current market both medicated nonmedicated; however, herbal shampoo popularized due to natural origin which is safer, increase consumer demand and free from side effects.

In synthetic shampoos, surfactants (synthetic) are added mainly for their cleansing and foaming property. But the continuous use of these surfactants leads to serious effects such as eye irritation, scalp irritation, loss of hair, and dryness of hairs. There are a number of medical plants with potential effects on hair used traditionally over years around the world and are incorporated in shampoo formulation. These medical plants may be used in extracts form, their powdered form, crude form, or their derivatives. A shampoo is a preparation of a surfactant (surface active agent) in suitable form – liquid, solid or powder which when under the specified conditions will remove surface grease, dirt, and skin debris from the hair shaft and scalp without adversely affecting the user.

Herbal shampoos for hair fall are made out of natural ayurvedic ingredients, natural oils, minerals, and herbal extracted compounds. These ingredients work on to improve the moisture in your hair by hydrating the follicles and roots of your hair [4-5].



Antidandruff Properties: Bhringraj is renowned for its various therapeutic properties, including those that contribute to its potential efficacy in addressing dandruff. The antidandruff properties of Bhringraj are attributed to its diverse bioactive compounds and their effects on the scalp. Here are some key properties that make Bhringraj a promising candidate for managing dandruff.

Anti-inflammatory effects: Bhringraj possesses anti-inflammatory properties that may help reduce inflammation on the scalp, which is often associated with dandruff. By calming irritated skin, Bhringraj contributes to a healthier scalp environment [4, 5].

These are various types of hair:

- Normal hair, oily hair, dry hair, varies from one human to other human.
- The problem of hair includes hair falling, white hair, dandruff and split end hair etc.
- The reason of hair problems are; o Tension, scalp infection, hormones distribution, food and large chemical shampoo use.

- In this direction we are presenting here polyherbal amla antidandruff shampoo for hair treatment with fewer side effects in a daily life.
- Herbal shampoos are shampoos infused with extracts of natural ingredients. The best thing about these shampoos is that they yield the best and long-lasting results.
- These shampoos are free from chemicals and cause no damage to the hair [6].

Today a large population both man and women use shampoo for washing the hair. One of the main functions of shampoo is to remove dirt on the hair. The dirt consists of sebum by the scalp, sweat residue, flakes of horny layer and residue from hair care cosmetics, dust and other external matter settled on the hair.

Various synthetic shampoo derivatives have been proved to cause harmful effect. Nowadays people are having awareness of their effects on hair. Due to these reasons the community is getting attracted towards herbal products due to their inexpensive nature and negligible side effects. Nowadays, the usefulness of herbs in the cosmeceutical production has been extensively increased and there is a great demand for the herbal cosmetics [7].

Ideal properties of herbal shampoo: To make the hair smooth and shiny. Produce good amount of foam. It should impart a pleasant fragrance to the hair. It should not cause any side effects.

It should not cause irritant to scalp, skin and eyes. Should completely, effectively remove dirt [8].

Advantages of herbal Bhringraj shampoo:

- It doesn't cause irritation to the eyes.
- It is cost friendly, not much expensive.
- Improving hair hygiene.
- Repair damaged hair.
- To make the hair smooth and shiny.
- Low toxicity

Botanical Overview:

Bhringraj (*Eclipta alba* (*L.*))

Synonyms: false daisy, bhringaraj, karisilakanni

Vernacular names: Bhringaraj “Ruler of bees” India, Sanskrit; Kesharaja/Keh "King of the hair" India and South Asia, Sanskrit/Assamese; Karisalankanni, “Dark-juice-leafed” Tamil Nadu and throughout, South Asia, Tamil; Yerba de Tago, “Herb of the ditch” North, South, and Central America, Spain, Spanish.

Biological source: Ecliptaprostrata (L.) commonly known as false daisy, bhringaraj, karisilakanni etc. is an annual herbaceous plant belonging to the family Asteraceae.

Cleansing Properties: Bhringraj has cleansing properties that can help remove impurities, excess oil, and dead skin cells from the scalp. Regular use of Bhringraj-based products may contribute to a cleaner scalp environment, reducing the likelihood of dandruff.

Morphological parts used: Woods, seeds, pericarp extracts, kernels etc. [9].

Taxonomical classification

- **Kingdom-** Plantae
- **Subkingdom-** Viridaeplantae
- **Infrakingdom-** Streptophyta
- **Division-** Tracheophyta

- **Subdivision -**Spermatophytina
- **Infra division-** Angiospermae
- **Class -**Magnoliopsida
- **Super order -**Asteranae
- **Order -**Asterales
- **Family** Asteraceae
- **Genus** Eclipta
- **Species** prostrata
- **Common name** False Lily, Bhringra [10]

Antimicrobial Action: Bhringraj exhibits antimicrobial properties, which can be beneficial in maintaining a balanced microbial environment on the scalp. This may contribute to the prevention of bacterial or fungal infections associated with dandruff.

Bhringraj Shampoo Formulation:

Ingredients: *Bhringraj Extract:* Bhringraj extract is the key ingredient. It can be obtained through extraction methods like cold pressing or steam distillation. Base Shampoo Formula: Use a mild, sulfate-free base shampoo to ensure gentleness on the scalp [10].

Aloe Vera Gel: Aloe Vera helps soothe the scalp and promotes hydration. It complements Bhringraj's anti-inflammatory properties.

Tea Tree Oil: Tea tree oil has antifungal and antimicrobial properties, which can further support the antidandruff effects.

Neem Extract: Neem is known for its antibacterial properties, helping maintain a healthy scalp.

Rosemary Essential Oil: Rosemary oil can stimulate blood circulation, promoting a healthier scalp.

Lavender Essential Oil: Lavender oil offers a pleasant scent and may contribute to scalp health.

Panthenol (Vitamin B5): Panthenol helps strengthen hair and improve moisture retention.

Preservatives and Stabilizers: Use natural preservatives like vitamin E or opt for other mild preservatives to extend the shelf life of the product.

pH Adjusters: Citric acid or other pH adjusters to ensure the shampoo falls within the desired pH range for hair[10,11].

Chemical Composition:

E. prostrata (Bhringraj) contains wide range of diverse phytochemical constituents which include coumestans, alkaloids, flavonoids, glycosides, polyacetylenes, and triterpenoids, phenolic acids, saponins, sterol, sesquiterpene lactones, proteins, amino acids, carbohydrates, and many more. Some major phytochemicals are shown in (Table 1) [12].

Table 1: Parts containing chemical constituents of *Eclipta prostrata.*

S.no.	Parts	Chemical constituents
1	Leaves	Wedelolactone1.6%Desmethylwedelolactone, Desmethylwedelolactone7glucoside,Stigmasterol
2	Roots	Hentriacontenol, Heptacosanol and Stigmasterol, Ecliptal, Eclabatin
3	Aerial plants	ß amyrin, Luteoin 7 -0 glucoside, Apigenin, Cinneroside, Sulpher compounds, Eclabasaponins I-VI
4	Stem	Wedelolactone
5	seeds	Sterols, Ecliptabine (alkaloid)
6	Whole plants	Resin, Ecliptine, reducing sugar, Nicotine, Stigmasterol, Triterpene saponin, Eclabatin, Ursolic acid, Oleanolic acid

Bhringraj Conditioner Formulation:

Ingredients:

Bhringraj Extract: Utilize Bhringraj extract as a primary ingredient.

Base Conditioner Formula: Choose a nourishing and moisturizing base conditioner that complements Bhringraj's properties [13].

Coconut Oil: Coconut oil adds an extra layer of nourishment and helps improve hair texture.

Shea Butter: Shea butter provides deep moisturization, especially beneficial for dry scalps.

Argan Oil: Argan oil contributes to shine and softness, enhancing the overall quality of the hair.

Hibiscus Extract: Hibiscus is known to stimulate hair growth and provide a natural shine.

Protein (Hydrolyzed Keratin or Silk Protein): Incorporate a protein source for strengthening and repairing damaged hair.

Glycerin: Glycerin helps retain moisture in the hair, preventing dryness.

Citrus Essential Oils: Citrus oils add a refreshing scent and may contribute to scalp health.

Preservatives: Include natural preservatives to maintain product integrity [14].

Procedure:

- Combine the base conditioner formula with Bhringraj extract.
- Add coconut oil, shea butter, and argan oil, ensuring even distribution.
- Incorporate hibiscus extract and protein source for added benefits.
- Integrate glycerin and essential oils for moisture and fragrance.
- Include natural preservatives to maintain product freshness.
- Thoroughly mix the ingredients and perform quality control checks before packaging [13,14].
- These formulations are general guidelines, and specific ingredient ratios may vary based on product goals, hair types, and other considerations. It is advisable to consult with cosmetic formulation experts and conduct stability and safety tests before finalizing and launching any product.

Oral Dosage: Creating an oral dosage formulation with Bhringraj involves considerations for dosage form, dosage strength, and additional ingredients that can enhance its bioavailability and efficacy. Here's a general guideline for formulating an oral dosage using Bhringraj [14].

Bhringraj Oral Formulation:

Ingredients:

BhringrajPowder or Extract: Use Bhringraj powder or extract obtained through a suitable extraction method. The choice depends on the desired concentration and form.

Capsule Shells or Tablets: Depending on preference and manufacturing capabilities, choose between vegetarian or gelatin capsule shells or compressed tablets.

Binder: Include a binder, such as microcrystalline cellulose, to ensure the tablet maintains its shape and integrity.

Fillers: Use fillers like lactose or cellulose to add bulk to the formulation and facilitate the manufacturing process.

Disintegrates: Incorporate disintegrates like croscarmellose sodium to promote the breakdown of the tablet in the digestive system for better absorption.

Flow Agents: Include flow agents like magnesium stearate to improve the flow ability of the powder during the manufacturing process.

Bioavailability Enhancers: Consider including bioavailability enhancers such as black pepper extract (piperine) to improve the absorption of active compounds from Bhringraj [15].

Procedure:

Bhringraj Extraction (If Using Extract): If using an extract, ensure that it is obtained through a reputable extraction method, and the concentration of active compounds is standardized.

Weighing and Mixing: Weigh the appropriate amounts of Bhringraj powder or extract, binder, fillers, and other excipients based on the desired dosage strength.

Granulation: Granulate the mixture if needed, especially if using wet granulation for tablet formation.

Tablet Compression or Capsule Filling: Compress the mixture into tablets using a suitable tablet press or fill it into capsules using capsule-filling equipment.

Coating: Optionally, apply a coating to tablets for improved aesthetics, taste- masking, or delayed release.

Quality Control: Perform quality control tests, including content uniformity, disintegration, and dissolution testing, to ensure the product meets specified standards.

Packaging: Package the tablets or capsules in appropriate packaging materials, ensuring that they are well-sealed to maintain product integrity.

Labeling: Include clear and accurate labeling that provides dosage instructions, recommended use, and any necessary precautions. It's important to note that formulating oral dosage forms requires adherence to Good Manufacturing Practices (GMP) and compliance with regulatory standards. Consulting with regulatory experts and conducting stability testing is essential before introducing any oral dosage formulation to the market. Additionally, individuals should consult healthcare professionals before incorporating herbal supplements into their routine, especially if they have underlying health conditions or are taking medications [13,14].

Material and Methodology:

Selection and collection of herbal materials: Bhringraj was collected from market. Left of the ingredient's

collects from the Shri RLT Institute of Pharmaceutical Science & Technology, Ekdil- Etawah. Mentha, Black Cumin, Xanthum Gum and Banana root powder was received from college laboratory. Tulsi and Lavender oil was collected from market.

Methodology:

Pre formulation study:

The pre-formulation stage of herbal shampoo development involves selecting suitable herbal ingredients based on their potential benefits for the scalp and hair. Various herbs, such as amla, reetha, bhringraj, neem, and fenugreek, are considered for their cleansing, conditioning, and hair growth properties. The choice of herbs depends on their specific properties and the desired effects on the hair and scalp. Additionally, different extraction methods, including maceration, solvent extraction, or steam distillation, are explored to obtain herbal extracts rich in active compounds. The pre-formulation process also involves pH balance adjustment, compatibility studies, and stability testing to ensure the efficacy and safety of the final product [11, 12].

Preparation method of herbal shampoo:

Decoction Method:

- Weighed all the ingredients according to the formula.
- Decoction of Bhringraj, Neem, Mentha, Black Cumin, Xanthum Gum, Banana root, Tulsi, Lavender Oil was prepared in one part of water.
- Filter it, by using muslin cloth. Collect filtrate.
- Decoction of Shikakai, and Ritha was prepared in another part of water.
- Filter it by using muslin cloth.
- Mixed to each other of above filtrate with constant stirring.
- Mixed gaur gum as a thickening agent for maintenance of consistency of herbal shampoo as like semisolid nature. Preservatives and perfume was added lastly [12,13].

Importance of this formulation:

- The selection of active ingredients for hair care shampoo is often based on the ability of the ingredient to prevent damage to skin as well as to improve the quality of the skin by way of cleansing, nourishing, and protecting the skin.
- It has not make the hand rough and chapped.
- It's not given any side effects or causes irritation to the eye.

Result and Discussion:

Physical appearance/visual inspection: The formulated herbal shampoo was brownish in red colour. It has a slight odour.

Clinical Studies and Trials: There were limited clinical studies specifically focused on Bhringraj for hair care, and findings were not as extensive as those for certain pharmaceutical interventions. Clinical research on herbal remedies can evolve over time, so it's advisable to check for the latest studies and reviews. Here are some studies available up to my last update [12, 14]

Efficacy of Bhringraj in Telogen Effluvium: A study published in the International Journal of Ayurveda research (2010) explored the efficacy of an Ayurvedic herbal formulation, including Bhringraj, in patients

with telogen effluvium (a common form of hair loss). The study reported a positive impact on hair regrowth and reduction in hair fall.

Anti-Inflammatory and Antioxidant Properties: Research published in the Journal of Ethnopharmacology (2009) investigated the anti-inflammatory and antioxidant properties of *Eclipta alba* extract. While the study was not hair-specific, it highlighted potential benefits that could indirectly support scalp health.

Hair Growth Promotion in Mice: A study in the Archives of Dermatological Research (2008) evaluated the hair growth-promoting effects of Eclipta alba (Bhringraj) in mice. The findings suggested a positive impact on hair growth, potentially linked to increased proliferation of hair follicle cells.

***Eclipta alba* Oil in *Alopecia areata*:** A study in the Journal of Ethnopharmacology (2014) investigated the therapeutic effects of *Eclipta alba* oil in patients with *Alopecia areata*. The results suggested that the oil could be a safe and effective topical treatment for this condition.

Antidandruff Activity: An article published in the Asian Pacific Journal of Tropical Medicine (2011) explored the antidandruff activity of herbal shampoos containing Bhringraj. The study reported positive effects on reducing dandruff and improving overall scalp health. It's crucial to interpret these findings with caution due to variations in study designs, sample sizes, and methodologies. Additionally, not all studies are specific to Bhringraj in isolation, as formulations often contain multiple herbal ingredients. As interest in herbal remedies for hair care grows, more research may emerge, shedding further light on the efficacy and mechanisms of Bhringraj. Before incorporating Bhringraj or any herbal remedy into a hair care routine, individuals should consult healthcare professionals, especially if they have underlying health conditions or are taking medications.

Comparisons with Conventional Hair Care Products: Comparing Bhringraj-based hair care products with conventional hair care products involves evaluating various aspects, including ingredients, mechanisms of action, potential benefits, and user experiences. Here's a comparison to highlight differences and potential advantages of Bhringraj products [16].

Bhringraj-Based Hair Care Products:

Ingredients:

Bhringraj products primarily contain *Eclipta prostrata* (Bhringraj) extract or oil along with other herbal ingredients chosen for their hair-nourishing properties.

Herbal formulations may include natural oils, plant extracts, and Ayurvedic herbs known for their traditional benefits in promoting scalp health and hair growth [15, 16].

Conventional Hair Care Products:

Ingredients:

Conventional hair care products often contain a mix of synthetic chemicals, preservatives, fragrances, and surfactants.

Common ingredients include sulfates, silicones, and synthetic preservatives, which may contribute to the product's texture, fragrance, and shelf life [16].

Mechanisms of Action:

Many conventional products focus on immediate visual effects, such as cleansing, conditioning, and providing a glossy finish, rather than addressing underlying scalp issues. Synthetic ingredients may have different mechanisms of action compared to the holistic approach of Bhringraj [17].

Synthetic Formulations:

Conventional products often use synthetic formulations, which may contribute to concerns such as dryness, irritation, or adverse reactions in some individuals. The use of synthetic ingredients allows for greater control over product consistency and texture [16, 17].

Future Research Directions:

Clinical Trials and Human Studies: Conducting rigorous clinical trials to validate the efficacy of Bhringraj-based antidandruff formulations in diverse populations. Investigating the long-term effects and comparative effectiveness of Bhringraj formulations against standard treatments through well-designed human studies.

Optimization of Formulations: Refining and optimizing the formulations of Bhringraj-based antidandruff shampoos, conditioners, and oral dosage forms for enhanced efficacy and user experience.

Synergistic Combinations: Exploring synergistic combinations of Bhringraj with other herbal ingredients known for their hair care benefits to create comprehensive and potent antidandruff formulations. Investigating potential interactions and complementary effects of Bhringraj with commonly used hair care ingredients [14,15].

Sustainability Practices: Investigating sustainable cultivation and harvesting practices for Bhringraj to address environmental concerns and ensure the long-term availability of this valuable botanical resource. Exploring eco-friendly packaging options for Bhringraj-based products to align with growing consumer preferences for sustainability. As research in herbal hair care progresses, these future directions aim to advance our understanding of Bhringraj and its potential applications in antidandruff formulations, fostering innovation and sustainability in the field of natural hair care[17].

Conclusion:

The exploration of Bhringraj (*Eclipta alba*) in herbal hair care formulations, with a specific focus on antidandruff shampoos, conditioners, and oral dosage forms, reveals a compelling potential for this botanical remedy in promoting scalp health and addressing dandruff issues. Combining traditional knowledge from Ayurveda with contemporary scientific scrutiny, this literature review provides a comprehensive overview of the multifaceted benefits and applications of Bhringraj in the realm of hair care.

Bhringraj's phytochemical composition, including flavonoids, alkaloids, and triterpenoids, underscores its therapeutic potential. Scientific studies have illuminated its antidandruff properties, showcasing anti-inflammatory, antifungal, and antimicrobial effects that contribute to its efficacy in alleviating this common scalp condition.

The formulation approaches explored in this review, such as antidandruff shampoos, conditioners, and oral dosage forms containing Bhringraj, offer promising alternatives to conventional synthetic products. These formulations leverage Bhringraj's natural properties to address dandruff while potentially minimizing side effects associated with synthetic ingredients. Mechanistic insights into Bhringraj's action on dandruff and scalp health provide a deeper understanding of how this herb contributes to the overall well-being of hair. By targeting inflammation, fungal overgrowth, and microbial imbalances, Bhringraj emerges as a holistic solution for individuals seeking natural remedies for dandruff management. Safety considerations are crucial, and the literature review underscores the importance of assessing the safety profile of Bhringraj in herbal hair care formulations. While Bhringraj is generally well- tolerated, understanding potential side effects and interactions is essential for ensuring consumer confidence and widespread adoption.

In conclusion, the exploration of Bhringraj in herbal hair care formulations for antidandruff purposes reveals a

promising avenue for natural and holistic solutions. Bridging traditional wisdom with contemporary scientific understanding, this review contributes valuable insights for researchers, formulators, and consumers seeking effective, safe, and natural alternatives in the realm of hair care. As the demand for herbal remedies continues to grow, Bhringraj stands as a beacon of hope in the pursuit of healthy and vibrant hair.

References:

1. Zambare Kk, Gonge Sb, Shewale Gb, Pawar Ps. Preparation And Evaluation of Polyherbal Shampoo. Skin. 2019; 158(168):171.
2. Potluri A, Harish G, Kumar Bp. Formulation and Evaluation Of Herbal Anti-Dandruff Shampoo. Indian Journal of Research In Pharmacy And Biotechnology. 2013 Nov 1; 1(6):835.
3. Lodha G. Formulation And Evaluation Of Polyherbal Shampoo To Promote Hair Growth And Provide Antidandruff Action. Journal of Drug Delivery And Therapeutics. 2019 Aug 30;9(4- A):296-300.
4. Yadav Ar, Mohite Sk. Formulation and Evaluation Of Antidandruff Shampoo. Research Journal of Topical and Cosmetic Sciences. 2020; 11(2):55-8.
5. Gawshinde A, Kamalpuria N, Farooqui N, Choursiya S. Formulation, OptimitziationAnd Evaluation Of Polyherbal Anti-Dandruff Shampoo. Asian Journal of Pharmacy And Technology. 2021; 11(3):220-4.
6. Arora P, Nanda A, Karan M. Shampoos Based On Synthetic Ingredients Vis-A-Vis Shampoos Based On Herbal Ingredients: A Review. International Journal of Pharmaceutical Sciences Review and Research. 2011; 7(1):42-6.
7. HalithSm, Abirami A, Jayaprakash S, Karthikeyini C, Pillai Kk, Firthouse Pm. Effect Of Ocimum Sanctum And Azadiracta Indica On The Formulation Of Antidandruff Herbal Shampoo Powder. Pharm Lett. 2009; 1:68-76.
8. Deepak B, Quazi A, Amol J, Kundan S, Ujwal H. Formulation And Evaluation Of Anti- Dandruff Shampoo. Ijesc. 2020; 10(3):25116-2.
9. Kaur G, Kriplani P, Dhingra A, Chopra B, Deswal G. Formulation And Evaluation Of Anti- Dandruff Polyherbal Powder Shampoo. Journal of Quality Assurance and Pharma Analysis. 2016; 2(1):115-21.
10. Prabha Ms, Sravani A, Spandana A, Ramarao N, Aruna Ms. Formulation And Evaluation Of Herbal Hair Powder Against Dandruff. Dermatitis. 2014
11. Snehal W, Nitin K. Preparation & Evaluation of Antidandruff Polyherbal Powder Shampoo. Pharmacophore. 2014 Jan 1; 5(1):77-84.
12. Dhayanithi S, Hoque E, Pharm B, Pallavi Nb, Pn K. Formulation and Evaluation Of Herbal Shampoo.
13. Patel P, Tiwari A. Formulation and Evaluation of Herbal Antidandruff Shampoo. International Journal of Pharmacy & Life Sciences. 2019 Feb 1; 10(2).
14. Kushwaha Rk, Maury S. A Review on Anti-Dandruff Activity of Herbal Shampoo.
15. Arora R, Singh Rk, Meenakshi B. Formulation and Evaluation of Herbal Shampoo By Extract Of Some Plants. Pharm Chem J. 2019; 6(4):74-80.
16. Patel IM, Talathi AD. Use of Traditional Indian Herbs for the Formulation Of Shampoo And Their Comparative Analysis. International Journal of Pharmacy and Pharmaceutical Sciences. 2016; 8(3): 28-32.
17. Goel N, Jain A, Budholiya P, Rao MH, Singh A, Siddiqui S, Mishra A. Formulation And Evaluation Of Herbal Anti-Dandruff Shampoo; World Journal of Pharmaceutical Research. 2022; 11(13): 1766-1776.

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A review: Phytochemical and Pharmacological potential of *Rauwolfia serpentina* (L.)

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Abstract: Rauwolfia bush, local to the orient from India to Indonesia, has been profoundly supported for the treatment of snakebite, bug stings, hypertension, sleep deprivation, mental issues, epilepsy, gastrointestinal problems, fever, and schizophrenia from the pre-vedic period in Ayurvedic arrangement of Indian medication. Rauwolfia having a place with the family Apocynaceae merits a particular, place in the pharmacopeia of present day medication. The foundations of Sarpagandha announced numerous significant dynamic standards extricated as alkaloids, flavonoids, glycosides, phlobatannins, phenols, starches, saponins sterols, tannins, and terpenes. In previous years it was announced as the best phytochemical, reserpine, which has been utilized in the treatment of systolic hypertension and has a few drug applications. This survey addresses data old to current methodology about the dynamic rule as well as therapeutic potential with underline organic instrument of *R. serpentina*. The current survey manage the huge measure of studies attempted in various parts of this plant in the space of plant's chemistry, and pharmacology and fundamentally analyzing its unfriendly after effects, toxicology gives an explored and archived strategy for the active ingredients.

Keywords: Indole alkaloids, Reserpine, Hypertension, *Rauwolfia serpentina*, Pharmacological activity, Sarpagandha

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1.1. Introduction The class name was chosen out of appreciation for Dr. Leonhard Rauwolf, a sixteenth century (21 June 1535 - 15 September 1596) German botanist, doctor, and explorer, who reported this plant as a potential source of therapeutic alkaloid schematic diagram has been represent in **[Figure 1]**. Rauwolfia (*Rauwolfia serpentina)*, likewise spelled ravolphia, is a restorative bush in the milkweed family. Practically all individuals from Apocynaceae are poisonous and utilized as restorative by significant in different clinical definitions because of the presence of cardiovascular glycosides and different biologically significant alkaloids [1, 2]. Underlying foundations of the plant *Rauwolfia serpentina* have been perceived in India and the Malay landmass (Mainland Southeast Asia) from old times as antidotes to the stings and bites of insects and poisonous reptiles. Mention of the plant is found in an old Hindu composition (1000 B.C.) as well as in the fantastic works of Charaka (second century, A.D.), under the Sanskrit name of "Sarpagandha." It has additionally been utilized as an energizer to uterine constrictions as a febrifuge, for loose bowels, the runs, madness, and a sleeping disorder. For a little more than a time of twenty years, its clinical application has been stretched out with progress to the treatment of hypertension.

Fig. 1: Dr Leonhard Rauwolf, (21 June 1535 – 15 September 1596)

In the modern edge period, Sarpagandha is utilized as a viable antihypertensive and it is the World's first antihypertensive medication. It is being articulated as the "Wonder medication of India" in 1949 when the British Heart Journal announced the plant to be "clinically powerful in treating hypertension." It has been utilized in the treatment of insanity in India for a really long time. Sen and Bose, Siddiqui and Siddiqui, and Chopra, *et al*., examined the pharmacological activity of the root separate and the indole alkaloid base individually [3, 4, 5]. Since the time the distribution of the aftereffects of these pharmacological examinations, the utilization of an alcoholic extract of the base of *Rauwolfia serpentina* for the treatment of hyperpiesis (constant and obsessive hypertension) and of specific types of insanity has expanded impressively. Rauwolfia serpentina *merits a clear spot in the pharmacopeia of present day" medication.* In any case, it is recognizable that very few clinical reports on the utilization of *Rauwolfia serpentina* have been distributed. We, consequently, distribute the following observations on the use of the standardized extract. The Indian doctor Rustom Jal Vakil answerable for acquainting Rauwolfia with Western medication. However, as of now in

India *Rauwolfia serpentina* is probably going to be a compromised restorative plant [6]. The Indian political pioneer Mahatma Gandhi was known to utilize Rauwolfia, supposedly utilizing the root to make a tea that he consumed in the evening to help relax following an occupied, over stimulated day. The author reviews the plant's science, and pharmacology and fundamentally inspecting its adverse side effects, toxicology gives an explored and reported strategy for activity for the active ingredients.

1.2. Medicinally Active Chemical Constituents of *R. serpentina* The phytochemicals of numerous types of Rauvolfia were at that point inspected and found as very good source of therapeutically significant alkaloids. *R. serpentina* root is accounted for to contain 0.7 - 3.0 % of complete alkaloids rule reserpine which is an indole alkaloid, present in the root. Henceforth, the root biomass production of this plant could be of monetary significance. All parts of the plant, including the stem and leaves, contain indole alkaloids, yet they are found in the highest concentration in the bark of the root [7, 8]. In light of the construction there are three types of alkaloids to be specific, weak basic indole alkaloids, alkaloids of middle basicity, and solid anhydronium bases [9]. The different alkaloids recognized in Rauwolfia include ajmaline, ajmalimine, ajmalicine, deserpidine, indobine, indobinine, reserpine, reserpiline, rescinnamine, rescinnamidine, serpentine, serpentinine, and yohimbine, serpentine apart from these substance different indole alkaloids are recognized in the roots, to be specific, isorauhimbinic acid, yohimbinic acid, N(b)-methylajmaline, 3 hydroxysarpagine, and N(b)- methylisoajmaline [10,11].

The presence of saponins is answerable for the hemolytic movement and cholesterol restricting property. *R. serpentina* is additionally wealthy in full scale and micronutrients which supports its therapeutic properties, i.e., calcium (Ca), phosphorus (P), potassium (K), magnesium (Mg), sodium (Na), iron (Fe), and zinc (Zn). Presently, it was seen that leaves of *Rauwolfia serpentina* contain useful minor components Ca, Co, Fe, K, Mg, Mn, Zn which are available inside the limit meanwhile the concentration of Ni is high. Harmful weighty metals Cd, Cu, and Pb are within the limit but the concentration of As and Cr are high. [**Tables 1** and **Figure 2, 3**] provide a concise depiction of the chemical composition.

Fig. 2: Images of *Rauwolfia serpentina*, showing various parts (A) *R. serpentina* whole plant, (B) flower spring (C) dried snake-like roots (D) dried seed

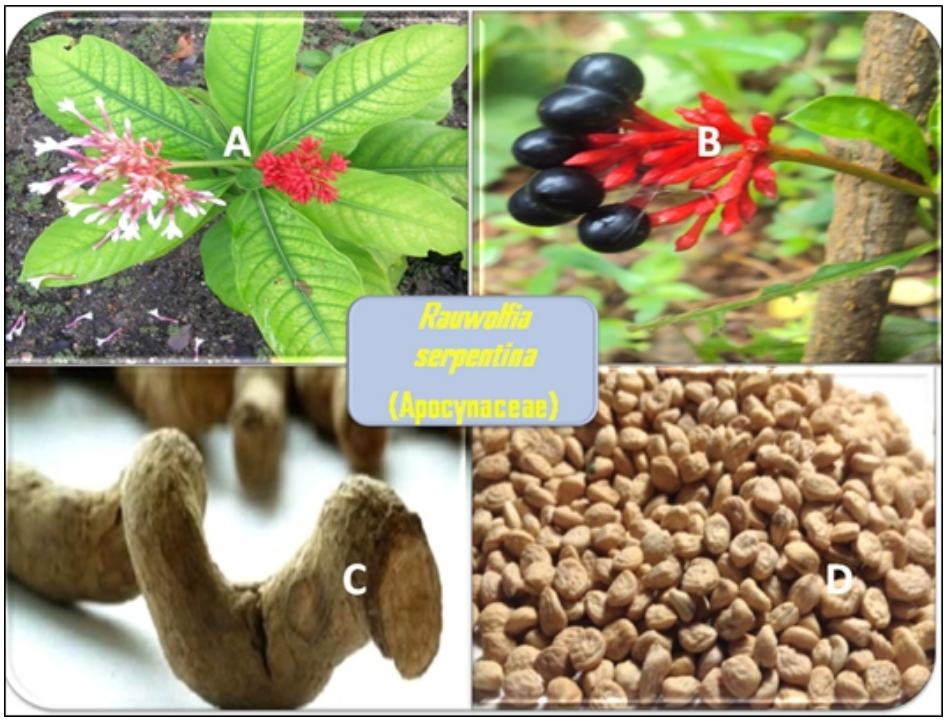

Table 1: Phytochemical of root bark and leaves of *R. serpentina* with their biological activity

S.no.	Phytochemicals	Molecular formula/ Molecular weight	Biological activity	Cited ref.
1	**Weakly bases indole type (pH 7-7.5)**			
	Reserpine	$C_{33}H_{40}N_2O_9$ / 608.7	Generally huge of all alkaloids as antihypertensive, an antipsychotic and normal sedative	[19, 20]
	Rescinnamine	$C_{35}H_{42}N_2O_9$ / 634.7	Diminished aldosterone emission and vasopressor action (Antihypertensive)	[21, 22]
	Despiridine	$C_{32}H_{38}N_2O_8$	Antihypertensive activity	[23]
2	**Tertiary indoline intermediate alkaloids basicity (pH 8)**			
	Reserpiline	$C_{23}H_{28}N_2O_5$ / 412.5	Treatment of psychosis and antihypertensive	[24]
	Ajmaline	$C_{20}H_{26}N_2O_2$ / 326.4	Antiarrhythmic impact by hindering the sodium channel	[25]
	Iso-ajmaline	$C_{20}H_{26}N_2O_2$ / 326.4	Antiarrhythmic compound Brugada condition and atrial or ventricular tachycardia	[26]
	Rauwolfinine	$C_{33}H_{40}N_2O_9$ / 608.7	Hypotensive properties	[27]
3	**Strongly bases anhydronium bases (pH 11)**			
	Serpentine	$C_{21}H_{20}N_2O_3$ / 348.4	Antipsychotic loss of motion of breath, misery of nerves and incitement of the heart (Tranquilizer)	[28]
	Serpentinine	$C_{21}H_{21}N_2O_3$ / 349.4	Sedative, diabetes and hypoglycemia	[29]
	Alsotonine	$C_{21}H_{20}N_2O_3$ / 348.4	Antipsychotic	[4]
4	**Other alkaloids**			
	Ajmalinine δ-yohimbine Raubasine	$C_{21}H_{24}N_2O_3$ / 352.4	Antihypertensive medication	[30]
	Ajmalicine	$C_{21}H_{24}N_2O_3$ / 352.43	Cerebral blood stream. It impacts in forestalling strokes, bringing down pulse and smooth muscles	[31]
	Acridone	$C_{13}H_9NO$ / 195.2	Cancer preventives, antibacterials and smooth muscle relaxants	[26]
	Chandrine		Cardiovascular activities and antiacetylcholine action	[32]
	Renoxidine	$C_{33}H_{40}N_2O_{10}$ / 624.7	Free radical scavenging activity	[33]
	Reserpinine Raubasinine Raubasinin	$C_{22}H_{26}N_2O_4$ / 382.5	Hypertension and mental issues	[34]
	Sarpagine	$C_{19}H_{22}N_2O_2$ / 310.4	Hypotensive to anticancer action	[35]
	Tetraphyllicine	$C_{20}H_{24}N_2O$ / 308.4	Antiarrhythmic impacts antihypertensive specialist	[36]
	Yohimbine	$C_{21}H_{26}N_2O_3$ / 354.4	Erectile brokenness, athletic execution, weight reduction, angina hypertension, diabetic, neuropathy	[37]
	18-beta-hydroxy-3-epi-alpha-yohimbine	$C_{21}H_{26}N_2O_4$ / 370.4	Sexual issues brought about by antidepressants nervousness athletic execution and stoutness	[38]
	Isorauhimbinic acid	$C_{20}H_{24}N_2O_3$ / 340.4	Inhibit cancer cells development	[39]
	Yohimbinic acid	$C_{20}H_{24}N_2O_3$ / 340.4	Inhibit cancer cells development	[40]
	N(b)-methylajmaline	$C_{21}H_{28}N_2O_2$ / 340.5	Cytotoxicity against the human promyelocytic leukemia (HL-60) cell lines	[41]
	D-Glucuronic acid	$C_6H_{10}O_7$ / 194.14	Counteractant, ATPase inhibitor, L-amino-corrosive oxidase inhibitor, Acute neurologic issues treatment Phospholipase A1, A2 inhibitor, 5'- Nucleotidase inhibitor	[42]
	Triacontanol	$C_{30}H_{62}O$ / 438.81	Antidote, Phospholipase movement, 5'nucleotidase inhibitor	[42]

5	**Other than alkaloids**			
	Coumarins	$C_9H_6O_2$ / 146.1	Antihypertensive antibacterial, antioxidant	[43]
	Lignans	$C_{22}H_{22}O_8$ / 414.4	Phytoestrogens, a brought down hazard of coronary illness, menopausal indications, osteoporosis and breast cancer	[44]
	Flavonoids (Kaempherol)	$C_{15}H_{10}O_2$ / 222.24	Digestive system decline the danger of heart infections, antioxidant and anti-inflammatory activities	[45]
	Phytosterols	$C_{29}H_{50}O$ / 414.7	In the human body and block cholesterol absorbed	[46]
	Saponins	$C_{58}H_{94}O_{27}$ / 1223.3	Stop bleeding and make it use in treating wounds	[47]
	Tannins	$C_{76}H_{52}O_{46}$ / 1,701.1	Traditional system of medicine for mucous membrane wounds and inflammation due to the presence of tannins in it	[48]
	Phenolic compounds	C_6H_6O / 94.1	Anti-diabetic and hypolipidemic, anti-microbial agent	[49]
	Resin (epoxy resin)	$C_{21}H_{25}ClO_5$ / 392.9	Yellow resin possessed the sedative and hypnotic properties of the serpentina root	[50]
	Starch	$C_{12}H_{22}O_{11}$ / 342.2	Dietary function	[51]
6	**Essential trace elements concentration**			
	Calcium	Ca / 340.240 ppm	Calcium is necessary for normal functioning of cardiac muscles, regulation of cell permeability, blood coagulation. Excess of calcium in blood results to calcification of several internal organs. Deficiency of calcium causes diseases like rickets, osteoporosis. It is also required for strong bones	[52]
	Phosphate	P / 118.24 ppm	Used to make the urine more acid, which helps treat certain urinary tract infections. Some phosphates are used to prevent the formation of calcium stones in the urinary tract	[53]
	Magnesium	Mg / 112.226 ppm	Magnesium is required for synthesis of protein and function of enzymes, production and energy transport, contraction and relaxation of muscles. Lack of magnesium is associated with abnormal irritability of muscles and convulsions and excess of magnesium cause depression in the central nervous system	[54]
	Potassium	K / 30.642 ppm	Potassium helps in the proper function of brain and nerves, so it helps in prevention of stroke. It regulates acid-base and water balance in the blood and tissues. It is required for bone and in prevention of osteoporosis. High potassium diet lowered blood pressure in individuals with raised blood pressure. Potassium is essential in protein bio-synthesis by ribosomes	[55]
	Manganese	Mn / 28.572 ppm	For glucose metabolism manganese is essential and its deficiency may cause glucose intolerance similar to diabetes mellitus in some species of animals. Its deficiency also results in tissue damage and impairs CNS functions. Excess of manganese causes pneumonia, affects reproductive system, which may lead to infertility, adverse effects primarily on the lungs and on the brain	[56]
	Sodium	Na / 2 ppm	Low sodium content that can be an added advantage due to the direct relationship of sodium intake with hypertension in human	[57]
	Silicate	Si / 3 ppm	Silicon is used for weak bones (osteoporosis), heart disease and stroke and alzheimer's disease	[58]

	Cobalt	Co / 0.163 ppm	It is a part of vitamin B12 which is essential for human health deficiency of cobalt causes pernicious anaemia, severe fatigue, and hyperthyroidism. Excess of cobalt causes cardiomyopathy, hyperglycemia, memory loss, allergic	[59]
	Nickel	Ni / 3.380 ppm	Nickel is required for production of insulin. It is component of several enzymes i.e., carbon monoxide dehydrogenase, urease, hepatic microsomal enzymes Excess of Ni causes allergic dermatitis known as nickel itch, which usually occurs when skin is moist. Nickel can cause cancer of different organs such as nose, prostate, lungs, thus it is carcinogen.	[60]
	Zinc	Zn / 14.656 ppm	Zn is an important trace element and one of the several important micronutrients that is essential for proper functioning of the body. It is within limit. High concentration of zinc is neurotoxin. Zinc is known to govern the contractibility of muscles and helps to avoid prostrate problems. Zinc acts as a co-factor for enzymes in the body. It also takes part in synthesis of DNA, proteins and in insulin biosynthesis, storage	[61]
	Iron	Fe / 162.382 ppm	Iron is required for synthesis of haemoglobin and myoglobin. Iron is essential components of many proteins and enzymes in the human body. Deficiency of iron causes anaemia, poor resistance to infection	[62]
7	**Harmful heavy metals concentration**			
	Arsenic	As / 3.172 ppm	Arsenic poisoning may cause death through enzyme inhibition, Excess of arsenic results in dermatitis, metabolic disorder, lung cancer, cardiovascular effects, neurology	[63]
	Chromium	Cr / 2.481 ppm	Chromium plays an important role in synthesis of fatty acids and cholesterol. Excess of Cr causes asthma, shortness of breath, liver and kidney damage	[64]
	Copper	Cu / 7.279 ppm	Copper is a component of many enzymes i.e., ceruloplasmin, cytochrome oxidase, lysyl oxidase, superoxide dismustase. Alzheimier's disease, Wilson's disease, Prion disease is due to the excess of copper. For normal synthesis of haemoglobin, traces of copper are required. Copper is need for neurotransmitter synthesis, formation of myelin	[65]
	Lead	Pb / 0.284 ppm	Lead has no beneficial effects in humans. Excess of lead causes anaemia, headache, central nervous system disorder, brain damage	[66]
	Cadmium	Cd / 0.162 ppm	Excess of cadmium damages kidneys and liver and causes high blood pressure, gastrointestinal irritation, vomiting	[66]
8	**Vitamin composition of *R. serpentina***			
	Thiamin	Vitamin B1 0.18±0.02 mg/100g	Helps the body's cells change carbohydrates into energy. It is essential for the metabolism of pyruvate	[67]
	Riboflavin	Vitamin B2 0.42±0.10 mg/100g	Reduce high blood pressure	[68]
	Niacin	Vitamin B3 0.02±0.10 mg/100g	nervous system, digestive system and skin healthy	[69]
	Ascorbic acids	Vitamin C 44.03±0.20 mg/100g	It is used in herbal medicines to treat many diseases. Lack of ascorbic acid hinders the normal synthesis of intercellular substances in the body, which includes, tooth dentin, collagen, and bone matrix. Ascorbic acid is essential for body's performance anemia, weakening of the endothelial wall of capillaries and pain in the joint can be related to the association of normal connective tissue metabolism and ascorbic acid	[68, 70]

1.3. Conventional and Modern Pharmacological View of *Rauwolfia serpentina* *Rauwolfia serpentina* was used in India as a folk drug for a seriously prolonged stretch of time to treat a wide number of diseases like febrile conditions, malaria, stomach pain, and looseness of the bowels uterine catalyst, febrifuge, solution for sensory system issues and snakebite envenoming is a dismissed tropical sickness which requires quick thought. Snake venoms are the most abundant source of this large number of enzymes represented in **[Table 2]** [12, 13, 14, 15]. The foundations of *Rauvolfia serpentina* are utilized in Ayurvedic drugs as a treatment for restoring hypertension, sleep deprivation, mental nervousness, gastrointestinal problems, expectation epilepsy, injury, tension, feeling, schizophrenia, narcotic sleep deprivation and psychosis [16, 17, 18].

Additionally, reserpine advance the amount and free corrosiveness of gastric emission alongside different pharmacological exercises incorporate antifungal, anti-arrhythmic, tranquilizing agent, anti-fibrillar activity, antiemetic, vasodilator, hypnotic, sympathomimetic, nematicidal, antidiuretic, hyperthermic, relaxant, sedative, anticontractile, anticholinergic and hypotensive.

Table 2: Pharmacological of *Rauwolfia serpentina* in various disorders

S.no.	Various disorders	Part used	Active constituents	Methods	Biological mechanism	Effective dose
	A. Traditional (3000 -1000 B.C.) view of Rauwolfia					
1	Snake and insect bites					
	Snake bite in Karnataka [71]	Roots buds with milk	Unknown	Applied on snake bit influenced region	The constriction of the digastric muscle will press of toxic substance organ. This makes the toxin to emerge from the toxic substance organ and streams into the adversaries body	Ordinary time period day
	Snake bite in Orissa [72]	Squeezed roots and rhizomes	Unknown	Applied on snake bit influenced region		Ordinary time period day
	Snake bite in Tamil Nadu [73]	Squeezed roots	Unknown	Oral medicine		Ordinary time period day
	Snake bite in Kanyakumari [74]	Decoction of rhizome and leaf	Unknown	Oral medicine		Ordinary time period day 50g/day
	Snake bite in Karnataka [75]	Squeezed roots	Unknown	Tied over the snake nibbled		Ordinary time period day
	Snake bite in Madhya Pradesh [76]	Squeezed roots and rhizomes	Unknown	Tied over the snake nibbled		Ordinary time period day
	Snake bite in West Ghats of Kerala [77]	Root and duck blossom alongside water	Unknown	Oral medicine		Twice a day at customary time frame days
	Snake bite in Uttar Pradesh [78]	Pressed roots	Unknown	Tied over the snake nibbled (as Antidote)		Ordinary time period day

2	Liver disease [79]	Root decoction	Unknown	Extract given orally	Vascular impediment, (Mechanism 1) intrinsic and versatile safe frameworks (Mechanism 2, 3) most significant hormonal impact (Mechanism 4)	Twice a day
3	Dysentery [80]	Paste of root	Unknown	Paste given orally	The reason for loose bowels is normally the microscopic organisms from variety Shigella, in which case it is known as shigellosis, or the one-celled critter Entamoeba histolytica; then, at that point, it is called amoebiasis	Children once day
4	Mental disorders [81]	Root decoction	Unknown	Oral medication	Organic elements comprise of anything actual that can cause antagonistic consequences for an individual's psychological well-being. Natural elements incorporate hereditary qualities, pre-birth harm, diseases, openness to poisons, mind deformities or wounds, and substance	Twice a day
5	Pneumonia [82]	Root decoction	Unknown	Oral medication	The neutrophils likewise discharge cytokines, causing an overall actuation of the resistant framework. This prompts the fever, chills, and exhaustion normal in bacterial pneumonia	Twice a day
6	Scabies [83]	Pressed roots	Unknown	Applied to the skin	Human scabies is brought about by a pervasion of the skin by the human tingle parasite	For eight hours
7	Spleen treatment [84, 85]	Root decoction	Unknown	Oral medication	It reuses old red platelets and stores platelets	Once a day
8	Headache [86, 87]	Root paste	Unknown	Applied above eyebrow	The aggravation pathways are clear, the ophthalmic division of the trigeminal nerve supports sensation inside the noggin and maybe supports why the highest point of the head is migraine, and the maxillary division is "facial torment"	As needed
9	Stomach pain [88]	Leaf of this plant	Unknown	Oral medication	Stomach torment normally begins with the excitement of tangible receptors in instinctive tactile neurons (nociceptors), which communicate nociceptive (torment) data by means of the dorsal horn of the spinal line to the focal sensory system (CNS), which is then incorporated in the cerebrum, coming about in a horrendous tangible	Twice a day

10	Skin diseases [89]	Paste of whole plant	Unknown	Applied to the skin	skin infections are portrayed by inclusion of the epidermis with disturbance of the respectability of the epidermal barrier	For eight hours
11	Loose motion [90]	Leaf extract	Unknown	Oral medication	The resistant reaction to fiery conditions in the entrail contributes considerably to improvement of looseness of the bowels	Twice a day
12	Chronic wound [90]	Root powder	Unknown	Applied to the skin	Organic and clinical comprehension of the systems that support wound fix	For five hours
13	Fever (Febrifuge) [90]	Root extract	Unknown	Oral medication	Accordingly, the nerve center raises the internal heat level's over the ordinary reach, consequently causing a fever	Twice a day
14	Malaria [90]	Squeezed roots	Unknown	Oral medication	The intestinal sickness parasite life cycle includes two hosts. During a blood feast, an intestinal sickness contaminated female Anopheles mosquito vaccinates sporozoites into the human host	Twice a day
15	Diarrhea [90]	Squeezed roots	Unknown	Oral medication	The runs is the inversion of the typical net absorptive status of water and electrolyte ingestion to discharge	Twice a day
16	Uterine energizer [90]	Root decoction	Unknown	Oral medication	The proper biomechanical capacity of the uterus is expected for the execution of human multiplication	Once a day
17	Nervous system disorders [90]	Squeezed roots and rhizomes	Unknown	Oral medication	Neurodegenerative problems are diseases described by a deficiency of sensory system working that are generally brought about by neuronal demise	At first the powdered root 20 to 60 grains one time each day
18	Periods related problems [90]	Root decoction	Unknown	Oral medication	Essential science of the period is a complicated, facilitated grouping of occasions including the nerve center, foremost pituitary, ovary, and endometrium	Once a day
	B. Modern view of Rauwolfia					
19	Anti-hypertension [91, 92]	Ethanolic extract of powder root	Reserpine and rescinnamine	Just patients with SP more than 160 and DP more than 95 mm/Hg 50 patient	Hypertension results from irregularities of the control frameworks that ordinarily direct pulse. These control frameworks incorporate vascular, cardiogenic, renal, neurogenic, and endocrine components that connect in a complex however coordinated way to accomplish pulse homeostasis	Low portion Rauwolfia (LDR) 0.5 mg and the last 2-3 mg of the alkaloid, 2-3 times day by day

20	Antipsychotic [93]	Extract of powder root	α-yohimbine, reserpiline, 10-methoxy tetrahydro alstonine, isoreserpili ne, and 10-deme thoxyreserp iline	Just determination of maniacal patients	Their restorative intensity scales with partiality for dopamine D_2 receptors, however there are signs that they act by implication, with dopamine D_1 receptors (and others) as conceivable extreme target	Parenteral infusion of 4-5 mg Rauwolfia separate was displayed to have a high proclivity for focal α_2 and dopamine D_2 receptors
21	Antibacterial [94]	Ethanolic extract of powder root	Ajmalicine Yohambaoi d Monoterpe noid	Bacterial societies 2-gram (+ve) and 3-gram (-ve) bacterial	Better comprehension of the component of activity (MOA) of AMPs is a significant piece of the disclosure of more powerful and less harmful AMPs. Many models and methods have been used to depict the MOA	Concentrate fixation employments 0.5 mg as compelling portion
22	Antibacterial potential [95]	Alcoholic extract	Indole alkaloid	Against *E.coli, S.typhi, S. aureus,* and *K. pneum oniae* utilizing the paper circle dissemination technique	alkaloids electron-donating ability is very important in inhibiting cell growth of bacteria because cell uses NADPH-dependent reductase to retain a intracellular reduced environment in the cells.	Least inhibitory conc. (MIC) was dictated by paper plate dispersion strategy found successful against *S. aureus*
23	*In-vitro* antimicrobial activity [96]	Aqueous extracts of roots	Reserpine Flavonoids Saponins Tannins	Agar well diffusion method	Agar well dispersion strategy has been utilized to decide the antimicrobial exercises and least inhibitory fixations (MIC) of various plant extricates against Gram-positive microbes Gram-negative microorganisms	Human pathogenic microscopic organisms and growths, it tends to be suggested for the control of irresistible gram-positive microbes at 100 mg/ml fixation
24	Quantification of reserpine content and antibacterial activity [97]	Methanol extracts	Reserpine Flavonoids Saponins Tannins	Agar well diffusion method	*R. serpentina* contain great measure of reserpine and displayed solid antibacterial action against the greater part of the tried human pathogenic microorganisms	Strong antibacterial movement against a large portion of the tried human pathogenic microscopic organisms removes up to 10 mg
25	Treatment of arterial hypertension [98]	Isolated a new active alkaloid root extract	Rescinnami ne	Observations in dogs	This disorder is a major risk factor for many common causes of morbidity and mortality including stroke, myocardial infarction, congestive heart failure, and end-stage renal disease	Directed either orally or i.v. measurement shifted from 1-2 mg

26	Herbo-mineral analysis [99]	Aqueous extracts	Determination of herb-minerals such Zn, Fe, Cu, Mn, Ca, K, Na, Co, Cr, Pb, Ni, Al, Cd, and Li	Inductively coupled plasma-nuclear discharge spectroscopy (ICP-AES)	Ayurvedic herbomineral definition arranged from spices, minerals and metals by calcinations process. Nano particles qualities of bhasma make them special and are fiercely prescribed to treat ongoing illnesses in most effective ways	Not really settled upsides of the greater part of the components in the example were in acceptable concurrence with the guaranteed values
27	Hematemesis and Melena [100]	Ethanolic extract of powder root	Reserpine	Reported in animals and man	Dealing with a significant intense gastrointestinal discharge are to treat hypovolemia by reestablishing the blood volume to typical, to make a determination of the draining site and its basic reason	Low dose Rauwolfia (LDR)
28	Vasomotor reflexes [101]	Crude root extract	Total alkaloids possesses	Impeding activity on pressure just as depressor reflexes starting from the carotid sinus	Instruments of vasomotor guideline. Connection of foundational to provincial vasomotor reflexes following feeling of specific interoceptive zones	Low dose Rauwolfia (LDR)
29	Cardiovascular and respiratory effects [102]	Crude root extract	"Serpasil"	Fifty mongrel dogs of both genders V.R. manometer	The most important normal pathogenetic venture by which wholesome variables impact cardiovascular sickness. Vascular aggravation is impacted by overabundance caloric admission (heftiness, insulin opposition)	Managed i.v. just a single infusion of Serpasil 0.5-1.0 mgm/kgm
30	Hypotension, sedation and bradycardia [103]	Ethanolic extract of powder root	Rescinnamine similar to that of resepine	Perception in dogs and rats and mice and by prolongation of pentobarbital-instigated dozing time in mice	Extreme vasodilation, or lacking narrowing of the veins (for the most part arterioles), causes hypotension	Low dose Rauwolfia (LDR)
31	Anti-diarrhoeal activity [104]	Leaf methanolic extract	Supports its traditional uses like Phenolic Flavonoids Saponins	Exploratory the runs instigated by castor oil in mice	work by diminishing the progression of liquids and electrolytes into the entrail and dialing back the development of the gut to diminish the quantity of defecations	Portions of 100, 200 and 400 mg/kg separates were given and created a portion subordinate decrease in digestive weight and liquid volume

32	Elicitation of pharmacological active phenolic compounds [105]	To evaluate the effect of three natural elicitors SA, MSA, ASA on Rauvolfia and to compare the efficiency of many solvent in phenolic compound extract	Improve phenolic concentration during extraction	Approach addresses an advantageous option in contrast to cell suspension or aqua-farming societies being material in wide horticultural practice	Phenolic compounds (PCs) goes about as a cancer prevention agent by responding with an assortment of free revolutionaries. The system of cell reinforcement activities included either by hydrogen molecule move, move of a solitary electron, successive proton misfortune electron move, and chelation of change metals	To further develop phenolic fixation during extraction
33	Anti-histaminase activity [106]	Methanolic extract of rhizomes/root	Serpentine	Guinea-pig ileum, uterus and inhibited histaminase	Allergy medicines stifle the receptor instigated wheal reaction (enlarging) and flare reaction (vasodilation) by hindering the limiting of receptor to its receptors or decreasing receptor movement on nerves, vascular smooth muscle, glandular cells, endothelium, and pole cells	Greatest reaction of serpentine with 10^{-8} and 10^{-7} g/ml
34	Platelet biological activity [107]	Methanolic extract of rhizomes	Raubasine or ajmalicine	*Ex-vivo* and the subs. were utilized as instigating specialists: adenosine di-phos, collagen, adr	Platelets are basically answerable for the total interaction. The principle work is to add to homeostasis box 3 cycles: bond, initiation, and collection	Raubasine has an inhibitory activity on the delivery response of the platelets
35	Antifungal activity [108]	Root extract	Alkaloids as well as rutin, oleoresin, sterol, oleic acid and unsaturated alcohols	Against *N. crassa* (culture Ema 5297 and EmA 5296) as well as mutation, segregation of the fungus or Vogel's minimal medium	The two principle components of activity of antifungals focusing on the cell divider are connected with the hindrance of chitin and β-glucan union	Critical developed inhibitory anti-fungal movement against *N. crassa* (Ema) and 10% which is reasonable for enlistment of change
36	Anti-inflammatory [109]	Stem and root were coarsely powdered using extraction solvents acetone, methanol and chloroform	Flavonoidal structure 3,5,7,4'-tetrahydroxy flavone *i.e.,* Kaempherol	Beginning communications between coursing leukocytes and endothelium are significant for resistant what's more, incendiary	(NSAIDs) produce their remedial exercises through hindrance of cyclooxygenase (COX), the compound that makes prostaglandins (PGs)	Late gauges show that dietary admission of flavonoids is on the request for 23 mg/day
37	Antipyretic effect [110]	Aqueous extract of the leaves	Reserpine and rescinnamine	Rabbits tainted with *Klebsiella aerogenes*	Antipyretics make the nerve center abrogate a prostaglandin-incited expansion in temperature. The body then, at that point, attempts to bring down the temperature, which brings about a decrease in fever	Portion of 1.2 g/kg^{-1} given orally created a lessening in temp. from 42ºC to 40ºC in around 2 hr

38	Treated of migraine headaches effectively [111]	Extract of root	Reserpine	220 chose patients cerebral pain against with mental	It additionally has been displayed to repress glutamate-intervened excitatory neuro transmission, work with GABA-A-interceded restraint, hinder carbonic anhydrase action, and diminish CGRP discharge from trigeminal neurons	Portion of 0.5-4mg, for multi month reserpine right now suggest
39	Tranquillizing agent [112]	Ethanolic extract of rhizomes /root	Reserpine	Intellectually inadequate patients chose	They are remembered to work by obstructing the neuro transmitter dopamine in the mind. This prompts a decrease of maniacal side effects	Portion of 0.5 - 4mg reserpine at present suggested
40	Childhood autism activity [113]	Ethanolic extract of rhizomes /root	Reserpine	Medically introverted youngsters between the periods of 3.5 and 9 years taken	The pathophysiology of cerebrum designs and cycles related with mental imbalance, and the neuropsychological linkages between mind constructions and practices	Reserpine has additionally been utilized for sedation yet offers no advantage over the phenothiazine
41	In improving pruritic and psychogenic dermatosis [114]	Aqueous extract of the leaves	Reserpine or Serpasil	Therapy of different dermatoses inpatients experiencing constant tingle is high	It is the communication among psyche and skin. The two disciplines are interconnected at the embryonal level through ectoderm. There is a mind boggling transaction among skin and the neuroendocrine and invulnerable frameworks	While treating blood vessel hypertension12 and in psoriatic joint pain, 13in which case both the psoriasis and the joint inflammation improved at the same time
42	Treatment of delirium tremens in alcohol and drug addicted patients [115]	Whole crude root extract	Reserpine	Intensely alcoholic patient	It restrains the activity of glutamate, which is an excitatory amino corrosive. Delayed liquor misuse brings about receptor up-guideline	The reserpine portion ought to be lower than 500 µg each day and, as a rule, lower than 250 µg each day suggested
43	Treatment of anxiety [116]	Whole crude root	Rauwolfia Reserpine Alseroxylon	Control of clear anxiety in meandering patients	Antidepressants lessen tension by expanding the convergence of synthetics (synapses) that the mind uses to impart	Clinical utilization of the Rauwolfia drugs are accounted for with minor harmful manifestations
44	Activity in agitation, excitement and acute hallucinatory [117]	Alseroxylon extract (whole root)	Pure reserpine	Seen in unsettling, energy, and intense illusory patients	There are something like three different pharmacological ways of prompting pipedreams (1) initiation of dopamine D2 receptors (D2Rs) with psychostimulants, (2) initiation of serotonin 5HT2A receptors (HT2ARs)	Suggested an everyday measurements lower than 0.75 mg of reserpine missing to negligible mental trip following a half year of treatment

45	Mosquito larvicidal activity [118]	Dry seeds of *R. serpentina* were extracted with five solvents graded Pet. ether, Benzene, EA, Acetone, Alcohol	Ajmaline Deserpidine Rescinnamine Serpentinine Reserpine	Against the hatchlings of *C. quinquefasciatus*	Component of larvicidal activity of elaidic corrosive, arachidic corrosive, and behenic corrosive may be because of obstruction with the octopaminergic framework	Most noteworthy mortality was displayed in 100 ppm of p.ether remove (61.00± 1.00) at 72 h
46	Sedative activity [119]	Extract dried powdered leaves and root bark ammoniated with methanol (1:10)	Ajmaline Peraksine Vomifoline Isoreserpiline	Cross bred albino rats (250-260 g) with rat hole-board method	Narcotics work by adjusting specific nerve interchanges in your focal sensory system (CNS) to your mind	concentrates of 12.5 or 25 mg/ kg and PVP combinations were given i.p. has narcotic exercises
47	Stroke induced experimental dementia [120]	Methanolic root bark extract	Phenolic compound like phenolic acid, flavanoids and tannins present in the plant	Morris water labyrinth test and raised in addition to labyrinth test. Toward the finish of all analysis mice mind were taken out and TBARS level, SOD	Stroke is a cerebrum illness that happens when blood stream stops that outcomes diminished oxygen supply to neurons	Organization of RS extra ordinarily at a portion of 20mg/kg and 40mg/kg; p.o. fundamentally lessened these change and show neuro defensive impact against oxidative pressure, infract size and learning and memory
48	Evaluation of DPPH-scavenging antioxidant potential [121]	Methanolic extract from the leaves	Flavonoidal structure Kaempherol	Potential was dictated by DPPH strategy and FRAP technique	The DPPH examine is utilized to foresee cancer prevention agent exercises by system in which cell reinforcements act to hinder lipid oxidation, so searching of DPPH extremist and subsequent ly determinate free revolutionary rummaging limit	0.5ml (50-5000 µg) of test arrangement was added to 1ml of DPPH arrangement independently
49	Antidiabetic and hypolipidemic [122]	Methanolic root extract	high quantity of total polyphenol compounds	Alloxan-induced diabetic mice	These specialists work by shutting potassium channels on the outer layer of beta cells, which causes a deluge of calcium particles into the cells and a subsequent surge of insulin from cell stockpiling vesicles	Oral organization of root powder portion level of 60 mg/kg
	Improves the glucose tolerance [123]	Methanolic root bark extract	Reserpine ajmaline	Male wister albino mice (20-30 g)	Further develops glucose resilience transcendently by diminishing glucose retention in the small digestive system. It most likely does this by repressing the impacts of digestive motility on liquid convection	Portion of 10-60 mg/kg and instigated no sedation in mice except for showed deadly impact by prompt sedation and mortality at dosages 100-250 mg/kg

50	Ameliorative effect on some biochemical parameters [124]	Hydro-methanolic roots extract	alkaloids such as reserpine, ajmaline and total polyphenol compounds	Type 1 alloxan induced diabetic mice selected	Propose that the fundamental atomic components of activity of BG-interceded mitigation of APAP-actuated hepatotoxicity	Use portion of 50, 100 and 150 mg/kg every treatment was rehashed for 14 days routinely concentrate on help the hypo glycemic and hypolipidemic potential
51	Hypoglycaemic and hypolipidemic activities [125]	Methanolic root extract	Total polyphenolic compounds	Alloxan - induced diabetic rats selected	Their system of activity intently looks like that of sulfonylureas (they act by controlling ATP-sub ordinate potassium diverts in pancreatic beta cells), since they animate the arrival of insulin from the pancreatic beta cells	Portion of 30 mg kg^{-1} for decreasing all out cholesterol, fatty substances alanine amino transferase
52	Hypolipidaemic activity [126]	Methanolic root extract	high quantity Polyphenolics	Experimental rabbits selected	This component represents the expansion in lipolysis (adjustment of apoCIII and lipoprotein lipase) and in HDL-cholesterol (balance of apoAI and apoAII qualities)	Oral treatment with 30 mg/kg for first - twelfth day
53	Hepatoprotective activity [127, 128]	Aqueous ethanolic extract of rhizomes	Antioxidant agents like total phenolics	Against paracetamol induced hepatic damage in rats was investigated	The insurance of liver cells against harmful materials including drugs, lipid peroxidation, and free extreme injury might diminish aggravation, further develop liver blood stream, and at last assistance in decrease of ascites and pulse	Day by day took care of 425 mg/kg^{-1}, p.o. for 7 days show critical impact of extract
		Methanolic extract of rhizomes and leaves	Antioxidant agents like total phenolic	CCl_4 induced hepatotoxicity model		Organization of 400 mg/kg MET of *R. serpentina*, huge
54	Breast cancer study [129]	Root powder extract	Rauwolfia derivatives Reserpine	Women breast selected for study	The growth develops on the grounds that the bosom disease cells contain proteins called estrogen receptors that become dynamic when estrogen atoms connect to them	Consistent at least 10 years term use have a raised danger of breast cancer growth by Reserpine
55	Anti-prostate cancer [130]	Root powder extract	Rauwolfia derivatives Reserpine	*In vitro* and *in vivo* against androgen-delicate human prostate malignancy cell line, LNCaP	Its sub-atomic system aimed at cell multiplica- tion control including cyclooxygenase-2(COX-2) prostaglandin E2 (PGE2) and cyclins /cdks pathways, and 3)	Growth volumes were diminished by 60%, 70% and 58% in the gatherings took care of the 75, 37.5 or 7.5 mg/kg Rauwolfia, individually

56	Influence of different sterilizing methods on isolation endophytic bacteria [131]	Root bark taken	Antioxidant agents like total phenolics	Surface cleansing strategies were led to segregate genuine endophytic microbes from the roots	Gainful impacts incorporate advancing host development and organic control of phytopathogens	Utilized to enhance the surface sanitization for the confinement of endophytes from *R. serpentina* studies decide the powerful endophytic microorganisms
57	Thyrotoxicosis activity [132]	Methanolic root extract	Total alkaloids Reserpine	16 cases: 3 male and 13 female patients	Thyroid chemical receptors work by restricting to explicit thyroid chemical responsive groupings in advertisers of target qualities and by managing record	Patients got three 1 mg "gendon" tablets every day
58	Regulation of hyper-thyroidism activity [133]	Root extract	Root possesses total alkaloids Reserpine Ajmaline	Guideline of hyperthyroidism in mice an increment in serum centralizations of both thyroid chemicals (thyroxine and triiodothyronine	The emission of T3 and T4, which happens in thyroid organ follicles, is typically constrained by thyroid animating chemical (TSH), a protein emitted from the front pituitary	Day by day organization of the plant separate (2.5 mg kg^{-1}) for 30 days diminished conc. of both thyroid chemicals, demonstrating the conceivable guideline of hyper-thyroidism by the plant remove
59	Effect on angina pectoris [134]	Methanolic root extract	Fraction of Alseroxylon and Rauwiloid	13 men and 2 ladies chose for study	Fundamental hidden instrument that prompts angina is an unevenness of myocardial oxygen organic market	Directed 4 mg/day of alseroxylon will accomplish a maximal helpful reaction
60	Anti-emetic activity [135]	Methanolic root extract	Fraction of Reserpine and alseroxylon	Dogs to determine action against apo-morphine - induced	Antiemetics work on the neural pathways engaged with heaving by obstructing explicit receptors that react to neuro transmitter particles, like serotonin, dopamine, and receptor	Low dose Rauwolfia (LDR) specific discouragement of the medullary emetic CTZ
61	Diuretic therapy in the treatment of hypertension [136]	Whole root extract of Rauwolfia	"Reserpine content"	62 unselected patents	They act by lessening sodium reabsorption at various destinations in the nephron, subsequently expanding urinary sodium and water misfortunes	Rautax utilize in this review as oral antihypertensive - saluretic drug that contain in every tablet 50mg of entire root extricate 400mg of flumethiazide and 400mg of potassium chloride

62	Reserpine content in response to geographical variation [137]	Rauwolfia Samples were collected from four different parts of southern India	"Reserpine content"	Different samples were extracted using CH_3OH extracts were subjected to HPLC analysis	Various elements like environment, height, precipitation and different conditions liable for development of plants might influence the substance of dynamic constituents	Significant variation in the content of reserpine has been recorded
63	Estimation of reserpine in plant by TLC, HP-TLC and HPLC [138]	Plant samples, including roots, leaves and callus	Determenta ion "Reserpine content"	The TLC analysis of all the samples, including roots, leaves and callus	The CAF of tests recommend that roots are wealthy in alkaloid content when contrasted with leaves and callus	The highest reserpine content was obtained from the *in-vitro* regenerated roots (33 mg/g^{-1}) and the least from the leaves
64	An efficient *in vitro* clonal propagation of reserpine content [139]	*In vitro* propagation measured in the different parts of plant including, leaf, stem, flower and root	Determenta ion "Reserpine content"	Effect of plant growth regulators Leaf callus 93.65% Stem callus 50.4% Shoots callus 25.4 Root callus 100%	*In vitro* different shoot societies were laid out utilizing shoot tip explants	90% of the total reserpine content was produced from the root, with the stem and leaf containing 10%
65	*In vitro* flowering in Rauwolfia [140]	Multiple shoot regeneration and flower induction *in vitro* have been achieved	Accomplis hed in this review utilizing blends of cytokinin and auxin	Murashige and Skoog medium	Various shoot recovery and bloom enlistment *in vitro* have been accomplished in this study utilizing mixes of cytokinin and auxin	Enhanced with 2.22 µm benzyl adenine (ba) + 2.32 µm kinetin (family) + 0.54 µm naphthalene acidic corrosive and 2.22 µm ba + 4.65 µm kinfolk under a 12 hr photoperiod
66	Determination of trace metals in the leaves [66]	The leaves of Indian medicinal plant *Rauwolfia serpentina* were digested with HNO_3 and $HClO_4$ (4:1)	The substance of minor component s, for example, As, Ca, Cd, Co, Cr, Cu, Fe, K, Mg, Ni, Mn, Pb and Zn	Determined by atomic absorption spectroscopy	Determined by atomic absorption spectroscopy	Helpful minor components Ca, Co, Fe, K, Mg, Mn, Zn are inside limit yet the grouping of Ni is high. Hurtful substantial metals Cd, Cu and Pb are inside limit however the convergence of As and Cr high
67	Neutralizing potential root extract against Naja naja venom [141]	Aqueous extract of *R. serpentina* root	D-glucuronic Triacontan ol Reserpine Gallic acid Oleic acid	*In vitro, in vivo* strategies and hostile to - toxin compounds were distinguished utilizing LCMS examination and their exercises were determe utilizing PASS programming	Checked for the cure properties against toxin by *in vitro* and *in vivo* strategies	About 0.14 mg of *Rauwolfia serpentina* plant extricate had the option to totally kill the deadly action of $2LD_{50}$ of naja toxin

68	Human kidney proximal tubule cells are vulnerable [142]	Root extract	Dietary support and for the safety of this herb reserpine and gallic acid	Utilized a human kidney cell line to research the conceivable adverse consequences of Rauwolfia on the renal framework	Human kidney proximal tubule cells are helpless against the impacts of *Rauwolfia serpentina*.	Results recommend more examinations are expected to research the wellbeing of this dietary enhance in both kidney and other objective organ frameworks
69	Development of suspension cultures and *ex-vitro* rooting [143]	Root and shoot of Rauwolfia with development chemicals mixes like IBA, BAP, KN, NAA, 2,4-D and TDZ for an axenic suspension culture	Yohimbine Reserpine	*Ex-vitro* developed shoots fluid MS media enhanced	Ex-vitro uncovering was conveyed from in-vitro developed shoots in various preparing blends under glass house conditions inside 10 days of manor with 95% of endurance rate	Result was discovered best for fast shoots development fluid MS media suppl. with BAP (2mg/l) + IBA (2mg/l) + KN (1mg/l)
70	Comparative phytochemical analysis of stem and root extracts [144]	Stem and root extracts (acetone and chloroform)	Occurrence of Alkaloids Flavonoids Glycosides Anthraquinon	Root and stem separates were tried for essential screening of phyto-synthetics	Nearly phytochemical investigation of stem and root separates (acetone and chloroform)	In this manner, the event of significant degree of alkaloids in the stem and root extract of *R. serpentina* may trustworthy for the biological activity
71	*In -silico* investigation on alkaloids of *R. serpentina* as potential inhibitors of 3-hydroxy-3-methyl-glutaryl-CoA reductase [145]	Isolated twelve alkaloids from the roots of *Rauwolfia serpentina*	Five alkaloids including compound 1 Ajmalicine 2 Reserpine 3 Indobinine 4 Yohimbine 5 Indobine	This reason, the (3D) swagger of the protein HMGCR (PDB ID: 1HW9) was download from Protein Data Bank (PDB) data set as an objective catalyst	this reason, the three-layered (3D) design of the protein HMGCR (PDB ID: 1HW9) was downloaded from Protein Data Bank (PDB) data set, as an objective catalyst	The alkaloids from serpentina can successfully stifle the cholesterol biosynthesis pathway through hindrance of HMGCR and can fill in as potential lead compounds for the advancement of new medications for HLD
72	Corrosion inhibition of carbon steel in HCl solution by some plant extracts [146]	Plant extracts of *Rauwolfia serpentina*	Tannins, org. amino acids, alkaloids, and pigments are known to exhibit inhibit action	*Rauwolfia serpentina* tried as consumption inhibitor for gentle steel in 1 M HCl and H_2SO_4 utilizing weight reduction strategy at three temp. 303, 313, 323K	Potentiodynamic polarization, electrochemical impedance spectroscopy, and scanning electron microscope (SEM)	Answered to hinder 98% the erosion of gentle steel in corrosive media potentio dynamic polarization, electrochemical impedance spectroscopy and checking electron magnifying instrument (SEM) examines

73	Analgesic activity [147]	Plant extracts of *Rauwolfia serpentina*	"Reserpine"	was screened by the formalin test and hot plate method	Principal mechanism of calcitonin's analgesic effect is probably a direct central action	Treatment of mice with different concentrates came about in the hinder of the formalin initiated provocative agony diminish paw volume
74	Anti-venomous activity[148]	Ethanolic extract of whole plant	"Reserpine"	Screened venom detoxifying activity in mice	Has completely neutralized the lethal activity of $2LD_{50}$ of venom by procoagulant, direct and indirect hemolytic activities	0.14 mg extract of R. serpentina has completely neutralized the lethal activity of $2LD_{50}$ of venom
75	Insecticidal activity [149]	Seed extracts with five solvents absolute alcohol, petroleum ether,	Indobinine Yohimbine Indobine	Against *Culex quinquefasciatus*	The protein and nucleic acid content of larvae were considerably reduced	Potent source to effect mosquito larvicidal activity
76	Immune enhancing activity [150]	Ethanolic extract of whole plant	Five alkaloids including compound 1 Ajmalicine 2 Reserpine 3 Indobinine	against *Aphanomyces invadans* infection in *Labeo rohita*	Indicating the ability of diet to enhance innate immunity and confer disease resistance	Increase in phagocytic, myeloperoxidase activity, the respiratory burst activity, WBC, biochemical parameters, lysozyme activity

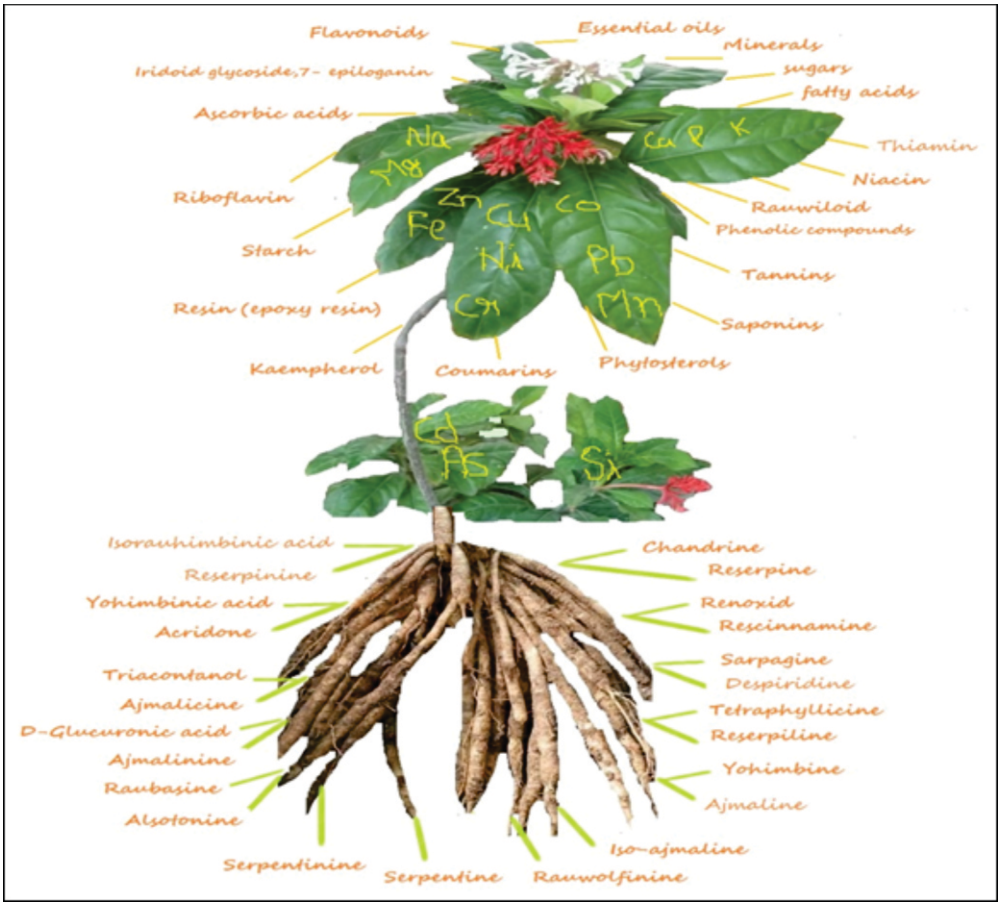

Fig.3: Demonstration of active constituents associated with the leaves, stem, and root of Sarpagandha

1.4. Side Effects Orally, the roots of the plant might cause unfavorable responses including nasal blockage, stomach cramps, looseness of the bowels, queasiness, spewing, anorexia, expanded gastric corrosive emission, sleepiness, exhaustion, laziness, eased back reflexes, and sexual dysfunction. The attending utilization of *R. serpentina* can build the danger of bradycardia and arrhythmias. In spite of the fact that there are not many reports of hypersensitive reactions from the utilization of plant roots, it might accelerate asthma.

The dose in bigger sums can accelerate mental misery and in incredibly enormous sums, Parkinson-like indications, extrapyramidal responses, and spasms might happen. Henceforth, these captivating discoveries will probably animate further interest in *R. serpentina*. A portion of the results of *R. serpentina* are faintness or sleepiness, absence of shortcoming or energy, powerlessness to focus or mental discouragement, uneasiness or gloom, early morning restlessness.

1.4.1. Other Common Side Effects Whenever taken enormous portion of indole alkaloids

- Dizziness
- Black, tarry stools, Stiffness
- Bloody vomit
- Chest pain, Headache Stomach cramps or pain
- Irregular heartbeat, Slow heartbeat
- Shortness of breath, Slow pulse
- Painful or difficult urination
- Skin rash or itching, Flushing of skin
- Trembling and shaking of hands and fingers
- Pinpoint pupils of eyes

1.5. Future perspective The present review is an instant resource and fills the gap on scientific research on discovery of novel drugs to the world of medicine. The ethnobotanical knowledge of various tribes indicated that, *R. serpentina* were reported as ethnobotanically important on snakebite, blood pressure, malarial fever, mental disease, nervous disorder, anthelmintic and respiratory problems. The members of species of Rauvolfia were recorded with various pharmacological activities, hypertension, antimicrobial efficiency, antioxidant properties, anti-inflammatory activity, anti-venomous activity, cytotoxic activity, sedative activity, insecticidal activity, antipsychotic activity etc. Although, in-depth investigation has to undertaken to understand the key features, structural activity relationships of phytocompounds, mode of action of drug on organisms, mass cultivation of Rauvolfia spp. due to heavy demand for their phytochemicals. One of the major advantages of using plants is that they do not show the deleterious side effects commonly associated with other drugs. There is need to save Rauwolfia species worldwide and development rehearses advance very large creation of roots for esteem expansion of medication research. A definite examination of *Rauvolfia serpentina* should be done on molecular level. The pharmacodynamics and pharmacokinetics of phytoconstituents should be perceived and judged.

1.5.1. Challenges and future aspects of medicinal plants Today medicinal plants are very important for the growth of new drugs. People are using herbal drugs because of its safety, efficacy and lesser side effects. Plants and plant products have utilized with varying success to cure and prevent diseases. At present demand of natural plants derived products are increasing day by day in global countries.

2.0. Conclusion The extensive literature survey revealed that *R. serpentina* is being used since pre-Vedic period to treat various ailments including hypertension, insomnia, psychological disorders, gastric disorders, epilepsy, wounds, fever, and schizophrenia. Research shows that *R. serpentina* is a potential source of compounds pertaining medicinal

applications. Recent studies also suggest a role of its various constituents for the wide array pharmacological and therapeutic properties. However, detail phytochemical, pharmacological, and clinical studies are required to validate the effect of *R. serpentina* and its constituent. It provides an interesting subject in the search for new drugs of natural origin.

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2.6. Conflict of interest We declare that we have no conflict of interest.

2.7. References

1. Sharma N, Chandel KP. Low-temperature storage of Rauvolfia serpentina Benth. ex Kurz.: an endangered, endemic medicinal plant. *Plant Cell Reports* 1992; 11(4): 200-3.
2. Singh R, Singh A, Rath S, Ramamurthy A. A review on sarpagandha-Whole herb v/s reserpine–Its alkaloid in the management of hypertension. *Int Ayur Med J* 2015; 3: 565-9.
3. Sen G. *Rauwolfia serpentina*, a new Indian drug for insanity and high blood pressure. *Ind Med World* 1931; 2:194-201.
4. Siddiqui S, Haider SI, Ahmad SS. A New Alkaloid from the Roots of *Rauwolfia serpentina*. *J Nat Prod* 1987; 50(2):238-40.
5. Chopra RN, Gupta JC, Mukherjee B. The pharmacological action of an alkaloid obtained from *Rauwolfia serpentina* Benth. A preliminary note. *Ind J Med Res* 1933; 21: 261-71.
6. Rj V. A clinical trial of *Rauwolfia serpentina* in essential hypertension. *Bri Heart J* 1949; 11(4):350-5.
7. Bhanwaria R, Singh B, Gochar R. Indian Snake Root and Devil Root as Distinctive Medicinal Plant for Curing Human Disease: Biology, Chemistry and Cultivation Practices of *Rauwolfia serpentina* and *Rauwolfia tetraphylla*. *Plants Nov Drug Mole* 2021; 445-465.
8. Chauhan S, Kaur A, Pareek RK. Pharmacobotanical and pharmacological evaluation of ayurvedic crude drug: *Rauwolfia serpentina* (Apocynaceae). *Int J Green Pharm* 2017; 11(4): S686-93. doi.org/10.22377/ijgp.v11i04.1344
9. Biradar N, Hazar I, Chandy V. Current insight to the uses of Rauwolfia: A review. *Res Rev J Pharmacogn* 2016; 3:1-4.
10. Abhijit D, De JN. *Rauvolfia serpentina* (L). Benth. ex Kurz.-a review. Asian journal of plant sciences. 2010; 9(6): 285-98. doi: 10.3923/ajps.2010.285.298
11. Surendran S, Raju R, Prasannan P, Surendran A. A Comprehensive Review on Ethnobotany, Phytochemistry and Pharmacology of Rauvolfia L.(Apocynaceae). *The Bot Rev* 2021; 87(3): 311-76.
12. Lobay D. Rauwolfia in the Treatment of Hypertension. *Integr Med* 2015; 14(3): 40-46.
13. Gawade BV, Fegade SA. Rauwolfia (reserpine) as a potential antihypertensive agent: A review. Int J Phar Phyto Res 2012; 2(1):46-49.
14. Tapre DN, Walde SR. A Review: Use of *Rauwolfia Serpentina* for antihypertensive activity. *Int J Sci Res* 2019; 8(9): 262 - 265
15. Singh P, Goswami B, Mittal D, Kumar P. A comparative review on "*Rauwolfia serpentina*" for antihypertensive potential in modern medicine. *J Biomed Phar Res* 2018; 7(4): 68-72.
16. Kiran K, Priya AJ, Devi RG. Medicinal and therapeutic uses of *Rauwolfia serpentina* Indian snakeroot. *Drug*

Invention Today 2018 2(10): 2674-2678.

17. Ghate VU, Gajendragadkar MP, Jadhav AB. Review of *Rauvolfia serpentina* (L.) Benth. Ex Kurz. *Int J Res* 2019; 8: 414-21.
18. Shitiz K, Gupta SP. *Rauwolfia serpentina*. *Him Med Plants* 2021; 1:111-49.
19. Pulliah T. Medicinal plants in India. Regency Publ., New Delhi, India. 2002:137-9.
20. Meenakshi B, Priyanka M. A novel protocol for micropropagation of *Rauvolfia serpentina*: in low concentration of growth regulators with sucrose and phenolic acid. *Int J Plant Sci* 2010; 5(1):93-7.
21. Li YC, Kong J, Wei M, Chen ZF, Liu SQ, Cao LP. 1, 25-Dihydroxyvitamin D3 is a negative endocrine regulator of the renin-angiotensin system. *The J clin invest* 2002; 110(2):229-38.
22. Wiens B, De Luca V. Molecular and biochemical characterization of a benzenoid/phenylpropanoid meta/para-O-methyltransferase from *Rauwolfia serpentina* roots. *Phytochem* 2016; 132: 5-15.
23. Wu P, Zhou Q, Liu XY, Xue F, Qin Y. Synthetic studies towards (–)-deserpidine: Total synthesis of the stereoisomer and derivative of (–)-deserpidine. *Chin Chem Lett* 2021; 32(1): 401-4. https://doi.org/10.1016/j.cclet.2020.02.009.
24. Srivastava SK, Agrawal AK, Singh SC, Khanna VK, Singh J, Nath C, Gupta MM, Gupta S, Verma RK, Pal A, Bawankule DU, inventors. Antipsychotic agents and standardized antipsychotic fractions from *Rauwolfia tetraphylla* and process of their isolation. United States patent US 9,018,226. 2015.
25. Böhme H, Lohse U. Age dependent ajmaline effect on type change in the electrocardiogram. *Zeit fur Alterns* 1968; 21(3):193-8.
26. Boga M, Bingul M, Ozkan EE, Sahin H. Chemical and biological perspectives of monoterpene indole alkaloids from Rauwolfia species. *In Stud Nat Prod Chem* 2019; 61: 251-299.
27. Kumar B, Kumar S, Bajpai V, Madhusudanan KP. Phytochemistry of Plants of Genus Rauvolfia. *CRC Press;* 2020.
28. Santos P, Herrmann AP, Benvenutti R, Noetzold G, Giongo F, Gama CS, Piato AL, Elisabetsky E. Anxiolytic properties of N-acetylcysteine in mice. *Beh Bra Res* 2017; 317: 461-9.
29. Gorman M, Neuss N, Djerassi C, Kutney JP, Scheuer PJ. Alkaloid studies–XIX: Alkaloids of some hawaiian rauwolfia species: The structure of sandwicine and its interconversion with ajmaline and ajmalidine. Tetrahedron. 1957; 1(4):328-37.
30. Srivastava A, Tripathi AK, Pandey R, Verma RK, Gupta MM. Quantitative determination of reserpine, ajmaline, and ajmalicine in *Rauvolfia serpentina* by reversed-phase high-performance liquid chromatography. *J Chrom Sci* 2006; 44(9):557-60.
31. Singh M, Kaur R, Rajput R, Mathur G. Evaluating the therapeutic efficiency and drug targeting ability of alkaloids present in *Rauwolfia serpentina*. *Int J Green Pharm* 2017; 11(3):132-142.
32. Reynolds AK, Presutti HJ, MacLeod DP. The Pharmacology of the rauwolfia alkaloids chandrine and Serpakrine. *Cana J Biochem Phys* 1960; 38(8): 889-97.
33. Gupta AK, Irchhaiya R, Chitme HR, Misra N. Free radical scavenging activity of *Rauwolfia serpentina* rhizome against CCl_4 induced liver injury. *Int J Pharm* 2015; 2: 123-6. doi: 10.13040/IJPSR.0975-8232.2(3).123-26.
34. https://pubchem.ncbi.nlm.nih.gov/compound/Pubescine
35. Rahman MT, Cook JM. The C-19 methyl substituted sarpagine-macroline-ajmaline alkaloids: Diversity, occurrence, bioactivity, and synthesis. *In Stud Nat Prod Chem* 2020; 64: 1-57.
36. Akbar S. *Rauvolfia serpentina* (L.) Benth. ex Kurz (Apocynaceae). In Hand book of 200 Medicinal Plants 2020; 1513-1520. https://doi.org/10.1007/978-3-030-16807-0_156
37. Bader FE. Rauvolfia alkaloids, XVII 3-Epi-α-yohimbine. *J Ame Che Soc* 1955; 77(13): 3547-3550.
38. https://doi.org/10.1016/B978-0-12-386454-3.00799-5

    https://pubchem.ncbi.nlm.nih.gov/compound/Isorauhimbinic-acid
39. https://doi.org/10.1016/B978-0-12-386454-3.00799-
40. https://drugs.ncats.io/drug/35FAV1EVE
41. Itoh A, Kumashiro T, Yamaguchi M, Nagakura N, Mizushina Y, Nishi T, Tanahashi T. Indole alkaloids and other constituents of *Rauwolfia serpentina*. *J Nat Prod* 2005; 68(6): 848-52.
42. Mollik MA, Hossan MS, Paul AK, Taufiq-Ur-Rahman M, Jahan R, Rahmatullah M. A comparative analysis of

medicinal plants used by folk medicinal healers in three districts of Bangladesh and inquiry as to mode of selection of medicinal plants. *Ethnob Res Appl* 2010; 8:195-218.

43. K.N. Venugopala, V. Rashmi, B. Odhav, Review on natural coumarin lead compounds for their pharmacological activity, *BioMed Res Int* 2013; 1-14.

https://doi.org/10.1155/2013/963248

44. Rodríguez-García C, Sánchez-Quesada C, Toledo E, Delgado-Rodríguez M, Gaforio JJ. Naturally lignan-rich foods: A dietary tool for health promotion? *Mole* 2019; 24(5): 917.

45. Yao LH, Jiang YM, Shi J, Tomas-Barberan FA, Datta N, Singanusong R, Chen SS. Flavonoids in food and their health benefits. *Plant foods hum nut* 2004; 59(3):113-22.

46. Sripakdee T, Mahachai R, Chanthai S. Phenolics and ascorbic acid related to antioxidant activity of maofruit juice and their thermal stability study. *Orie J Chem* 2017; 33(1):74.

47. Lohani H, Andola HC, Bhandari U, Chauhan N. HPTLC method validation of reserpine in *Rauwolfia serpentina* - a high value medicinal plant. *Res* 2011; 3(3): 34-37.

48. Das S, Saraf A, Sharma D, Sohal JK. Qualitative screnning of bioactive secondary metabolites present in *Withania somnifera* and *Rauwolfia serpentina* root and stem extract with pharmacological importance. *Int J Res Ana Rev* 2019; 6: 69-74.

49. Schlittler E, Saner H, Müller JM. Reserpinin, ein neues Alkaloid aus*Rauwolfia serpentina* Benth. *Exper* 1954; 10(3):133-4.

50. Rungsung W, Dutta S, Mondal DN, Ratha KK, Hazra J. Pharmacognostical Profiling on the Root of *Rauwolfia serpentina*. *Int J Pharmacogn Phytochem Res* 2014; 6: 612-6.

51. Agoha RC. Medicinal plants of Nigeria, offset Drakkerij. *Faculfcitder Wiskunde in Naturwetenschappen, the Netherlands* 1974; 41-33.

52. Lanham-New SA. The balance of bone health: tipping the scales in favor of potassium-rich, bicarbonate-rich foods. *The J nut* 2008; 138(1):172S-7S.

53. Tucker KL. Osteoporosis prevention and nutrition. *Curr Osteop Rep* 2009; 7(4):111-7. https://doi.org/10.1007/s11914-009-0020-5

54. Booth SL, Dallal G, Shea MK, Gundberg C, Peterson JW, Dawson-Hughes B. Effect of vitamin K supplementation on bone loss in elderly men and women. *The J Clin Endoc & Metab* 2008; 93(4):1217-23.

55. He FJ, MacGregor GA. Beneficial effects of potassium on human health. *Physiologia plantarum*. 2008; 133(4):725-35.

56. F.M. Hussain, M.M.A. Arif, H. Sheikh, and A.J. Nawaz, Trace element status in type 2 diabetes, Bangl. J. Med. Sci. 8(3), 12-17 (2009).

https://www.rxlist.com/manganese/supplements.htm

57. L.K. Dahl, Salt and Hypertension, Ame. J. Clin. Nutr. 25, 231-238 (1972).

58. https://www.medicinenet.com/silicon/supplements-vitamins.htm

59. A. Elbetieha, A.S. Thani, and K. Rawdah, Effects of chronic exposure of cobalt chloride on the fertility and testes in mice, J. Appl. Bio. Sci. 2, 1-6 (2008).

60. A.G. Diwan, A.B. Pradhan, D. Lingojwar, K.K. Krishna, P. Singh, and S.I. Almelkar, Serum zinc, chromium and magnesium levels in type-2 diabetes, Int. J. Diabet. Dev. Countri. 26, 122-123 (2006).

61. R.C. Agoha, Medicinal plants of Nigeria, offset Drakkerij, Faculfcitder Wiskunde in Naturwetenschappen, The Netherlands, 1974, 41-33.

62. R. Harisaranraj, K. Suresh, and S. Saravanababu, Evaluation of the chemical composition *Rauwolfia serpentina* and *Ephedra vulgaris*, Adv. Biol. Res. 3,174-8 (2009).

63. W.H. Zhang, Y. Cai, C. Tu, and L.Q. Ma, Arsenic speciation and distribution in an arsenic hyper accumulating plant, Sci. Tot Enviro. 300, 167-177 (2002).

64. S.A. Katz, and H. Salem, The toxicology of chromium with respect to its chemical speciation: A review, J. Appl.Toxi.13, 217-224 (1992).

65. N.S. Amin, T. Kaneco, and K. Ohta, Slurry sampling electrochemical atomic absorption spectrometric determination of copper in herbal medicines samples with a molybdenum tube atomizer, Microchem. J. 74,181-

186 (2003).

66. G. Jaya and G. Amit, Determination of trace metals in the leaves of *Rauwolfia serpentina* by using atomic absorption spectroscopy, Int. J. Ch. Stu. 4(3), 94-969 (2016).

67. A. Uraku and V. Nwankwo, Phytochemical and nutritional composition analysis of *Murraya Koenigii* Linn. leaves, Br. J. Pharm. Res. 6,174-80 (2015).

68. D.E. Okwu, Phytochemicals and vitamin content of indigenous spices of Southeastern, Nigeria, J. Sustain. Agricu. Enviro. 6(1), 30-37 (2004).

69. A. Gurib-Fakim, Medicinal plants: Traditions of yesterday and drugs of tomorrow, Mol. Aspects. Med. 27, 1-93 (2006).

70. M. Levine, New concepts in the biology and biochemistry of ascorbic acid. N. Engl. J. Med. 314, 892-902 (1986).

71. M. Parinitha, G.U. Harish, N.C. Vivek, T. Mahesh, and M.B. Shivanna, Ethno-botanical wealth of Bhadra wild life sanctuary in Karnataka, 2004, 37-50. http://hdl.handle.net/123456789/9336

72. C. Pattanaik, Some phytotherapeutic claims by tribals of Rayagada district, Orissa, India, Ethnobota. Leaflets. 2006 (1), 20 (2006).

73. S.K. Srivastava, H. Pandey, Traditional knowledge for Agro ecosystem management, Ind. J. Trad. Knowl. 5(1), 122-131 (2006).

74. S. Jeeva, S. Kiruba, B.P. Mishra, N. Venugopal, S.S. Dhas, G.S. Regini, C. Kingston, A. Kavitha, S. Sukumaran, A.D. Raj, and R.C. Laloo, Weeds of Kanyakumari district and their value in rural life. 2006, 501-509. http://hdl.handle.net/123456789/6936

75. H.M. Prakasha, M. Krishnappa, Y.L. Krishnamurthy, S.V. Poornima, Folk medicine of NR Pura taluk in Chikmagalur district of Karnataka, 2010, 55-60.

76. A. Arjariya, K. Chaurasia, Some medicinal plants among the tribes of Chhatarpur district (MP) India, Ecoprint: Int. J. Eco. 2009, 55-60.

77. Rajith NP, Ramachandran VS. Ethnomedicines of Kurichyas, Kannur district, Western Ghats, Kerala, 2010, 249-253.

78. P.K. Singh, V. Kumar, R.K. Tiwari, A. Sharma, C.V. Rao, and R.H. Singh, Medico-ethnobotany of 'chatara' block of district sonebhadra, Uttar Pradesh, India, Adv. Biol. Res. 4(1), 65-80 (2010).

79. M. Anisuzzaman, A.H. Rahman, M. Harun-Or-Rashid, A.T. Naderuzzaman, and A.K. Islam, An ethnobotanical study of Madhupur, Tangail, J. Appl. Sci. Res. 3(7), 519-30 (2007).

80. A. Dey and J.N. De, Ethnobotanical aspects of *Rauwolfia serpentine* (L). Benth. Ex. Kurz. in India, Nepal and Bangladesh, J. Med. Plant. Res. 5(2), 144-150 (2011).

81. S.K. Behera, A. Panda, S.K. Behera, and M.K. Misra, Medicinal plants used by the Kandhas of Kandhamal district of Orissa. 2006, 519-528.

82. S.K. Rai, Medicinal plants used by Meche people of Jhapa district, eastern Nepal, Our nature. 2(1), 27-32 (2004).

83. R.K. Mahanta, S.D. Rout, and H.K. Sahu, Ethnomedicinal plant resources of Similipal biosphere reserve, Orissa, India. Zoos. Print. J. 21(8), 2372-4 (2006).

84. A. Biswas, M.A. Bari, M. Roy, and S.K. Bhadra, Inherited folk pharmaceutical knowledge of tribal people in the Chittagong hill tracts, Bangladesh. 2010, 77-89.

85. J. Singh, A.K. Singh, and R. Pravesh, Product ion and trade potential of some important medicinal plants: an overview. In: Proceeding of first national interactive meet on medicinal and aromatic plants, CIMAP, Lucknow, India, 2003, 50-8.

86. C. Muthu, M. Ayyanar, N. Raja, and S. Ignacimuthu, Medicinal plants used by traditional healers in Kancheepuram District of Tamil Nadu, India. J. Ethnobio. ethnomedi. 2(1), 1-10 (2006).

87. R.N. Chopra, S.L. Nayar, I.C. Chopra, Glossary of Indian medicinal plants, (NISCIR, CSIR, Delhi 2002).

88. A. Ghosh, Ethnomedicinal plants used in West Rarrh region of West Bengal, (2008).

89. A.K. Meena, P. Bansal, and S. Kumar. Plant-herbal wealth as a potential source of Ayurvedic drugs, Asi. J. Tradi. Medi. 4(4), 152-170 (2009).

90. P.K. Mukherjee, N.K. Nema, P. Venkatesh, and P.K. Debnath, Changing scenario for promotion and development of Ayurveda-way forward, J. ethnopharmacol. 143(2), 424-34 (2012).

91. Surendran, S., Raju, R., Prasannan, P. *et al.* A Comprehensive Review on Ethnobotany, Phytochemistry and Pharmacology of *Rauvolfia* L. (Apocynaceae). *Bot. Rev.* 87, 311–376 (2021).https://doi.org/10.1007/s12229-021-09262-2

92. A. Chatterjee and S. Bose, Serpine-a new isomeride of yohimbine isolated from *Rauwolfia serpentina* benth, Experientia. 10(6), 246-7 (1954).

93. V.S. Bhatara, Gupta, S., Khanna, V.K., Maurya, A., Bawankule, D.U., Shukla, R.K., Pal, A.,Srivastava, S.K., 2012. Bioactivity guided isolation of antipsychotic constituents from the leaves of Rauwolfia tetraphylla L. Fitoterapia 83: 1092-1099.

94. A.R. Bunkar, Phytochemical and antimicrobial study of *Rauwolfia serpentina*, Int. J. Bio. Res. 2(2), 13-16 (2017).

95. V. Upadhyay, Deepika, P. Singh, and P. Kaushik, Bioevaluation of antibacterial potential of Sarpgandha (*Rauwolfia serpentina*), Enviro. Cons. J. 10(1/2), 109-111 (2009).

96. A.K. Owk and M.N. Lagudu. *In-vitro* antimicrobial activity of roots of *Rauwolfia serpentina* L. Benth. Kurz. Notu. Scien. Biologi. 8(3), 312-6 (2016). doi: 10.15835/nsb.8.3.9831

97. J.S. Negi, V.K. Bisht, A.K. Bhandari, D.S. Bisht, P. Singh and N. Singh, Quantification of reserpine content and antibacterial activity of *Rauvolfia serpentina* (L.) Benth. Ex. Kurz. Afri. J. Microbio. Res. 8(2), 162-166, (2014). doi: 10.5897/AJMR2013.5847

98. G. Lemieux, A. Davignon, and J. Genest. Treatment of arterial hypertension with rescinnamine, a new alkaloid isolated from *Rauwolfia serpentina*. Can. Med. Associ. J. 74(2), 144 (1956).

99. I.A. Abu-Yousef, C. Gunasekar, N. Abdo, S. Narasimhan, and S.M. Kanana, Herbo-mineral analysis of *Rauwolfia serpentina*. Int. J. Appl. Chem. 5(2), 103-15 (2009).

100. L.E. Hollister, Hematemesis and Melena Complicating Treatment with Rauwolfia Alkaloids AMA Arch Intern Med. 99(2), 218-221(1957). doi:10.1001/archinte.1957.00260020054009

101. G.K. Ray, P.K. Roy, and S.R. Dasgupta, The action of *Rauwolfia serpentina* on vasomotor reflexes, Naunyn – Schmiedebe. Arch. 219, 310-314 (1953). https://doi.org/10.1007/BF00246406

102. J.H. Trapold, A.J. Plummer, and F.F. Yonkman, Cardiovascular and respiratory effects of serpasil, a new crystalline alkaloid from *Rauwolfia serpentina* Benth. in the dog, J. of Pharmacol. Experi. Ther. 110 (2), 205-14 (1954).

103. G. Cronheim, W. Brown, J. Cawthorne, M.I. Toekes, and J. Ungari, Pharmacological studies with rescinnamine, a new alkaloid isolated from *Rauwolfia serpentine,* Proceedi. Soci. Experime. Bio. Med. 86 (1), 120-124 (1954).

104. I.I. Ezeigbo, M.I. Ezeja, K.G. Madubuike, D.C. Ifenkwe, I.A. Ukweni, N.E. Udeh, and S.C. Akomas, Antidiarrhoeal activity of leaf methanolic extract of *Rauwolfia serpentina*, Asi. Pac. J. Tro. Biomedi. 2 (6), 430-432 (2012). https://doi.org/10.1016/S2221-1691(12)60070-7.

105. V.D. Nair, R. Panneerselvam, R. Gopi, and S. Hong-Bo, Elicitation of pharmacologically active phenolic compounds from *Rauvolfia serpentina* Benth. Ex. Kurtz. Industrial crops and products. 45, 406-15 (2013).

106. K.S. Sachdev, R. Aiman, and M.V. Rajapurkar, Antihistaminase activity of serpentine, Brit. J. Pharmacol. 16, 146-152. (1961).

107. J. Neuman, A.M. de Engel, and M.P. Neuman, Pilot study of the effect of raubasine on platelet biological activity, Arzneimittel-forschung. 36(9), 1394-1398 (1986).

108. A.L. Ray, Antifungal activity of *Rauwolfia serpentina* root extract against *Neurospora crassa* and genetic study of induced mutants Bangladesh, J. Sci. Ind. Res. 54(3), 241-246 (2019).

109. M.A. Read, Flavonoids: naturally occurring anti-inflammatory agents. Ame. J. Path. 147(2), 235 (1995).

110. O.O. Amole and A.O. Onabanjo, Antipyretic effect of *Rauwolfia vomitoria* in rabbits, Nig. J. Nat. Prod. Med. 3, 77-78 (1999). doi: 10.4314/njnpm.v3i1.11768

111. A.P. Friedman, Treatment of headache with reserpine, Neurol. 5 (11), 805 (1955).

112. D. Healy and M. Savage, Reserpine exhumed, Br. J. Psychia. 172, 376-378 (1998).

113. E. Lehman, J. Haber, and S.R. Lesser, The use of reserpine in autistic children. J. Nerv. Ment. Dis. 125 (3), 351-356 (1957).

114. R.J. Ferrara and H. Pinkus, Alseroxylon in the treatment of pruritic and psychogenic dermatoses, AMA. Arch. Derm. 72(1), 23-28 (1955).

115. M. Avol and P.J. Vogel, Treatment of delirium tremens with reserpine (serpasil): a preliminary report. JAMA.

159(16), 1516-1520 (1955).

116. P. Lowinger, *Rauwolfia serpentina* in the control of anxiety, Psychia. Quar. 31(3), 445-453. (1957).
117. I.E. Sommer, C.W. Slotema, Z.J. Daskalakis, E.M. Derks, J.D. Blom, and van der Gaag M, The treatment of hallucinations in schizophrenia spectrum disorders, Schizophr. Bullet. 38(4), 704-14 (2012). doi: 10.1093/schbul/sbs034
118. D. Das and G. Chandra, Mosquito larvicidal activity of *Rauvolfia serpentina* L. seeds against *Culex quinquefasciatus* Say. Asi. Paci. J. Tro. Med. 5(1), 42-5 (2012).
119. Mittal B, Meenakshi Sharma A, Gothecha V K (2012) Phytochemical and pharmacological activity of Rauvolfia serpentina - a review. J. Ayu. Her. Med. 2: 427-434
120. N. Kanyal, Role of *Rauwolfia serpentina* in stroke induced experimental dementia. Ind. J. Pharm. Biol. Res. 4(1), 19-30 (2016).
121. S.R. Hussain, J. Gillard, and P. Gillard, Hydroxyl radical scavenging activity of flavonoids, Phytochem. 26(9), 2489-2491. (1987).
122. M.B. Azmi and S.A. Qureshi, Methanolic root extract of *Rauwolfia serpentina* benth. improves the glycemic, antiatherogenic, and cardioprotective indices in alloxan-induced diabetic mice, Adva. Pharmaco. Sci. 2012, 1-11. doi:10.1155/2012/376429
123. M.B. Azmi and S.A. Qureshi, Methanolic root extract of *Rauwolfia serpentina* improves the glucose tolerance in wister mice, J. Food. Drug. Analy. 20(2), 484-488 (2012).doi:10.6227/jfda.2012200208
124. M.B. Azmi, S.A. Qureshi, S.D. Ahmed, H.A. Mudassir, F. Imtiaz, S. Rais, A.A. Khan, and M. Ahsan Ameliorative effect of hydro-methanolic extract from roots of *Rauwolfia serpentina* on some biochemical parameters of type 1 diabetic mice, Pak. J. Pharm. Sci. 31(2S), 663-668 (2018).
125. S.A. Qureshi, A. Nawaz, S.K. Udani, and B. Azmi, Hypoglycaemic and Hypolipidemic activities of *Rauwolfia serpentina* in alloxan-induced diabetic rats. Int. J. Pharmaco. 5, 323-326 (2009). doi: 10.3923/ijp.2009.323.326
126. S.A. Qureshi and S.K. Udani, Hypolipidaemic activity of *Rauwolfia serpentina* Benth. Pak. J. Nutr. 8 (7), 1103-1106 (2009).
127. A.K. Gupta, H. Chitme, S.K. Dass and N. Misra, Hepatoprotective activity of *Rauwolfia serpentina* rhizome in paracetamol intoxicated rats. J. Pharmaco. Toxic. 1(1), 82-88 (2006). *doi:* 10.3923/jpt.2006.82.88
128. A. Dey, J.N. De, *Rauwolfia serpentina* (L). Benth. Ex. Kurz. - A review, Asi. J. Plant. Sci. 9, 285-98 (2010).
129. J.L. Stanford, E.J. Martin, L.A. Brinton, and R.N. Hoover, Rauwolfia use and breast cancer: a case-control study, J. Nat. Can. Inst. 76(5), 817-22 (1986).
130. D.L. Bemis, J.L. Capodice, P. Gorroochurn, A.E. Katz, and R. Buttyan, Antiprostate cancer activity of a beta-carboline alkaloid enriched extract from *Rauvolfia vomitoria*, Int. J. Oncolo. 29(5), 1065-1073. (2006).
131. S. Shukla and V. Wahla, Influence of different sterilizing methods on isolation endophytic bacteria from *Rauvolfia serpentine*, Phar. Innovat. J. 8(1), 38-41(2019).
132. H.J. Kuschke and H. Gruner, Reserpin als Thyroxin-Antagonist, Klin Wochenschr. 32, 563-564 (1954). https://doi.org/10.1007/BF01484941
133. S. Panda and A. Kar, Regulation of hyperthyroidism by *Rauwolfia serpentina* root extract in mice, Phar. Pharmaco. Commu. 6(11), 517-20 (2000). https://doi.org/10.1211/146080800128735629
134. S. Chauhan, A. Kaur, R. K. Pareek, Pharmacobotanical and pharmacological evaluation of Ayurvedic crude drug: *Rauwolfia serpentina* (Apocynaceae), Int. J. Green Phar. 11(04) 687 -693 (2018).
135. C.L. Malhotra and R.K. Sidhu, The anti-emetic activity of alkaloids of *Rauwolfia serpentine*, J. Pharmaco. Experi. Therap. 116 (1), 123-129 (1956).
136. J.C. Hutchison, J.R.R.B. Lutz, and S. Pezzi, Diuretic therapy in the treatment of hypertension, Angio. 11(3), 193-9 (1960). https://doi.org/10.1177/000331976001100307
137. V.H. Kumar, S. Shashidhara, and C.E. Rajendra, Reserpine content of *Rauwolfia serpentina* in response to geographical variation, Int. J. Pharm. Bio Sci. 1(4), 434 (2010).
138. G.S. Panwar and S.K. Gurum, Alkaloid profiling and estimation of reserpine in *Rauwolfia serpentina* plant by TLC, HP-TLC and HPLC, Asi. J. Plant. Sci. 10(8), 393-400 (2011).
139. G.S. Panwar, I.H. Attitalla, and S.K. Guru, An efficient *in vitro* clonal propagation and estimation of reserpine

content in different plant parts of *Rauwolfia serpentina* L. Amer. Eur. J. Sci. Res. 6(4), 217-22 (2011).

140. S. Mondal, J.T. Silva, and P.D. Ghosh, *In vitro* flowering in *Rauvolfia serpentina* (L.) Benth. ex. Kurz. Int. J. Plant. Develop. Bio. 5(1), 75-7 (2011).

141. .H. Rajasree, R. Singh, C. Sankar. Anti venom activity of ethanolic extract of *Rauvolfia serpentina* against *Naja naja* (Cobra) venom, Int. J. Drug. Disc. Herb. Res. 3, 521-524 (2013).

142. M.E. Mossoba, T.J. Flynn, S. Vohra, P.L. Wiesenfeld, and R. L. Sprando, Human kidney proximal tubule cells are vulnerable to the effects of *Rauwolfia serpentina*. Cell. Bio. Toxic. 31(6), 285-93 (2015).

143. A. Kad, A. Pundir, S. Sharma, and H. Sood, Development of suspension cultures and *ex-vitro* rooting in *Rauwolfia serpentina* for rapid and large scale multiplication. Int. J Innov. Res. Sci. Engi. 3, 135-43 (2017).

144. V. Vaishnav and D. Sahoo, Comparative phytochemical analysis of stem and root extracts from *Rauwolfia serpentine*, Int. J. Adv. Sci. Res. Manag. 5 (1), 5-7 (2020).

145. M.B. Azmi, S. Sultana, S. Naeem, and S.A. Qureshi, *In silico* investigation on alkaloids of *Rauwolfia serpentina* as potential inhibitors of 3-hydroxy-3-methyl-glutaryl-CoA reductase. Sau. J. Biol. Sci. 28, 731-737 (2021).

146. A. Singh, E. E. Ebenso, and M.A. Quraishi, Corrosion inhibition of carbon steel in HCl solution by some plant extracts, Int. J. Corrosion. 2012, 1- 20. doi:10.1155/2012/897430

147. C.T. Sulaiman, C.K. Jyothi, J.K. Unnithan, K.M. Prabhukumar, and I. Balachandran, Identification of suitable substitute for Sarpagandha (*Rauvolfia serpentina* (L.) Benth. ex Kurz) by phytochemical and pharmacological evaluation, Beni-Suef. Univer. J. Basic. Appl. Sci. 9(1), 1-1 (2020).

148. Rajasree P H, Singh R, Sankar C (2013) Anti-venom activity of ethanolic extract of Rauwolfia serpentina against Naja naja (Cobra) venom. Int J Drug Dis Herb Res. 3: 521-4.

149. Kapoor R T (2014) Evaluation of insecticidal potential of root extracts of Rauvolfia tetraphylla against Musca domestica. Rom. J. Biol. 1: 13

150. Yogeshwari G, Jagruthi C, Anbazahan S M, Mari L S S, Selvanathan J, Arockiaraj J, Dhayanithi N B, Ajithkumar T T, Balasundaram C, Ramasamy H (2015) Herbal supplementation on immune response in Labeo rohita against Aphanomyces invadans. Aquaculture 437: 351-359.

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A review: Hepatoprotective & Other Pharmacological Potential of *Annona squamosa*

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Abstract: Liver is the key organ of the body. It is the largest gland in the body and weighing between 1 and 2.3kg. It is situated in the upper part of the abdominal cavity. Occupying the greater part of the right hypochondriac region one part of the epigastria region and extending into the left hypochondriac region. Its upper and anterior surfaces are smooth and curved to fit the undersurface at the diaphragm. .Liver injury is not a single entity; the lesion observed depends not only on the chemical agent involved but also on the period of exposure. After acute exposure one usually finds lipid accumulation in the hepatocytes, cellular necrosis, or hepatobiliary dysfunction, whereas cirrhotic or neoplastic changes are usually considered to be the result of chronic exposures.

Key words: Liver, chemical agent, Lipid, Accumulation, Cellular necrosis

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Introduction:

It is estimated that about 7,500 plants are used in local health traditions in, mostly, rural and tribal villages of India. Out of these, the real medicinal value of over 4,000 plants is either little known or hitherto unknown to the mainstream population. The classical systems of medicine such as Ayurveda, Siddha, Unani and Tibetan use about 1,200 plants. A detailed investigation and documentation of plants used in local health traditions and pharmacological evaluation of these plants and their taxonomical relatives can lead to the development of invaluable plant drugs for many dreaded diseases. Random screening of plants has not proved economically effective. Liver is a vital organ play a major role in metabolism and excretion of xenobiotics from the body. Liver injury or liver dysfunction is a major health problem that challenges not only healthcare professionals but also the pharmaceutical industry and drug regulatory agencies. Liver cell injury caused by various toxic chemicals like certainanti-biotic, chemotherapeutic agents, carbon tetrachloride (CCl_4), thioacetamide (TAA) etc, excessive alcohol consumption and microbes is well studied. The available synthetic drugs to treat liver disorders in this condition also cause further damage to the liver. Hence, Herbal drugs have become increasingly popular and their use is widespread. Herbal medicines have been used in the treatment of liver diseases for a long time. A number of herbal preparations are available in the market. Medicinal plants play a key role in the human health care. About 80% of the world population relies on the use of traditional medicine which is predominantly based on plant materials. The traditional medicine refers to a broad range of ancient natural health care practices including folk/tribal practices as well as Ayurveda, Siddha and Unani.

These medical practices originated from time immemorial and developed gradually, to a large extent, by relying or based on practical experiences without significant references to modern scientific principles. [1, 2]

Hepatoprotective herbs:

Herbal-based therapeutics for liver disorders has been in use in India for a long time and has been popularized world over by leading pharmaceuticals. Despite the significant popularity of several herbal medicines in general, and for liver diseases in particular, they are still unacceptable treatment modalities for liver diseases.

The use of natural remedies for the treatment of liver diseases has long history, starting with the Ayurvedic treatment, and extending to the Chinese, European and other systems of traditional medicines. The 21st century has seen a paradigm shift towards therapeutic evaluation of herbal products in liver disease models by carefully synergizing the strengths of the traditional systems of medicine with that of the modern concept of evidence based medicinal evaluation, standardization and randomized placebo controlled clinical trials to support clinical efficacy.

A large number of plants and formulations have been claimed to have hepatoprotective activity. Nearly 160 phytoconstituents from 101 plants have been claimed to possess liver protecting activity. In India, more than 87 plants are used in 33 patented and proprietary multi-ingredient plant formulations. In spite of the tremendous advances made, no significant and safe hepatoprotective agents are available in modern therapeutics. The present review is aimed at compiling data based on reported works on promising phytochemicals from medicinal plants that have been tested in hepatotoxicity models. The hepatoprotective activity is probably due to the presence of flavonoids in all few herbal plants. The results of this study indicate that extracts of leaves and plants extracts of some medicinal plant have good potentials for use in hepatic disease. The present review study gives evidential explore mechanism of action of medicinal plants against experimentally induced hepatotoxicity. Hence the review study is concluded that the herbal drug possesses hepatoprotective activity and it has been proved by different animal models give many links to develop the future trials. [3, 4]

Plant profile:

Scientific Classification:

Kingdom Plantae - Plants

Subkingdom Tracheobionta – Vascular plants

Super division Spermatophyta – Seed plants

Division Magnoliophyta – Flowering plants

Class Magnoliopsida – Dicotyledons

Subclass Magnoliidae

Order Magnoliales

Family Annonaceae – Custard-apple family

Genus Annona L. – *Annona*

Species *Annona squamosa* L. – sugar apple [5]

The plant *Annona Squmosa*is commonly called Custard Apple in English and Sharifa or Seetaphal in Hindi in India. *Annona squamosa* is a multipurpose tree with edible fruits and could be a supply of healthful and industrial products. This plant is acknowledged to possess varied medicative properties. The *Annona squamosa* may be massive or little evergreen tree or straggly woody plant,4 to 7m tall, introduced into Bharat and Srilanka mostly, found wild and cultivated in various parts, up to an altitude of 900m. The leaves of the plants are somewhat hairy when young, oblong and 8 to 15 centimeters in length with petiole 1 to 1.5 centimeters long. The flowers of plants occur one by one within the axils of the leaves. Flowers are about 2.5 centimeters long. They are three angled, pendulous, hairy and greenish-white or yellowish in color. The fruit is large, somewhat heart shaped and 6 to 9 centimeters in length. The outside of the fruits is marked by polygonal tubercles. When the fruits are ripe, it is a light yellowish green. The flesh is white, sweet, soft and juicy and has a mild very agreeable flavor. The figure shows the various parts of the plant *Annona squamosa*. Ayurvedic practitioners use stem and leaf extracts as autochthonous uterotonic drug. [6]

Phytoconstituents from *Annona squamosa*:

Pharmacological potential of *Annona squmosa:*

Antioxidant property:

Free radical scavenging potential of ethanolic extracts of leaves of *Annona squamosa* by using different antioxidant models of screening was reported, the extract showed only moderate scavenging activity of superoxide radicals and anti-lipid peroxidation potential, which was performed using rat-brain homogenate. [7]

Anti-headlice activity:

Cream is prepared by the petroleum ether extract of *Annona squamosa* seeds and reported as anti-headlice activity. The custard apple cream maybe, therefore, suitable for to be used as an alternative therapy to treat the headlice. [8]

Antidiabetic activity:

Some researchers reported that the *Annona saquamosa* extract supplementation is beneficial in controlling the blood glucose level, improves the plasma hypoglycaemic agent, lipid metabolism and is beneficial in preventing diabetic complication from lipid peroxidation and antioxidant system in experimental diabetic rats; therefore, it could be useful for prevention or early treatment of diabetes. *Annona squamosa* leaves extract lowered blood glucose with simultaneous increase in the plasma insulin and C-peptide levels. In addition, *Annona squmosa* extract could influence protein metabolism and marker enzymes in STZ-induced diabetic rat. [9]

Mosquitocidal activity:

The methanolic extract of leaves of *Annona squamosa* tested for mosqutocidal effect against *C. quinquefasciatus*. The result suggests the potential mosquitocidal effect of *Annona squamosa* on *C. quinquefasciatus*. [10]

Antifertility activity:

Postcoital antifertility activity of *Annona squamosa* was reported in the seed extract, while aerial parts are inactive. [11]

Hepatoprotective activity:

The hepatoprotective activity of leaves of *Annona squamosa* was reported against isoniazid rifampicin induced hepatotoxicity. The alcoholic and aqueous extract of leaves of plant tested against isoniazid-rifampicin induced hepatotoxicity. [12]

Antiandrogeni and anti-spermatogenic activities:

Some worker evaluated ant androgenic activities of *Annona squamosa* with the respective reversibility in male albino rats. The stem bark extract feeding caused a marked reduction the number of spermatocytes and spermatids in the testis.

Cytotoxic activity: Compounds cytogenesis isolated from the bark of *Annona squamosa* showed selective cytotoxic activity against the human pancreatic tumor cell line, PACA-2, with potency 10-100 time that of Adriamycin. [13]

Antimicrobial activity:

Based on research on the antibacterial activity of the ethanol extract of *Annona squmosa* leaves and DMSO which were tested in vitro with the agar plate method against clinical isolates of *P. aeruginosa* and *E. coli*. It was shown that there was a mechanism of inhibition of the growth of these two microbes due to the treatment of *Annona squmosa* leaf ethanol extract.[14]

Antifungal activity:

Annona squmosa leaves extract is revealed to be capable of inhibiting the growth of Fusarium oxysporum 46 and especially Colletotrichum capsici. [15]

Anti-inflammatory activity:

Maintenance of urolithiasis using the ethanolic extract of *Annona squmosa* have almost the same comparison than the clinical treatment. Pain in urinary tract inflammation can be reduced by the pharmacological activity of anti-inflammatory and analgesic compounds from A. squamosa leaf extract. Smooth muscle contractions of the urinary tract have been shown to be relaxed by restoring impaired kidney function, normalizing urine and serum parameters, and restoring damaged cells. In association with the assessment of the ethanol extricate of atemoya takes off, there was a reduction in leukocyte relocation as a parameter of inflammatory activity. [16]

Neuroprotective activity:

Annona squmosa leaf has many benefits. Based on a study conducted by Porwal *et al*. related to neuron protection, it was stated that sugar apple leaf extract contains anonaine can help in treating epilepsy, mood disorders, and memory problems. The results of the phytochemical test of *Annona squmosa* leaf extract using petroleum and ethanolic showed that *A. squamosa* leaf contains phenols components. Phenols play an important role in preventing neurodegenerative disease conditions. [17]

Immunomodulatory activity:

Annona squmosa leaf water extract has a possibility to be a strong immunostimulant with a nonspecific immune mechanism. The immunomodulatory movement of leaf extract watched in *Annona squmosa* was showed in *Clarias batrachia* fish in haematological parameters. There was a critical increase within the concentration of extract (10ml)

50% and (15ml) 100%. At that point analysed haematological parameters in fish blood and found an increase within the number of TEC, haemoglobin levels, TLC counts and the number of Differential Leukocytes. Haematological lists such as haemoglobin, blood cell counts (RBC and WBC) revealed critical changes due to the treatment of ethanol extract of A. squamosa leaves and fruit. The important increase in WBC assay in treated mice observed in this study may be due to stimulation of the immune system. [18]

Conclusion:

Annona squmosa plant is a type of plant that was first known in Mexico and is now widely found in India. A. squamosa plants grow well in the lowlands and the tropics. The leaves *Annona squmosa* is a type of plant that is still rarely used. *Annona squmosa* has a lot of benefits for humans such as for health functions based on the previous studies that have shown that their leaves have high nutritive value. However, research on *Annona squmosa* leaves needs to be further developed to be able to convince and increase the information that A. squamosa leaves have many benefits, especially in the prevention and treatment of disease

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References:

1. Solikhah TI, Solikhah GP, Susilo RJK. *Aloe vera* and Virgin Coconut Oil (VCO) accelerate healing process in domestic cat suffering from scabies. Iraqi J Vet Sci. 2021; 35(4):699-704.
2. Safira A, Savitri SL, Putri ARB. Review on the pharmacological and health aspects of Hylocereus or Pitaya: An update. J Drug Deliv Ther. 2021; 11(6):297-303.
3. Khairullah AR, Solikhah TI, Ansori ANM. Review on the pharmacological and health Aspects of *Apium Graveolens* or Celery: An Update. Syst Rev Pharm. 2021; 12(1):606-612.
4. Kalidindi N, Thimmaiah NV, Jagadeesh NV, Nandeep R, Swetha S, Kalidindi B. Antifungal and antioxidant activities of organic and aqueous extracts of *Annona squamosa* Linn. Leaves. J Food Drug Anal. 2015; 23(4):795-802.
5. Al-Nemari R, Bacha AB, Al-Senaidy A. Selective cytotoxic effects of *Annona squamosa* leaves against breast cancer cells via apoptotic signalling proteins. Plants 2020; 9:1-14.
6. Shukry WM, Galilah DA, Elrazek AA, Shapana HA. Mineral composition, nutritional properties, vitamins, and bioactive compounds in *Annona squamosa* L. grown at different sites of Egypt. Ser Bot Environ Sci. 2019; 1(1): 7-22.
7. Fincan M. Extract ability of phenolics from spearmint treated with pulsed electric field. J Food Eng. 2015; 162: 31-37.
8. Morais-Braga MFB, Carneiro JNP, Machado AJT. Phenolic composition and medicinal usage of *Psidium Guajava* Linn.: Antifungal activity or inhibition of virulence? Saudi J Biol Sci. 2017; 24(2): 302-313.
9. Moreira SA, Alexandre EMC, Pintado M, Saraiva JA. Effect of emergent non-thermal extraction technologies on bioactive individual compounds profile from different plant materials. Food Res Int. 2019; 115:177-190.
10. Moreira SA, Alexandre EMC, Pintado M, Saraiva JA. Ethanolic Noni leaf extract dechlorophyllised using sedimentation process: antioxidant, antibacterial properties and efficacy in extending the shelf-life of striped catfish slices. Int J Food Sci Technol. 2021; 56(6): 2804-2819.
11. Olatunde OO, Tan SL Della, Shiekh KA, Benjakul S, Nirmal NP. Ethanolic guava leaf extracts with different

chlorophyll removal processes: anti-melanosis, antibacterial properties and the impact on qualities of Pacific white shrimp during refrigerated storage. Food Chem. 2021; 341: 1-11.

12. Gajalakshmi S, Divya R, Divya Deepika V, Mythili S, Sathiavelu A. Pharmacological activities of *Annona squamosa*: A review. Int J Pharm Sci Rev Res. 2011; 10(2):24-29.

13. Verma RS, Joshi N, Padalia RC, Singh VR, Goswami P, Chauhan A. Characterization of the leaf essential oil composition of *Annona squamosa* L. from foothills of north India. Med Aromatic Plants. 2016; 5(5):1-5.

14. Vanitha V, Umadevi KJ, Vijayalakshmi K. Determination of bioactive components of *Annona squamosa* L leaf by GC-MS analysis. Int J Pharm Sci Drug Res. 2011; 3(4):309-312.

15. Vyas K, Manda H, Sharma RK, Singhal G. An update review on *Annona squamosa*. Int J Pharm Ther. 2012; 3(2):107-118.

16. Johns T, Windust A, Jurgens T, Mansor SM. Antimalarial alkaloids isolated from *Annona squamosa*. Phytopharmacology. 2011; 1(3):49-53.

17. Chandel SS, Dikshit SN, Sharma HG. Collection and evaluation of custard apple (*Annona squamosa* L.) genotypes in Chhattisgarh plains. J Pharmacognosy Phytochemistry. 2018:149-152.

18. Nguyen MT, Nguyen VT, Le VM. Assessment of preliminary phytochemical screening, polyphenol content, flavonoid content, and antioxidant activity of custard apple leaves (*Annona squamosa* Linn.). IOP Conf Ser Mater Sci Eng. 2020;736:0

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JOHP

A review: Pharmacological potential of leaf of *Triumfetta rhomboidea*

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Abstract: Plants have been one of the important sources of medicine even since the dawn of human civilization. Inspite of tremendous development in the field of allopathy during 20th century, plants still remain one of the major sources of drug in the modern as well as traditional system of medicine throughout the world. *Triumfetta rhomboidea* is commonly known as Burr bush, a popular Indian medicinal plant, has long been used commonly in Ayurvedic system of medicine. The plant has been found to possess diverse number of pharmacological activities. The present paper gives an account of updated information on its traditional uses, ethnobotany, phytochemistry and its pharmacological activities. The review reveals that wide range of phytochemical constituents have been isolated from the plant and it possesses important activities like Diuretic, analgesic, Anti-Inflammatory, anti-tumour, antioxidant, antiulcer and antimicrobial have also been reported. These reports are very encouraging and indicate that this plant has great potential to be developed as drug by pharmaceutical industries.

Keywords: *Triumfetta rhomboidea*, Pharmacological activities, Ethnobotany

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Introduction: Throughout the ages, humans have relied on Nature for their basic needs for the production of food-stuffs, shelters, clothing, means of transportation, fertilizers, flavours and fragrances, and, not the least, medicines. Plants have formed the basis of sophisticated traditional medicine systems that have been in existence for thousands of years and continue to provide mankind with new remedies. Although some of the therapeutic properties attributed to plants have proven to be erroneous, medicinal plant therapy is based on the empirical findings of hundreds and thousands of years. [1] The genus *Triumfetta* comprises certain herb and under shrubs. It contains about eight species which are distributed in the tropics, of which three yield useful fibers. [2]

Triumfetta rhomboidea belonging to family Tiliaceae is commonly known as Burr bush or Burweed[4] found throughout tropical & sub-tropical India & Ceylon. [3,4] It is a very common weed growing wild and freely on Matheran Hills.

Taxonomic classification [5]

Kingdom: Plantae

Super Division: Tracheobionta

Super division: Spermatophyta

Division: Magnoliophyta

Class: Magnoliopsida

Subclass: Dilleniidae

Order: Malvales

Family: Tiliaceae

Genus: Triumfetta

Species: *Triumfetta rhomboidea*

Pharmacological Potential of *Triumfetta rhomboidea*

Antibacterial activity: The ether and 90 per cent ethanolic extract of leaf showed antibacterial activities against three Gram positive bacteria, *Staphylococcus aureus*, *Enterococcus faecalis, Bacillus cereus* and three Gram negative bacteria *Klebsiella pneumoniae, Pseudomonas aeruginosa, Escherichia coli*. [6]

Diuretic Activity: The methanol & petroleum ether extract showed potent diuretic activity. Methanol extract at dose of 100 and 200 mg/kg increases excretion of sodium and potassium ion compared to the control in a dose dependent manner while petroleum ether extract at dose of 200 mg/kg showed significant excretion of sodium in urine. Both the extracts showed significant increased total volume of urine in a dose dependent manner. [7]

Analgesic & anti-inflammatory Activity: Methanolic extract of *Triumfetta rhomboidea* leaf (50-400 mg/kg, i.p.) caused statistically significant inhibition of the egg albumin induced odema in Wistar *albino rats* & the number of acetic acid induced writhing in mice. Both the effect was dose dependent. It was reported that *Triumfetta rhomboidea* can be recommended for acute inflammatory disorders & diseases associated with pains. [8]

Anti-tumour activity: The methanolic extract of *Triumfetta rhomboidea* leaf showed significant antitumor activity against Dalton's Ascites Lymphoma bearing Swiss albino mice. Intra-peritoneal administration of extract (100 & 200 mg/kg) reduced the tumor volume, packed cell volume & viable cell count in dose dependent manner. [9]

***In vitro* antioxidant activity:** The ethanol extract of *Triumfetta rhomboidea* exhibited potent DPPH and ABTS radical scavenging activity with IC_{50} values 16.56 and 39.00 mg/ml, respectively. It also showed significant in vitro antioxidant activity against H_2O_2 radical with IC50 values 97.80 mg/ml and moderate against nitric oxide radical with IC_{50} value 345.50 mg/ml, respectively. [10]

Antimicrobial activity The essential oil of the aerial parts of *Triumfetta rhomboidea* was analysed by GC and GC-MS and assayed for its antibacterial and antifungal activities. The main constituents identified were trans-caryophyllene

(22.4%), kessane (14%) and caryophyllene oxide (13%). The antimicrobial tests showed a mild activity against *Escherichia coli* and *Enterococcus hirae*. [11]

Anti-larvae activity: The crude extract of *Triumfetta rhomboidea* leaves did not show anti-larvae activity against various species of mosquito larvae. [12]

Antiulcer activity: Root extract of *Triumfetta rhomboidea* showed significant antiulcer activity. [13]

Antiviral activity: 80% ethanolic extract of leaf exhibited promising antiviral activity against polio, coxsackies, semliki forest, herpes, and measles virus. Extract significantly reduced viral titre. [14]

Ecbolic activity: *Triumfetta rhomboidea* showed ecbolic property on the gravid mammalian uterus. [15]

CONCLUSION

In recent years, ethnobotanical and traditional uses of natural compounds, especially of plant origin received much attention as they are well tested for their efficacy and generally believed to be safe for human use. They obviously deserve scrutiny on modern scientific lines such as phytochemical investigation, biological evaluation on experimental animal models, toxicity studies and investigation of molecular mechanism of action of isolated phytoconstituents. *Triumfetta rhomboidea* is reported to possess antibacterial, diuretic, analgesic & anti-inflammatory, anti-tumour, *in vitro* antioxidant activity, antimicrobial, anti-larvae, antiulcer, antiviral and embolic activities but number of other pharmacological activities are yet to be explored. In future studies the isolated principles from plant material needs to be evaluated in scientific manner using specific experimental animal models and clinical trials are to be done to understand the molecular mechanism of action, in search of lead molecule from natural resources.

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References:

1. Gurib-Fakim Ameenah, Medicinal plants: Traditions of yesterday and drugs of tomorrow, Mol Aspec Med, 2006, 27, 1-93.
2. The Wealth of India: A Dictionary of Indian raw materials & industrial products. First supplement series, vol 10 (Sp-W), 2003; 387-388.
3. Chopra RN, Nayar SL and Chopra IC, Glossary of Indian Medicinal Plants, 1st edn (National Institute of Science Communication and Information Resources (CSIR), New Delhi, India) 2002, 249.
4. Kirtikar KR and Basu BD, Indian Medicinal Plants, 2nd edn, vol 1 (Bishen Singh Mahendra Pal Singh, Dehra Dun, India) 1993, 546-548
5. Plants.usda.gov [homepage on the Internet]. United states Department of Agriculture: Natural resources Conservation services, [updated 2011 Apr 25; cited 2011 May
6. Devmurari VP, Ghodasara TJ and Jivani NP, Antibacterial activity and phytochemical study of ethanolic extract of *Triumfetta rhomboidea* Jacq, Inter J of Pharm Tech Res, 2010, 2(2), 1182-1186.
7. Ullewar Meenal P, Bukkawar Amit R and Bagade Archana B, Preliminary screening of diuretic activity of *Triumfetta rhomboidea* Jacq leaves extracts in rats. Res J Pharmaceutica Bio & Chem Sci, 2010, 1(3), 469-473.
8. Uche FL and Okunna BU, Phytochemical constituents, analgesic and anti-inflammatory effects *Triumfetta rhomboidea*, Asian Pacif J Tropica Med, 2009, 2(5), 26-29.
9. Sivakumar P, Kumar Sambath R, Sivakumar T, Nethaji R and Vijyabaskaran M, Antitumor & Antioxidant activities of *Triumfetta rhomboidea* against Dalton's Ascites Lymphoma bearing Swiss albino mice, Res J Med

Sci, 2008, 2(4), 203-208

10. Sivakumar P, Kumar RS, Sivakumar T, Perumal P and Jayakar B, *In vitro* antioxidant activity of ethanol extract of *Triumfetta rhomboidea*. Inter J Pharm & Tech, 2010, 2(3), 665-673.

11. Mevy JP, Bessiere JM, Rabier J, Dherbomez M, Ruzzier M, *et al*., Composition and antimicrobial activities of the essential oil of *Triumfetta rhomboidea* Jacq., Flav & Frag J, 2006, 21(1); 80-83.

12. Mangalat Sarath, Narayanan Varun and Janardhanan Minija. Herbal Larvicides to control mosquito larvae. Nat prod rad, 3(1), 24-26.

13. Pradhan D, Panda PK and Kar DM, Study of antiulcer activity of roots of *Triumfetta rhomboidea*, J Sci and Pharm, 2003, 5, 18-21.

14. Vlietinck AJ, Hoof LV, Totte J, Lasure A, Berghe DV *et al*., Screening of hundred Rwandese medicinal plants for anti-microbial and anti-viral properties, J of Ethnopharmacol, 1995, 46, 31-47.

15. Osore H, Ecbolic properties of *Triumfetta rhomboidea* on the gravid mammalian uterus, East Afr Med J, 1982, 59(11), 733-736

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A research: Screening for novel ligands Dopamine D1 receptor –an HTS approach

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Abstract: Due to absence of brain penetrable selective ligands (Agonist and antagonist) of Dopamine receptor D, its challenge to elucidate the physiological role of this receptor and also in different CNS pathologies such as ADHD, Parkinson's, Major depression Schizophrenia and bipolar disorder. High-throughput screening (HTS) campaigns is a starting point for many drug discovery programs. With the advent of HTS, the pharmaceutical industry is anticipating a rush of new potential drugs mined from the millions of uncharacterized small molecules held in chemical repositories. Now a day, several new technological innovations have been designed not only to increase throughput (eg. miniaturization and combinatorial strategies) but also to increase the amount of data derived from a single assay point (multi label screening and high-content Screening [HCS] methods). These technologies coupled with extensive computational speed and integrated bioinformatics programs, have increased the number and output of HTS laboratories dramatically in the same period. So, HTS has been proven to be a valuable and evolving Technique that has greatly changed the drug discovery program. The aim of present study To screen various compounds (synthetic and natural products) on D_1 receptor for agonistic and antagonistic action using HTS approach , validate the active "HITS" define the selectivity and specificity and determine the in vivo efficacy of ligand using pre-clinical mouse models of D_1receptor action.

Keywords: HTS approach, D_1receptor, screening, ligand, GPCR, *In-vivo*

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Introduction: G protein-coupled receptors (GPCRs) are seven transmembrane receptor (7-TM Receptors, or Serpentine Receptors) traverse the cell membrane seven times. As their name implies GPCRs interact with G-proteins in the plasma membrane-which causes a conformation change in GPCR by binding of an external signaling molecule. G-proteins are specialized proteins with the ability to bind the nucleotides guanosine triphosphate (GTP) and guanosine diphosphate (GDP). The G- proteins that associate with GPCRs are heteromeric, meaning they have three different subunit: an alpha subunit, a beta subunit and a gamma subunit, an alpha subunit is further divided into following types: Gay this stimulate adenyl cyclase, G this activates phospolipase C which generate second messenger andG. This inhibit the adenyl cyclase lowering the cAMP level in cell.G protein alpha subunit binds either GTP or GDP depending on whether the protein is active (GTP) or inactive (GDP) GPCR family constitutes the largest class of cell surface receptors and GPCR are the targets for more than 50% of the marketed drug [1]. The therapeutic importance of these receptors has driven researchers to design a number of high throughput screens aimed at the discovery of new drug candidates [2].

In addition to the characterized GPCRs, it is estimated that mammalian genome contains about 1,000 genes that encode for approximately 10,000 GPCRs [3]. Dopamine (3-hydroxytyramine) is a catecholamine neurotransmitter in brain. It is a metabolite of amino acid tyrosine. In brain dopaminergic neuronal cell bodies are confined to four sites and from there projections go to the whole brain Four major Dopaminergic pathways have been identified in the mammalian brain: the nigrostriatal, mesolimbic, mesocortical and tuber or infundibular systems that originate from the A9 (nigrostriatal). A10 (mesolimbic and mesocortical, often collectively termed the mesocorticolimbic pathway). And AS (tuberoinfundibular) groups of dopamine-containing cells respectively. These neurons are critically involved in various vital central nervous system functions, including voluntary movement, feeding, affect, reward, sleep, attention, working memory, and learning.

In the periphery, dopamine plays important physiological roles in the regulation of olfaction, retinal processes, hormonal regulation, cardiovascular functions, sympathetic regulation, immune system, and renal functions, among others. Because dopamine is involved in a variety of critical Physiological action of dopamine is mediated by five distinct but closely related dopamine receptors [4]. Based upon their structural, pharmacological, and biochemical properties, these receptors are classified as DI-class dopamine receptors [DI like family: D1 and D5 [5] and D2-class dopamine receptors (D2 like family: D2, D3, and D4) [6] (Table 1). The individual members of the subfamilies of the D1-and D2-class receptors share a high level of homology in their transmembrane domains and have distinct pharmacological properties. It is commonly accepted that the DI-class dopamine receptors (D1 and D5) activate the Gs/olf family of G proteins to stimulate cAMP production by adenylyl cyclase (AC) and are found exclusively post synaptically on dopamine receptive cells, such as GABAergic medium spiny neurons (MSN) in the striatum. The D2-class dopamine receptors (D2, D3, and D4) couple to the C Family of G proteins and thus induce inhibition of AC [7].

Table 1: Dopamine Receptor families

Dopamine receptor family	Dopamine receptors	G protein coupling
DI Like Family	D1R	-
	D5R	Gsα
D2 Like Family	D2R	Giα
	D3R	Giα
	D4R	Giα

High-throughput screening (HTS) campaigns is a starting point for many drug discovery programs. With the advent of HTS, the pharmaceutical industry is anticipating a rush of new potential drugs mined from the millions of uncharacterized small molecules held in chemical repositories. Now a day, several new technological innovations have been designed not only to increase throughput (eg. miniaturization and combinatorial strategies) but also to increase the amount of data derived from a single assay point (multilabel screening and high-content Screening [HCS] methods). These technologies coupled with extensive computational speed and integrated bioinformatics programs, have increased the number and output of HTS laboratories dramatically in the same period. So, HTS has been proven to be a valuable and evolving Technique that has greatly changed the drug discovery program.

Materials and methods: Plasmid is an extracellular small circular double stranded DNA that replicate independently of chromosomal DNA within bacteria. Plasmids carry genes that may provide benefit for survival of organism, and can be transmitted from one bacterium to another by a horizontal gene transfer. Plasmids serve as important tools in genetics and biotechnology labs, where they are commonly used to multiply (make many copies of) or express particular genes. The gene to be replicated is inserted into copies of a plasmid containing genes that make cells resistant to particular antibiotics and a multiple cloning site (MCS), which is a short region containing several commonly used restriction sites allowing the easy insertion of DNA fragments at this location. This plasmid containing desired gene can be transformed to get colonies containing the plasmid with the cloned gene. Plasmid DNA is purified from Escherichia coli using alkaline lysis method by denaturation of plasmid DNA.

The bacterial cultures having plasmid with Dopamine 1 Receptor (DIR) gene and pGloSensor 22F CAMP plasmid were inoculated in 100ml Luria-Bertani broth (Hi Media) and was kept at 37°C on a shaking platform for overnight. After overnight shaking at 37°C, Glycerol stocks were prepared by adding 500µl of bacterial freezing media to the bacterial culture (1:1) in a cryovial (SPL lifescience) and was kept at -80°C. The left culture was pelleted by spinning tubes containing culture media at 12000 rpm for 10 minutes at 4°C. Supernatant was discarded and the pellet was resuspended in re suspension buffer (RNase added, 4°C by vortexing. Plasmid DNA was then isolated from this resuspended culture using kit (GE healthcare) for isolation of plasmid DNA. Briefly, after re suspension the cells were lysed in lysis buffer for five minutes and then were neutralized by adding neutralization buffer.

The neutralized lysate was loaded onto the pre equilibrated column for clearance. After lysate clearing, the column is washed with wash buffer and plasmid DNA was eluted by adding elution buffer. Plasmid DNA was precipitated from the transcluent by adding isopropenol (Sigma Aldrich). The precipitate was loaded onto the finalizer (Nucleobond, Macherey-Magel) and washed with 70% ethanol (4°C). After washing, finalizer was dried to remove the residual ethanol and plasmid DNA was eluted in 5mM tris HCl (pH8.5)

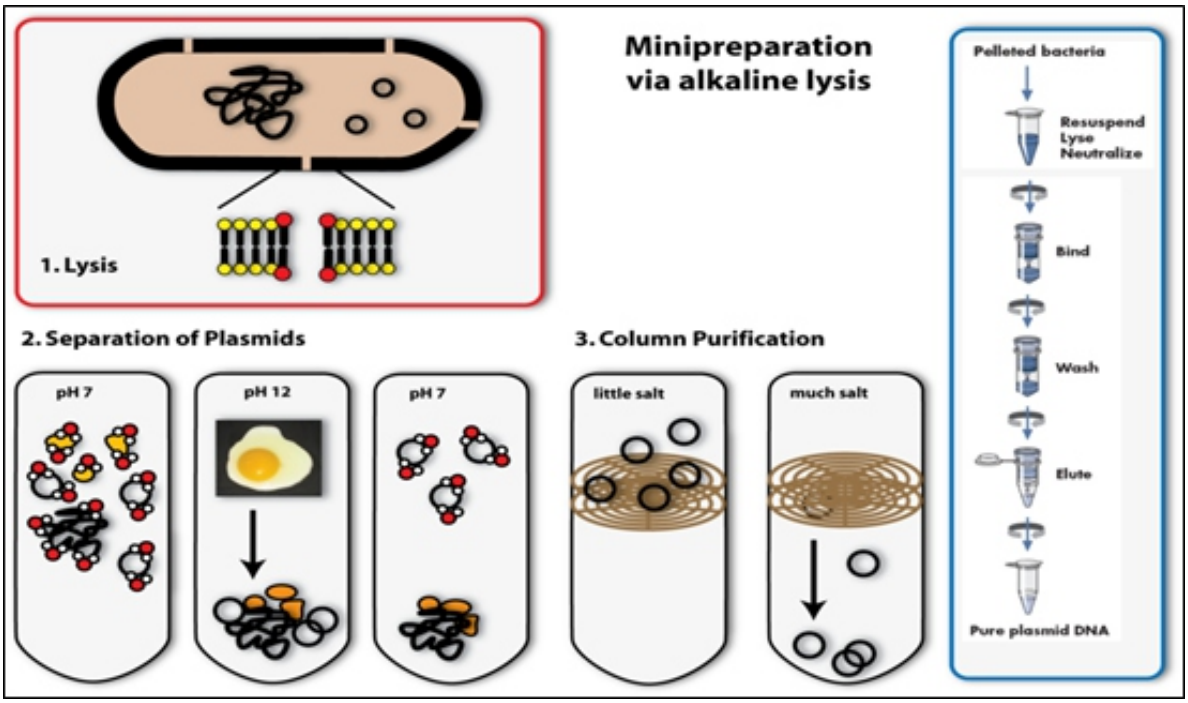


Fig. 1: isolation of plasmid DNA by mini kit

Quantitative and qualitative analysis of plasmid DNA: The Quality plasmid DNA was estimated using agarose gel electrophoresis on 1 agarose gel. Gel electrophoresis is a method for separation molecules (DNA, RNA and proteins) on the basis of molecular mass by applying an electric field. Plasmid DNA is a lightly super coiled circle and during isolation, most of the DNA remains super coiled, but a certain amount sustains single-strand nicks. Because of presence of nick in only one of the strands, the DNA remains circular, but the nick permits rotation around the phosphordiester backbone and the supercoils are released. On an agarose gel, supercoiled DNA sustains less friction than nicked circular DNA.

Therefore, for the same over-all size, supercoiled DNA movesfaster than open-circular DNA. So, an uncut plasmid produces two bands on a gel. Representing the supercoilled and nicked circular conformations.The quantity of plasmid DNA was estimated by Nanodrop 2000c (Thermo Fisher: UV Spectrophotometer) using one microliter of plasmid DNA. The ratio of absorbance at 260nm and 280 mm is used to measure the purity of DNA and RNA. A ratio of 260/280 1.8 is generally accepted as pure for DNA; a ratio of 260/280-2 is generally accepted for RNA. If the ratio is lower in either case, it may indicate the presence of impurities or protein. Before starting the software 'sample input surface' was cleared with distilled water to remove any dried sample that might be present. The 1 ul DNA sample was loaded on sensor and measured the concentration.

Agarose gel electrophoresis:

Preparation of 1% agarose gel:

The gel casting tray (Bangalore Genie, India) was wiped and combs were adjusted to make the wells in the gel.1 g of agarose (Invitrogen) was added to 250 ml flask containing 100 ml of IX TAE buffer (pH 8.5) (Annexure I) and boiled till agarose gel completely dissolved to give a clear solution. 10 µl of ethidium bromide (10 mg/ml) (Amnion Biosciences) was added to the gel solution and mixed thoroughly by gentle swirling. The agarose solution was cooled to 60°C and poured in the gel casting tray avoiding any bubble formation. The gel was allowed to set completely at room temperature for 30 minutes and combs were removed carefully. The gel was placed in the horizontal submarine electrophoresis chamber (Bangalore Genie, India) containing IX TAE buffer (pH 8.5).

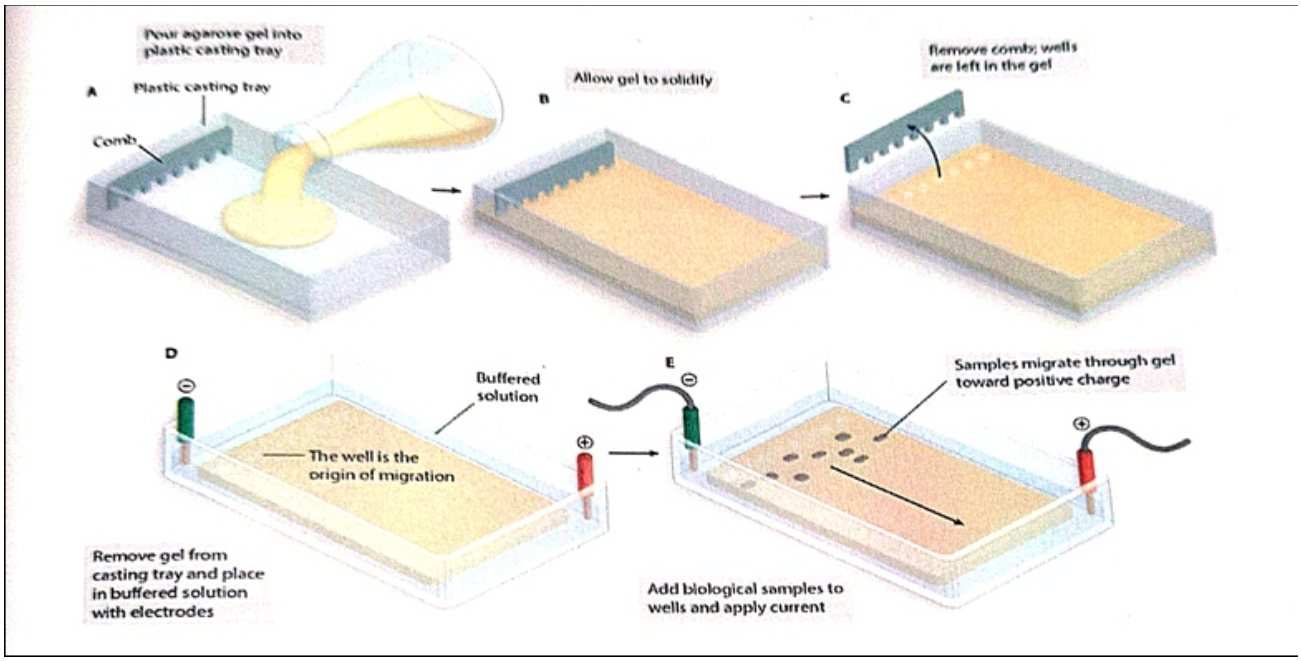


Fig. 2: Preparation of agarose gel and loading of DNA sample.

Loading of DNA samples:

2 ul of each DNA sample was mixed with 3 ul of 6X gel loading buffert Annexure 1) and were loaded in the wells. 0.5ug DNA marker (Gene Ruler 1kb DNA ladder, Ready to Use, SM1163 Fermentas was loaded in the first well of the gel. The lid of electrophoresis chamber was closed and electric leads were connected. The electrophoresis was done at 100 V for 30 minutes. After completion of electrophoresis. The gel was removed from the chamber and analysed under UV transilluminator and photographed.

Characterization of plasmid DNA:

Isolated plasmid DNA was verified by restriction digestion with restriction enzymes corresponding to the restriction sites used to clone the receptor.

Restriction digestion analysis:

Restriction enzymes bind specifically to double stranded DNA and cleave it at specific sites within or adjacent to a particular sequence known as recognition sequence. These recognition sequences are four, five, or six nucleotide long and display two fold symmetry. Enzyme Kpl recognizes 5-GGTAC CC-3 sequence and Xhol recognizes recognition sequence 5'-CTGGAG-3'sequence. Double digestion of 6765bp DIR plasmid with Kpal and Xhol, yields two fragments of 5427bp and 13338bp. Restriction enzyme Nhel recognizes 5-G CTAGC-3 sequence and BamHI recognizes recognition sequence 5'-G GATTC-3′ sequence. Double digestion of 6990bp pGloSensor 22F CAMP plasmid with Nhel (1910) and Bumi (4293) restriction enzymes yields two fragments of 4607bp and 2383bp.

Setting of Restriction Digestion Reaction:

To set up restriction digestion, 10X buffer was thawed and mixed thoroughly before starting the reaction setting. lug of each plasmid was added to the pre labelled 0.5ml microcentrifuge tubes (Axygen Scientific, Inc.). The Restriction Digestion master mixture was prepared by adding nuclease free water, 10X buffer and restriction enzyme in the sequence. The reaction master mixture was mixed gently and 18µl was distributed to each tube containing 2 ul of plasmid DNA. The contents of the microcentrifuge tubes were spun for 10-15 seconds and incubated at 37°C for two hours. After two hour of incubation, 5 ul of 6X gel loading buffer (Annexure 1) was added to the tubes to stop the digestion reaction. The samples were analyzed on 1.5% agarose gel.

Characterization of DIR plasmid by Restriction Digestion method:

Plasmid containing DIR was verified by digesting plasmid DNA Kpnl and Xholrestriction enzymes. The details of restriction digestion mixture are mentioned in the Table 2. The fragment size obtained after double digestion was- 5427bp and 13338bp.

Table 2. Restriction Digestion master mixture to verify DIR containing Plasmid

S.No.	Reagents	Volume(µl) (for 1 reaction)
1	Nuclease free water	13.5
2	10X buffer 4 (NEB)	2.0
3	BSA (100X)	0.5
4	Kpnl restriction enzyme (10U/µl)(NEB)	1.0
5	Xhol restriction enzyme (10U/ µl) (NEB)	1.0
5	Plasmid DNA(500µg)	2.0
Total		20

Characterization of pGloSensor 22F CAMP plasmidby Restriction Digestion:

pGlo sensor 22F CAMP plasmid was verified by digesting plasmid DNA with Nhel and BamI restriction enzymes. The details of restriction digestion mature are mentioned in the **Table 2**.The fragment size obtained after double digestion was-4607bp and 2183bp.

Table 3. Restriction Digestion master misture to verify GloSensor 22F cAMP plasmid

S.No.	Reagents	Volume (µl) (For 1 reaction)
1.	Nuclease free water	14.5
2.	10X buffer 4 (NEB)	2.0
3.	Nhel Restriction Enzyme (10U/µl)	1.0
4.	BamHI Restriction Enzyme (10U/µl)	1.0
5.	Plasmid DNA(500µg)	2.0
Total		20

Restriction digestion reaction products analysis:

Restriction digestion products were analysed on 1.5% agarose gel.

Preparation of 1.5% agarose gel:

The gel casting tray (Bangalore Genie, India) was wiped and combs were adjusted to make the wells in the gel 1.5 g of agarose (Invitrogen) was added to 250 ml flask containing 100 ml of IX TAE buffer (pH 8.5) (Annexure 1) and boiled till agarose gel compl.cly dissolved to give a clear solution 10 µl of ethidium bromide (10 mg/ml) (Ammion Biosciences) was added to the gel solution and mixed thoroughly by gentle swirling The agarose solution was cooled to 60°C and poured in the gel casting tray avoiding any bubble formation. The gel was allowed to set completely at room temperature for 30 minutes and combs were removed carefully. The gel was placed in the horizontal submarine electrophoresis chamber (Bangalore Genie, India) containing IX TAE buffer (pH 8.5).

Loading of restriction digestion reaction products:

Restriction digestion products were mixed with 5 ul of 6X get loading haffer and inded the well 1kp molecular weight marker (Fermentas) was loaded in the first wall of the gel. The lid of electrophoresis unit was closed and electric leads were connected. The dectroplicitous was det 100 V for 40 minutes. After completion of electrophoresis, the gel was removed from the chamber and analysed under UV transilluminator and photographed. The plasmids were verified conding to the size of the fragments obtained after digestion (**Table 4**)

Table 4: Loading of restriction digestion reaction products

Plasmid DNA	Restriction enzyme	Incubation temperature	No. of Fragments obtained	Fragment size(bp)
D1R	Kpnl, Xhol	37^0C	2	5427,1338
pGloSensor 22F cAMP	Nhel, BamH1	37^0C	2	2383, 4607

Culturing and Maintenance HEK293T cell line:

HEK293T cells (NCCS, Pune) were cultured in Dulbecco's Modified Eagle Medium (DMEM) with 4.5g/l Glucose 4.0mM, L-glutamine; Sodium Pyruvate (Cell Clone) supplemented with 10% FBS at 37°C and 5% CO_2in a humidified incubator.At 90-95% confluency, media was aspirated using sterile serological pipette (Coming) and cell monolayer was washed using 10 ml of 1X PBS (pH7.4) (Annexure 1). After washing, 2ml of 0.05% trypsin-EDTA, prewarmed to room temperature, was added to the cell monolayer and was spread throughout the flask, so as to coat the cell surface evenly. The flask was then kept at 37°C for 40 seconds for efficient trypsinization. After cells started dislodging from the flask surface, 10ml of DMEM supplemented with 10% FBS (complete DMEM media; prewarmed to 37°C)was added to the flask to neutralize action of trypsin and was mixed gently by repeated pipetting to break cell aggregates. The trypsinized cell suspension was then transferred to 15ml centrifuge tube (Tarsons, India) and was spun at 200 X g for five minutes at room temperature to get cell pellet. The supernatant was discarded and cell pellet was resuspended in 10ml of complete DMEM media. The cell number was determined using using hemocytometer and cells were plated at the density of 10X 10" in tissue culture treated 15cm cellculture dish (Nunc) in DMEM containing 10% FBS prewarmed to 37°C. The dish was then incubated at 37°C in tissue culture incubator with 5% CO for overnight. After overnight scubation, cells were transfected.

Transient Transfection of HEK293Tcells using transfection reagent:

Transfection is the process of introducing nucleic acids into eukaryotic cell by nonviral methods. It is a method to neutralize or obviates the issue of introducing negatively charged molecules (DNA or RNA) into cells with a negatively charged membrane. Chemicals like calcium phosphate and DEAE-dextran or cationic lipid based reagents coat the DNA, neutralizing or even creating an overall positive charge to the molecule. HEK293Tcells were transiently transfected with DIR, 22F CAMP and YFP plasmid. 20µg of total DNA was mixed (DIR, Glo, and YFP) with transfection reagent in a ratio of 1:4 in incomplete DMEM and was incubated for five minutes at room temperature. After incubation, the transfection mix was added to the dish drop wise and the dish was again kept at 37°C in tissue culture incubator with 5% CO2 for overnight.

Glo Sensor Assay:

The Gle Sensor CAMP Assay is a method to detect and measure CAMP activities using genetically encoded biosensor variants with CAMP binding domains fused to mutant forms of firelly (Photinus pyralis) luciferasewhich is capable of modulation of its luminescence activity dependent on reversible allosteric interaction with ligand. Upon binding to CAMP, conformational changes occur that promote large increases in light output. Following pre- equilibration with substrate, cells transiently or stably expressing a biosensor variant can be used to assay GPCR function using a live-cell, non-lytic assay format, which enable simple kinetic measurements of cAMP accumulation in living cells.

Equilibration with luciferase substrate luciferin:

After over night incubation, media was aspirated from the culture dish and 10ml drug buffer (IX ov HBSS and 20mM HEPES, pH 7.4) was added to the transiently transfected HEK293T cells. The cells were dislodged from the dish by pipeting in drug buffer The dulcelge ol wapension was then taken in 15mil sentofage tabe Carsons, India and was span at 200X H temperature for five minutes to get cell pellet. The supernatant was discarded and the coll pellet was resuspendal in luciferin solution (10uguly. The 125µl of resuspended cells were plated in 96 well plate and plates were kept at 37°C in se culture mcubator with 5% CO_2 90 minutes

Compound Preparation and addition to the pre-equilibrated cells:

Stock solution of test compounds was prepared in DMSO Cigma Aldrich) at concentration of 10mM and stored at -20°C. For primary screening, test compound was diluted to 60M (6X) in drug buffer (Annexure 1). Primary screening in agonest mode was done using 10um concentration of each compound, for antagonist mode compounds were added half an hour before and then dopamine was added, where 50 percent inhibition would suggest that the compound is acting as

antagonist The concentration response curves of dopamine (Sigma Aldrich) and DIR selective agonist SKF38398 (Sigma Aldrich) were prepared by serially diluting compound 10X in drug buffer (Annexure 1). A 10M forskolin (Sigma Aldrich) solution was used as positive control in theassay. After drug preparation, 25µl of dopamine and SKF were added to the cells in first six lines in triplicate. Test compounds were also added in triplicates (10µM final concentration). After drug addition, the cell plate was incubated at 37°C in tissue culture incubator with 5% CO_2 for 15-20 minutes to get a steady state condition.

Luminescence measurement:

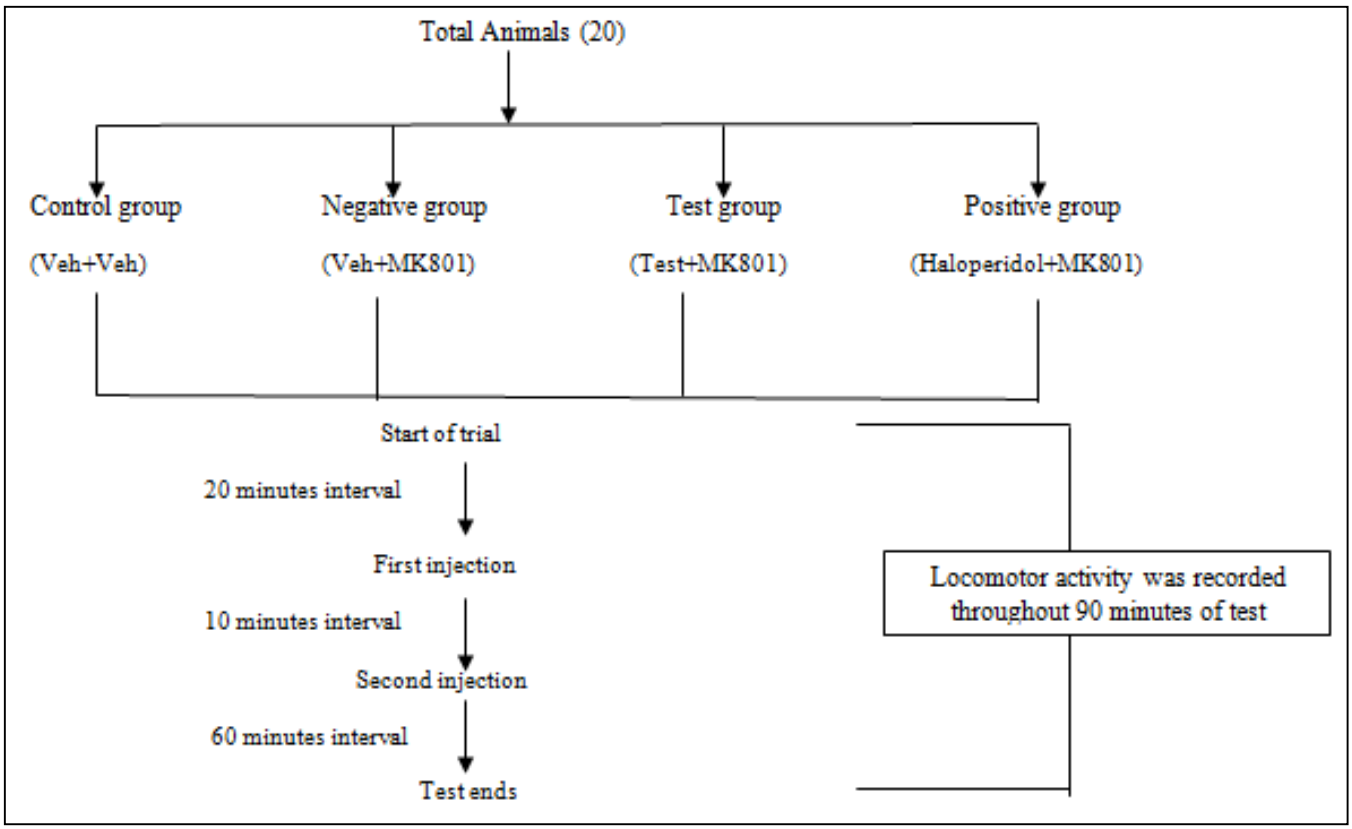
After drug addition, the luminescence was measured using multimode plate reader (BMG, Labtech) and standard curves of drug concentration vs. relative luminescence unit (RLU) were plotted using Graph Pad Prism 5.

***In vivo* testing of D2R antagonism for locomotor activity:**

Experimental Animals C57/BL6 strain mice (25-30gm) were procmel from CDICI becoding centre. Mice were placed separately in polypropylene cages (five per capci randomly with paddy husk bedding. The animals were maintained under dandant Labratory conditiones empre 232°C. *Relatively humidity*: 55: 10% and 12hrs light and 12 hrs dark cycles throughout all the experiments. The animals were shifted to the naushchavioral taboratory one hour prior to experiments.

Experimental Design:

In order to do *in vivo* screening of D2R antagonist 4 test groups were designed. In each group there were 5 mice of average weight 23.73 g (figure). Each group was administered with 2 injections each as given in figure Test duration was of 90 minutes and data was recorded after every 5 min. Detailed procedure is given in the **figure 6**.



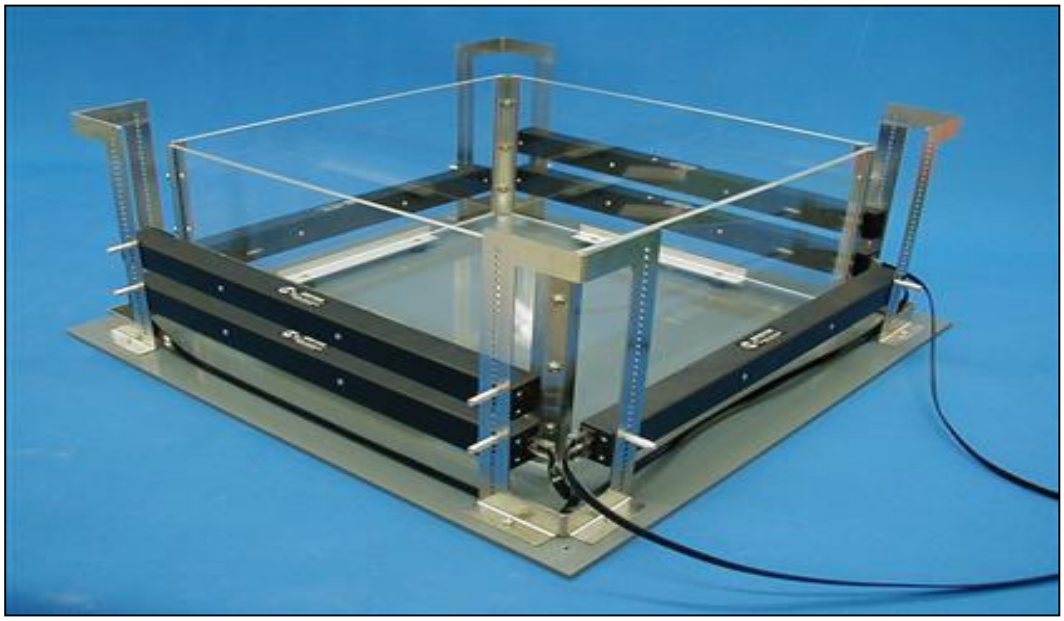


Fig. 6: Detailed procedure of locomotor activity

Animal Activity Meter: Opto – 4 auto Varimex:

Grouping of animals/injections:

Group-I: Control group (vehicle vehicle)

Group II: Negative group/Vehicle MK801)

Group-III: Test group (Test compound MK801)

Group-IV: Positive group (Haloperidol MK801)

Drugs and Chemicals:

MK801 was given 0.5 mg/kg ip

Saline was given per 67-21-3 ml per kg ip

Test compound was given mg/kg ip

Haloperidol was given 0.5 mg/kg ip

All the compounds were dissolved in DMSO

Solutions and Reagents:

0.5M EDTA (pH 8.5) **Volume: 250 ml**

46.252 g of EDTA (Mol Wt 372.2) (Sigma Aldrich) was dissolved in 170 ml double dild and its pH was adjusted to 8.5 by adding sodium hydroxide (NH) peliates (Menck, day with continuus stirring on magnetic stimer. The final volume of the solution was adjuta 250 ml with double distilled water. The solution was filtered, autoclaved and 4°C

1M Tris-HCl (pH 8.5) **Volume: 1000 ml**

121.1 g of Tris buffer (Machery Nagel) was dissolved in 800 ml of double distilled water. Its pH adjusted to 8.5 with concentratal HC (Rankem, India) and final volume was adjusted to 1000 ml with double distilled water. The solution was filtered, autoclaved and stored at 4°C

Tris EDTA (TE) buffer (pH 8.5) **Volume: 1000 ml**

1M Tris-HCl (pH 8.5)	1000µl
0.5M EDTA (pH 8.5)	200µl

Both constituents were mixed and final volume was raised to 100 mil by adding 94.5 ml of distilled water. The solution was filtered, autoclaved and stored at 4°C

50X Tris Acetate EDTA (TAE) buffer (pH 8.5) **Volume: 50 ml**

Tris base (Mol. Wt. 121.1) (Sigma Aldrich)	121.09g
Glacial acetic acid (Sigma Aldrich)	28.55 ml
0.5 M 50mM EDTA (pH 8.0)	18.60gm

The above constituents were dissolved inwarm double distilled water. The final volume adjusted to 50 ml with double distilled water. The solution was filtered, autoclaved and stored room temperature.

Ethidium Bromide (10 mg/ml) **Volume 1 ml**

10 mg ethidium Bromide (Mol WL 304 3) (Amresco) was dissolved in 1 ml of double distilled and stored at 4°C in dark bottle.

Gel loading buffer (6X) **Volume: 50 ml**

Glycerol (Sigma Aldrich)	25ml
1M Tris 50mM	2500µl
Bromophenol blue (Sigma Aldrich)	25mg
10%SDS	500µl

The above constituents were dissolved in double distilled water. The final volume was adjusted 50 ml of double distilled water and stored at 4°C

10X PBS solution **Volume: 1000ml**

KCl (Sigma Aldrich)	2g
KH_2PO_4(Sigma Aldrich)	2.4g
NaCl (Sigma Aldrich)	80g
Na_2HPO_4	11.45g

The above constituents were dissolved in 800 ml of double distilled water. The final volume was adjusted to 1000 ml, autoclaved and stored at room temperature.

0.5M HEPES (pH 7.4) **Volume: 100ml**

11.95 gm HEPES (Merck) was dissolved in 80 ml distilled water. Its pH was adjusted to 7.4 by adding HCI and final volume was adjusted to 100 ml with distilled water. The solution was filtered and stored at 4°C.

1 X Drug Buffer (pH 7.4) **Volume: 1000ml**

HBSS (Gibco)	960ml
0.5M HEPES 20mM	40ml

Both constituent were mixed. Its pH was adjusted to 7.4 by adding KOH and stored at 4°C.

Results: Quantitative and qualitative analysis of plasmid DNA

The quantity of plasmid DNA was estimated using Nanodrop 2000c (Table 5)

Table 5: Quantitative details of Plasmid DNA

Plasmid DNA	Conc(ng/µl)	A_{260}	A_{280}	A_{260}/ A_{280}
D_1	310	6.20	3.32	1.87
Glo	1112	6.15	3.38	1.81

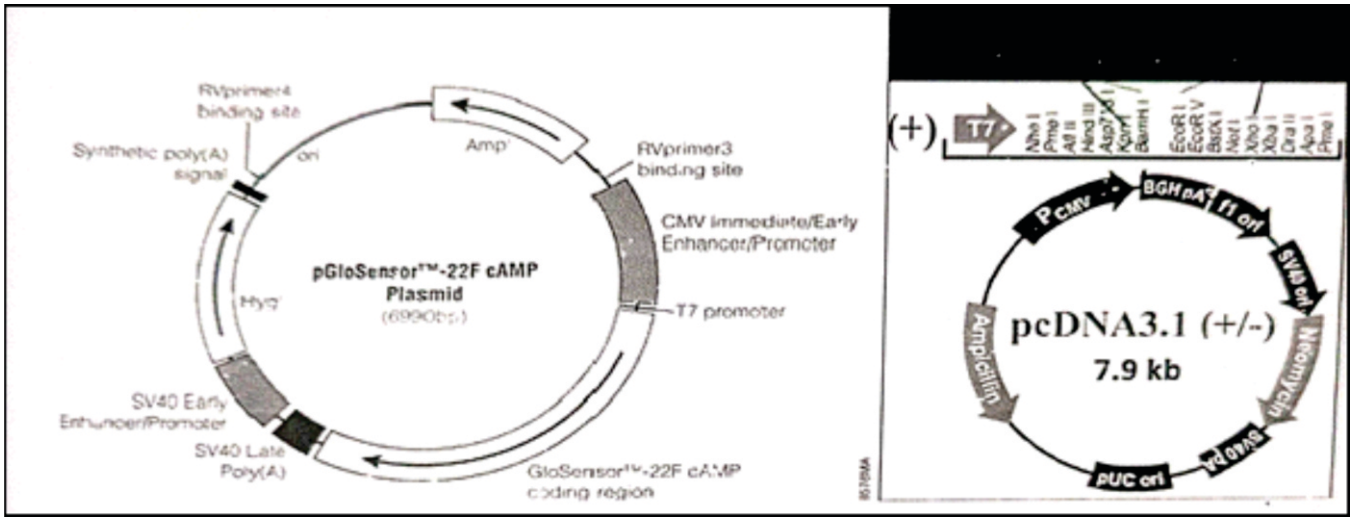


Fig. 7: Restriction digestion map of plasmid constructs D1R and Glosensor

DIR plasmid construct was in pcDNA3 format (6765hp) which was verified by restriction digestion using Kpnl and Xhol restriction enzymes which yielded two fragments of 5427bp and 1338bp.Glo(6990bp) was digested with Nhel and BamHI restriction enzymes which yielded two fragments of 4607bp and 2383bp. Digested Plasmid DNA were analyzed on 1.5% agarose gel (**Fig. 8**).

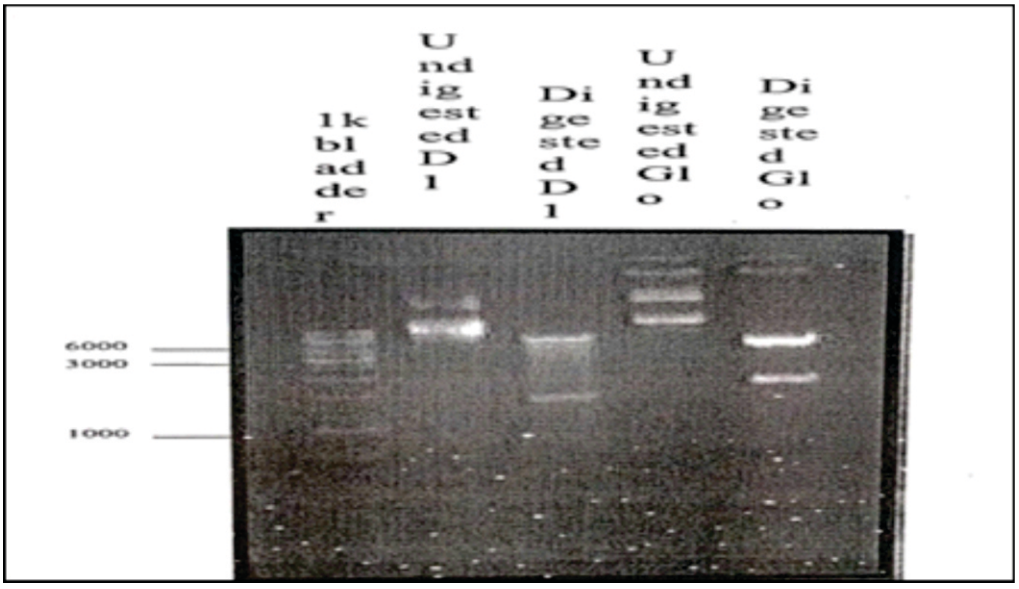


Fig. 8: Restriction digestion of D1R and Glo plasmids

Transfection in HEK293T cells:

HEK293T cells were transfected with green Fluorescent protein (GFP) in order to see transfection efficiency with our transfection reagent. Visualization and imaging was done using fluorescent microscope (**Fig. 9**). It was found that the transfection efficiency with our transfection reagent was greater than 80%.

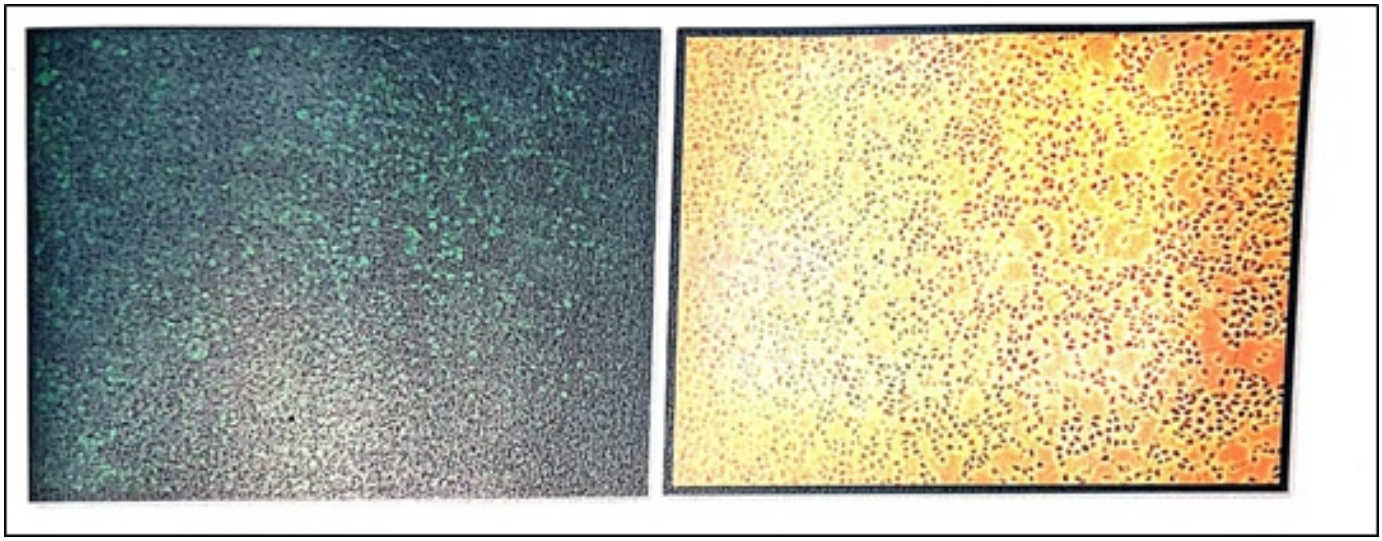


Fig. 9: Transfected HEK293T with green fluorescent protein (left) and same under bright field (right)

Glo sensor Assay:

We screened 20 compounds which were received from CDRI chemistry department for screening of important scaffolds on GPCRs. The screening was done in agonist as well as antagonist mode on DIR. On primary screening we found one compound active in agonist mode (**Table 6**) while 3 in antagonist mode (**Table 7**). On active compounds we did secondary screening (agonist **Table 8** and antagonist **Table 9**) for all the positive hits but it was not reproduced in the secondary screening. For all assays, dose response curve of Dopamine and SKF38393 had concentration of 10 micro molar to 10 Pico molar.

	1	2	3	4	5	6	7	8	9	10	11	12
A	←	Drug buffer	→	←	DA 10mm	→	←	SKF	→	←	FSK	→
B-11				←	C1	→	←	C8	→	←	C20	→
C-10				←	C2	→	←	C9	→	←	C19	→
D-9				←	C3	→	←	C10	→	←	C18	→
E-8				←	C4	→	←	C11	→	←	C17	→
F-7				←	C5	→	←	C12	→	←	C16	→
G-6				←	C6	→	←	C13	→	←	C15	→
H-5				←	C7	→	←	C14	→			
	← Dopamine →			← compounds →			← compounds →			← compounds →		

Fig. 6: Drug plate for primary screening

	1	2	3	4	5	6	7	8	9	10	11	12
A	586	824	3122	66160	67193	64567	66160	67193	64567	66160	7641	137169
B	4965	4626	6049	7097	8107	7970	7865	8100	8942	9997	9632	103333
C	6625	6673	6082	4434	4282	3910	4631	4861	5007	7315	6753	7655
D	20829	13759	12824	1821	1008	1032	1972	2036	2119	6690	7213	8640
E	48613	52174	45256	9946	6741	10324	5438	5157	5619	6411	6792	7872
F	116822	114392	106140	7948	1962	1992	7653	8236	7978	5743	5995	5993
G	152397	148938	143316	19405	11237	16695	8646	7481	7057	13427	19449	13114
H	17294	165606	151609	92266	17480	55689	10759	9274	10297			

Table 6: Luminescence data of primary screening of compounds in agonist mode. C_7 was identified as hit (shaded

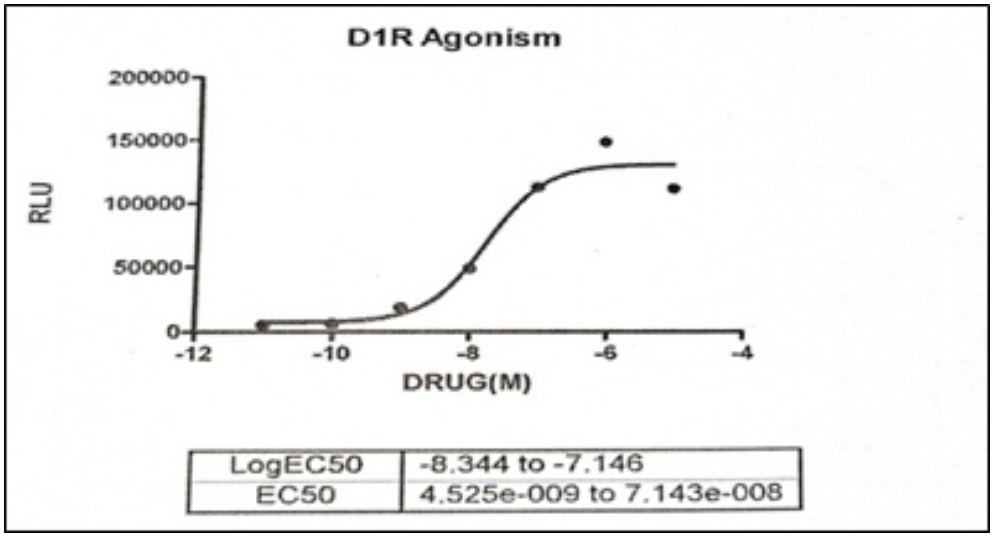


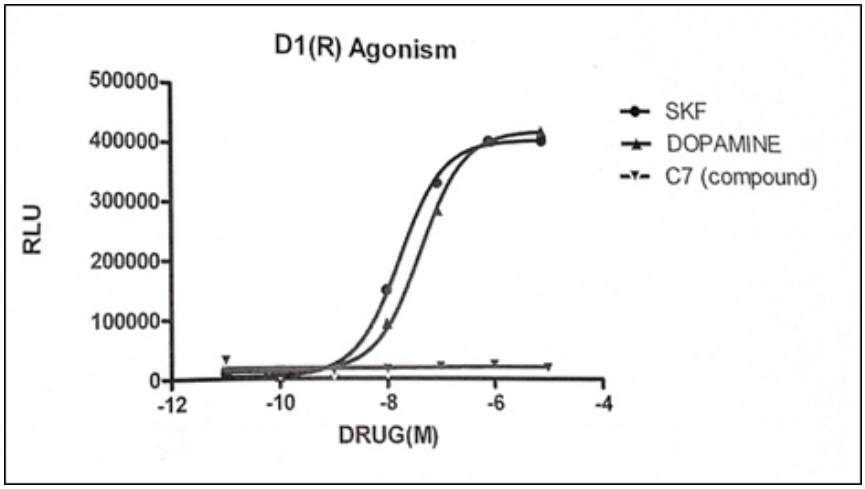
Fig. 11: Dose response curve of Dopamine as agonism. Data were plotted from table 6

Drug buffer			FSK			Dopamine			SKF		
2450	2084	2991	29472	21690	22989	25096	21661	2091	2450	2084	2991
2979	3466	15363	20324	16153	1654	29852	19564	8482	1775	13018	1261
3596	3882	3086	19916	16965	26790	29322	28519	23990	29073	24510	27467
5061	5217	15938	22617	16589	18182	28316	28676	18174	19800	22377	23498
17414	13544	131775	27959	18194	20064	25218	26861	22284	20208	20372	23658
41351	33400	300124	26968	20553	21671	29029	25143	24112	30073	28621	28510
68096	53289	369070	34880	25471	25588	29442	30429	28967	30195	33468	31532
98924	56691	53096	38445	17153	31505	32194	35199	33376			
Dopamine			Compounds			compounds			compounds		

Table7: Luminescence data of secondary screening of compounds in agonist mode. C_1, C_2, C_3 and C_{20} was idetified as hit (shaded)

Drug buffer			FSK			Dopamine			SKF		
2450	2084	2991	29472	21690	22989	25096	21661	2091	2450	2084	2991
2979	3466	15363	20324	16153	1654	29852	19564	8482	1775	13018	1261
3596	3882	3086	19916	16965	26790	29322	28519	23990	29073	24510	27467
5061	5217	15938	22617	16589	18182	28316	28676	18174	19800	22377	23498
17414	13544	131775	27959	18194	20064	25218	26861	22284	20208	20372	23658
41351	33400	300124	26968	20553	21671	29029	25143	24112	30073	28621	28510
68096	53289	369070	34880	25471	25588	29442	30429	28967	30195	33468	31532
98924	56691	53096	38445	17153	31505	32194	35199	33376			
Dopamine			Compounds			compounds			compounds		

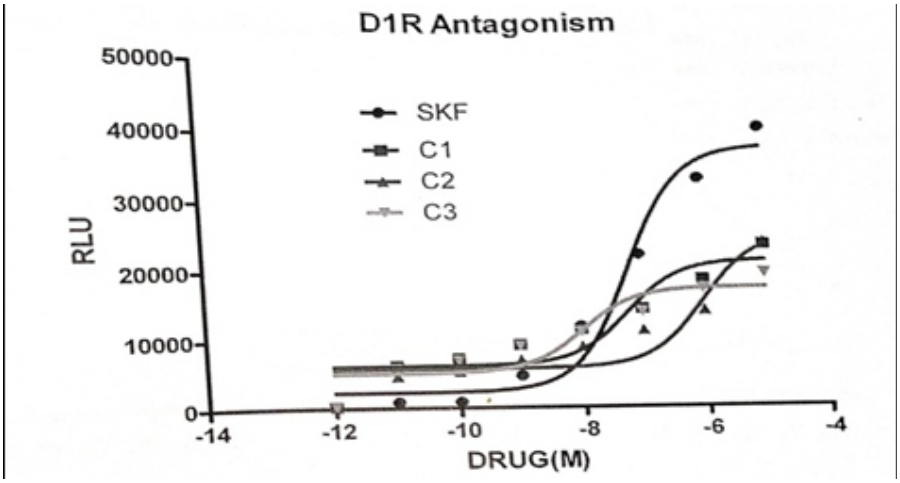
Table 8: Luminescence data of secondary screening of C7 compounds. Compound C7 was not active as agonist



	SKF	Dopamine	C7(compound)
LogEC50	-7.925 to -7.521	-7.451 to -7.204	-19.38 to 5.313
EC50	1.189e-008 to 3.014e-008	3.541e-008 to 6.255e-008	0.0 to 205727

Drug buffer			Dopamine 10um			FSK			Skf		
168	180	410	6439	6379	6873	3774	3744	3611	7020	7048	8186
695	742	1220	5409	6383	6652	6479	6167	1213	5358	5751	6185
638	740	1176	6431	7465	7612	7453	7213	1226	6568	6903	7179
3915	4657	5250	8645	9350	9262	9396	9630	1588	8730	8872	9267
12272	11272	11635	11262	12130	10740	12537	12016	1942	10529	11145	10935
24815	21656	20332	15012	14077	13849	15746	14957	2774	13395	13871	14214
36093	33594	30405	20275	17814	17700	19311	19183	3710	16579	17934	17105
43101	41960	36880	25132	22437	23282	26075	24137	21542	19644	20536	17884
SKF			C1			C2			C3		

Table 9: Luminescence data of secondary screening of C1, C2 and C3 compounds were not active as antagonist



SKF	C1	C2	C3
-7.199	-7.240	-6.013	-7.977
6.330e-008	5.750e-008	9.714e-007	1.055e-008

In vivo **testing of D2R antagonism for locomotor activity** Locomotor activity of Mk801, haloperidol, vehicle and compound are shown in figure and 14 MK801 is a NMDA receptor blocker which mimics psychosis in mice MKX01 increased psychosis activity in mice (**Figure 12 and 13**) Halopendol is an antipsychotic drug which reduced the psychosis activity induced by MK801 in mice as compared to MK801 alone (**Figure 13 and14**) Test compound reduced psychosis activity more as compared to haloperidol (**Figure 12 and 13**).

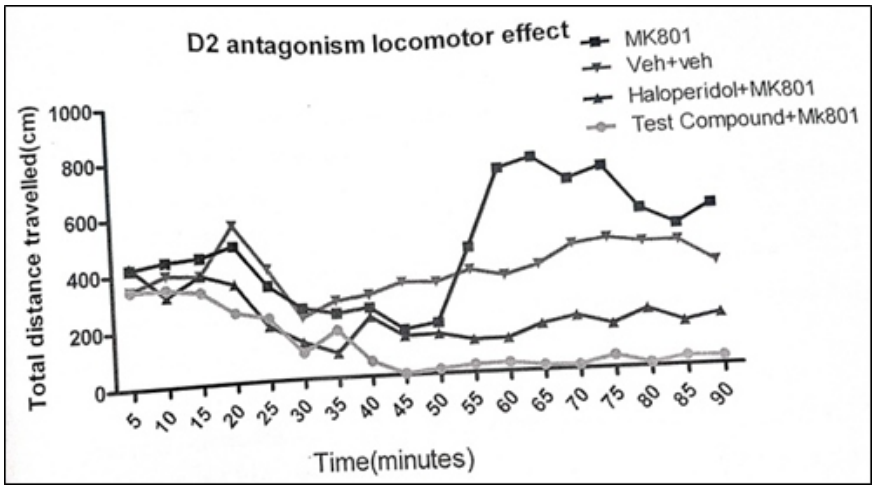


Fig. 14: Locomotor effect of mk801, haloperidol and test compounds in C57 mice

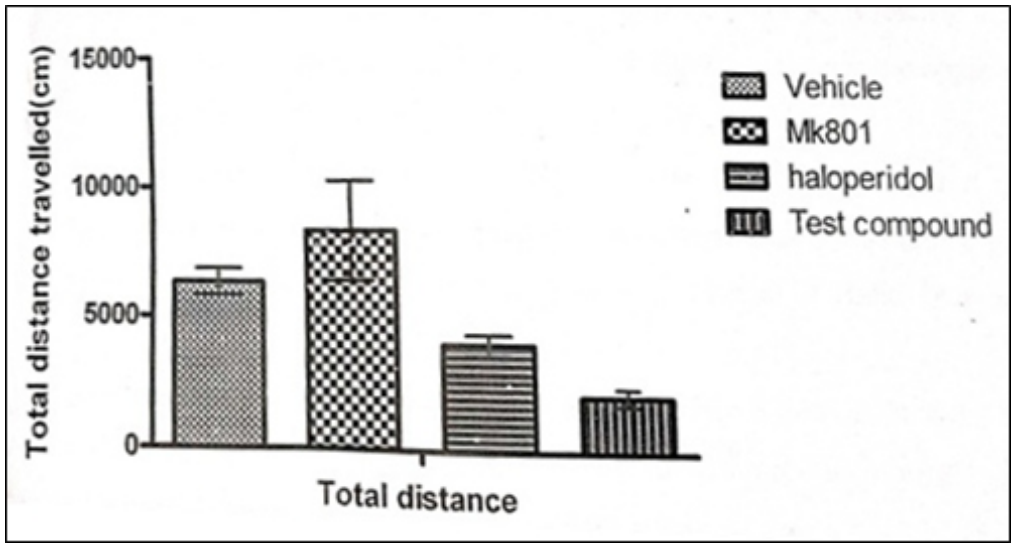


Fig. 15: Suppression of mouse locomotor activity by haloperidol and a novel D2 antagonist (Test compound). Total distance versus time interval (left) and total distance travelled during the 90 minutes session (right).

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Reference:

1. Andersen et al., 1990 Dopamine receptor agonists: selectivity and dopamine D1 receptor efficacy European al of Pharmacology: Molecular Pharmacology Volume 188, Issue 6, 12 June 1990, 335-347.
2. Wess, J. Molecular basis of receptor/Gprotein-coupling selectivity. Pharmacol Ther, 80, 1998, 231-264.
3. Howard, AD, McAllister, G. Feighner, SD, Liu, Q. Nargund, RP.Van der Ploeg, LHT and Patchett, AA Orphan

G-protein-coupled receptors and natural ligand discovery.

4. Tiberi and Caron (1994) High agonist independent activity is a distinguish feature of Dopamine D, B receptor subtype. J.Biol chem 269 27925.

5. Sokoloff P. Giros B, Martres MP. Andrieux M. Besancon R. Filon C. Bouthenet ML, Souil E, and Schwartz JC (1992b) Localization and function of the D3 dopamine receptor. Arzneimittelforschung 42:224-230.

6. Josu Li, Yuhong Ning: Warren hedley, Brian Saunders. Yong Sheng Chen Nicole Tindi), Timo Hannauy, and Shankar Subramanium The molecule pages Database Nature 420 716-712, 2002

7. Rondou P. Haegeman G. and Van Craenenbroeck K (2010) The dopane D4 receptor biochemical and signalling properties. Cell Mol Life Sci 67:1971-1986.

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A review: Hydrogel as drug delivery system: a new phase in pharmaceutical field

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ABSTRACT
Water-insoluble polymer chains form a network known as hydrogel, which is occasionally observed as a colloidal gel with water acting as the dispersion medium. Crosslinked polymer networks, or hydrogels, are able to absorb large volumes of aqueous liquids. These gels more closely mimic real tissue than any other kind of synthetic biomaterial because of their high water content. A number of methods for creating hydrogels have been documented, including co-polymerization and crosslinking of co-monomers with the use of a multifunctional co-monomer as a crosslinking agent. The polymerization reaction is started by a chemical initiator. Hydrogels are employed in certain parts of the human body. The body contains some environmental factors, like high temperatures and low pH. For site-specific controlled drug delivery, pH-sensitive and/or temperature-sensitive hydrogels can be employed. Hydrogels with molecular selectivity, such glucose or antigens, have potential applications in medication administration and biosensors. Homo- and co-polymeric hydrogels have been created using novel synthetic techniques for a variety of medication, peptide, and protein delivery uses. This article's goal is to provide a succinct overview of the uses of hydrogels in the pharmaceutical industry, as well as information on the material's characteristics, preparation process, benefits, and drawbacks.

Key words: Polymer, Hydrogel, Drug delivery, Toxicty

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Introduction:

Hydrogels are three-layered, cross connected organizations of water-solvent polymers. Hydrogels can be produced using for all intents and purposes any water-solvent polymer, enveloping many substance pieces and mass actual properties. Further-more, hydrogels can be figured out in different actual structures, including chunks, microparticles, nanoparticles, coatings, and movies. Therefore, hydrogels are generally utilized in clinical practice and trial medication for many applications, including tissue designing and regenerative medication, diagnostics, cell immobilization, detachment of biomolecules or cells, and boundary materials to manage natural attachments. The special actual properties of hydrogels have started specific interest in their utilization in drug conveyance applications. Their exceptionally permeable design can without much of a stretch be tuned by controlling the thickness of cross connections in the gel lattice and the fondness of the hydrogels for the watery climate in which they are enlarged. Their porosity likewise allows stacking of medications into the gel grid and ensuing medication discharge at a rate reliant upon the dispersion coefficient of the little particle or macromolecule through the gel organization. Without a doubt, the advantages of hydrogels for drug conveyance might be generally pharmacokinetic especifically that a stop definition is made from which tranquilizes gradually elute, keeping a high neighborhood centralization of medication in the encompassing tissues over a lengthy period, despite the fact that they can likewise be utilized for foundational conveyance. Hydrogels are additionally commonly exceptionally biocompatible, as reflected in their fruitful use in the peritoneum and different locales in vivo. Biocompatibility is advanced by the high water content of hydrogels and the physiochemical likeness of hydrogels to the local extracellular grid, both compositionally (especially on account of carb based hydrogels) and precisely. Biodegradability or disintegration might be planned into hydrogels by means of enzymatic, hydrolytic, or ecological (for example pH, temperature, or electric field) pathways; nonetheless, corruption isn't generally alluring relying upon the time scale and area of the medication conveyance gadget. Hydrogels are likewise moderately deformable and can adjust to the state of the surface to which they are applied. In the last setting, the muco or bioadhesive properties of certain hydrogels can be worthwhile in immobilizing them at the site of use or in applying them on surfaces that are not even. In spite of these numerous beneficial properties, hydrogels likewise have a few restrictions. The low rigidity of numerous hydrogels restricts their utilization in load bearing applications and can bring about the untimely disintegration or stream away of the hydrogel from a designated nearby site. This impediment may not be significant in numerous average medication conveyance applications (for example subcutaneous infusion). More significant, maybe, are issues connecting with the medication conveyance properties of hydrogels. The amount and homogeneity of medication stacking into hydrogels might be restricted, especially on account of hydrophobic medications. The high water content and huge pore sizes of most hydrogels frequently bring about somewhat fast medication discharge, north of a couple of hours to a couple of days. Simplicity of utilization can likewise be dangerous; albeit a few hydrogels are adequately deformable to be injectable, many are not, requiring careful implantation. Every one of these issues essentially limits the viable utilization of hydrogel-based drug conveyance treatments in the center. In this survey, we center around ongoing improvements resolving three key clinically pertinent issues in regards to the utilization of hydrogels for drug conveyance: working with the in vivo use of medication eluting hydrogels, expanding their term of medication delivery, and widening the scope of medications which they successfully deliver. (1-6].

Classification of Hydrogels:

The classification of hydrogel system is elaborated as follows **(Figure 1)**

1. In the light of the strategy for arrangement, hydrogels are grouped into:

A) Homopolymer hydrogels

B) Co-polymer hydrogels

C) Multi polymer hydrogels

2. In light of the ionic charges hydrogels can be arranged into:

A) Impartial hydrogels

B) Anionic hydrogels

C) Cationic hydrogels

D) Ampholytic hydrogels

3. In view of the construction hydrogels can be arranged into:

A) Nebulous hydrogels

B) Semi-glasslike hydrogels

C) Hydrogen fortified hydrogels

4. In view of the system controlling the medication discharge they are arranged into:

A) Dispersion controlled discharge frameworks

B) Expanding controlled discharge frameworks

C) Synthetically controlled discharge frameworks

D) Climate responsive frameworks

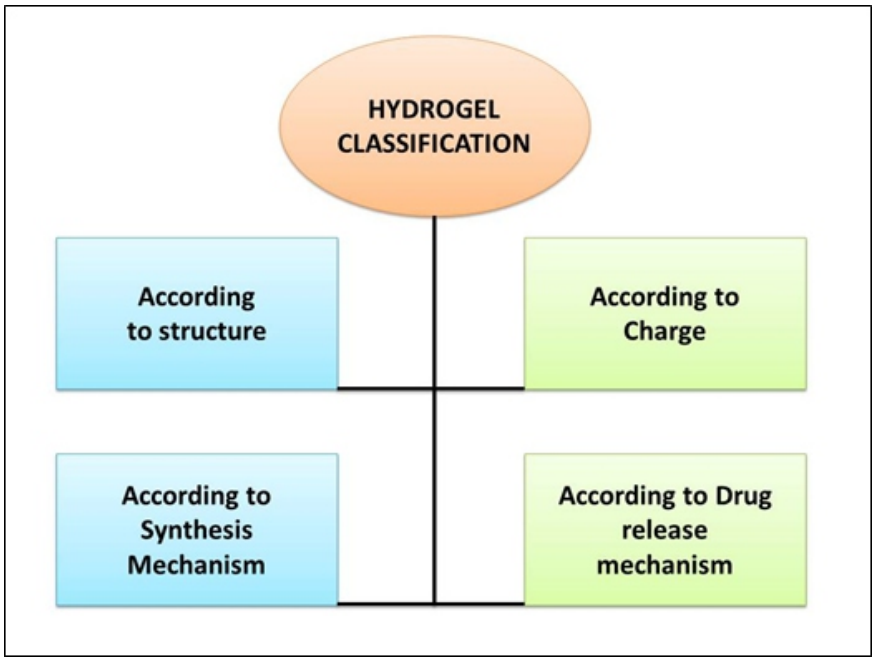

Fig. 1: Classification of Hydrogels

Properties of hydrogel:

Hydrogels are water enlarged polymer networks, with a propensity to guzzle water when set in fluid climate. This capacity to expand, under organic circumstances, makes it an optimal material for use in drug conveyance and immobilization of proteins, peptides, and other natural mixtures. Because of their high water content, these gels look like normal living tissue more than some other sort of manufactured biomaterial. These organizations, have a three layered structure, crosslinked together either genuinely (snares, crystallites), or synthetically (tie-focuses, intersections). Insoluble crosslinked immobilization of design dynamic. This permits specialists, biomolecules actually, and considers its delivery in obvious explicit way. In this manner the hydrogels biocompatibility and crosslinked structure are liable for its changed applications

Physical, Chemical& Toxicological Properties of Hydrogels:

1. Factors influencing expanding of hydrogels:

The crosslinking proportion is perhaps of the main element that influences the expanding of hydrogels. It is characterized as the proportion of moles of crosslinking specialist to the moles of polymer rehashing units. The higher the crosslinking proportion, the seriously crosslinking specialist is consolidated in the hydrogel structure. Profoundly crosslinked hydrogels have a more tight construction, and will grow less contrasted with similar hydrogels with lower crosslinking proportions. Crosslinking obstructs the portability of the polymer chain, subsequently bringing down the enlarging proportion. The synthetic design of the polymer may likewise influence the enlarging proportion of the hydrogels. Hydrogels containing hydrophilic gatherings swell to a more serious level contrasted with those containing hydrophobic gatherings. Hydrophobic gatherings breakdown within the sight of water, accordingly limiting their openness to the water atom. Thus, the hydrogels will grow significantly less contrasted with hydrogels containing hydrophilic gatherings. Expanding of naturally touchy hydrogels can be impacted by unambiguous upgrades. Enlarging of temperature-touchy hydrogels can be impacted by changes in the temperature of the expanding media. Ionic strength and pH influence the enlarging of ionic strength and pH-touchy hydrogels, separately. There are numerous other explicit upgrades that can influence the expanding of other ecologically responsive hydrogels.

Elements of Swelling:

The enlarging energy of hydrogels can be delegated dissemination controlled (Fickian) and unwinding controlled (non-Fickian) expanding. At the point when water dispersion into the hydrogel happens a lot quicker than the unwinding of the polymer chains, the enlarging energy is dissemination controlled.

Mechanical properties:

Mechanical properties of hydrogels are vital for drug applications. For instance, the uprightness of the medication conveyance gadget during the lifetime of the appli-cation is vital to get FDA endorsement, except if the gadget is planned as a biodegradable framework. A medication conveyance framework intended to safeguard a delicate remedial specialist, like protein, should keep up with its trustworthiness to have the option to safeguard the protein until it is delivered out of the framework. Changing the level of crosslinking has been used to accomplish the ideal mechanical property of the hydrogel. Expanding the level of crosslinking of the framework will bring about a more grounded gel. Nonetheless, a more significant level of crosslinking makes a more weak design. Subsequently, there is an ideal level of crosslinking to accomplish a generally solid but versatile hydrogel. Copolymerization has likewise been used to accomplish the ideal mechanical properties of hydrogels. Integrating a co monomer that will add to H-holding can expand the strength of the hydrogel.

Cytotoxicity and *in-vivo* toxicity:

Cell culture techniques, otherwise called cytotoxicity tests can be utilized to assess the harmfulness of hydrogels. Three normal measures to assess the poisonousness of hydrogels incorporate concentrate weakening, direct contact and agar dispersion. The majority of the issues with poisonousness related with hydrogel transporters are the unreacted monomers, oligomers and initiators that filter out during application. Accordingly, a comprehension the poisonousness of the different monomers utilized as the structure blocks of the hydrogels is vital. The connection between synthetic designs and the cytotoxicity of acrylate and methacrylate monomers has been concentrated broadly. A few measures have been taken to tackle this issue, remembering changing the energy of polymerization for request to accomplish a higher transformation, and broad washing of the subsequent hydrogel. The arrangement of hydrogels with next to no initiators has been investigated to kill the issue of the remaining initiator. The most regularly utilized method has been gamma illumination. Hydrogels of PVA have been likewise made without the presence of initiators by utilizing warm cycle to instigate crystallization. The gems framed go about as physical crosslinks. These gems will actually want to

ingest the heap applied to the hydrogels.

Fabrication Techniques for Hydrogels:

Hydrogels are polymeric organizations. This suggests that crosslinks must be available to keep away from disintegration of the hydrophilic polymer chain in fluid arrangement **(Figure 2)**. The different strategies for crosslinking are as per the following:

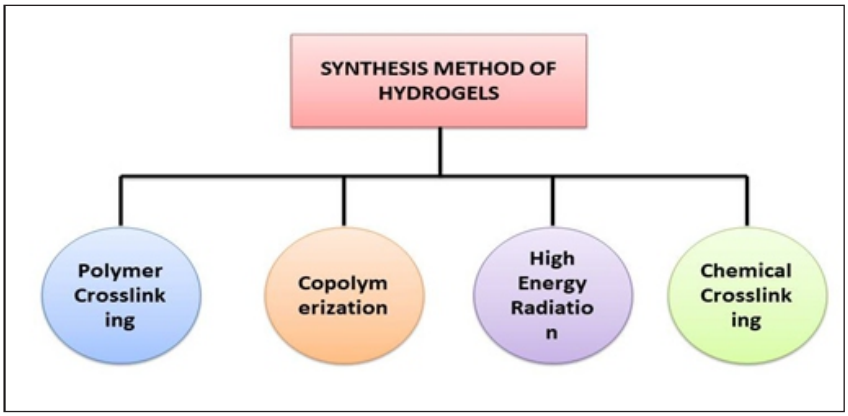

Fig. 2: Elaboration of Synthesis methods of Hydrogel

Crosslinking of Polymers:

In this strategy synthetically crosslinked gels are shaped by extremist polymerization of low atomic weight monomers, or expanded homopolymers, or copolymers within the sight of crosslinking specialist. This response is for the most part completed in answer for biomedical applications.

Copolymerization/Crosslinking Responses:

Copolymerization responses are utilized to create polymer gels, numerous hydrogels are delivered in this style, for instance poly (hydroxyalkyl methylacrylates).

Crosslinking by High Energy Radiation:

High energy radiation, for example, gamma and electron bar radiation can be utilized to polymerize unsaturated mixtures. Water dissolvable polymers derivatized with vinyl gatherings can be changed over into hydrogels utilizing high energy radiation.

Crosslinking Utilizing Chemicals:

As of late another strategy was distributed utilizing a catalyst to orchestrate Stake based hydrogels. A tetrahydroxy Stake was functionalized with expansion of glutaminyl gatherings and organizations were shaped by expansion of transglutaminase into arrangement of Stake and poly (lysine cophenylalanine). The combination of hydrogel in industry is Comprise of suspension arrangement and endlessly turned around emulsion polymerizations.

Uses of Hydrogel:

- Presently utilized as frameworks in tissue designing. When utilized as platforms, hydrogels might contain human cells to fix tissue.
- Naturally delicate hydrogels. These hydrogels can detect changes of pH, temperature, or the convergence of metabolite and delivery their heap as consequence of such a change.
- Utilized in expendable diapers where they "catch" pee, or in clean napkins.
- Contact focal points (silicone hydrogels, polyacrylamides). Normal fixings are for example polyvinyl liquor, sodium polyacrylate, acrylate polymers and copolymers with a wealth of hydrophilic groups.Natural hydrogel materials are being examined for tissue designing, these materials incorporate agarose,
- As frameworks.

- Control-discharge conveyance Give ingestion, desloughing and debriding limits of necrotics and fibrotic tissue.
- Hydrogels that are receptive to explicit atoms, for example, glucose or antigens can be utilized as biosensors as well as in DDS. Methylcellulose, hylaronan, and other normally determined polymers.

Advantages of Hydrogel:

a) Ensnarement of microbial cells inside polyurethane hydrogel globules with the benefit of low harmfulness.

b) Hydrogel is more versatile and more grounded than accessible hydrogels of comparable non-abrasiveness. Poly (methyl acrylate-co hydroxyethyl acrylate) hydrogel embed material of solidarity and delicateness.

c) Hydrogel-based microvalves have various benefits over regular microvalves, including moderately straightforward manufacture, no necessity, outer power no incorporated gadgets, enormous relocation (185 µm), and huge power age (22 mN).

d) Ecologically touchy hydrogels. These hydrogels can detect changes of pH, temperature, or the centralization of metabolite and delivery their heap as consequence of such a change. e) Normal hydrogel materials are being researched for tissue designing, these materials incorporate agarose, methylcellulose, hylaronan, and other normally determined polymers. (26-27)

Disadvantages of Hydrogel:

The primary drawbacks are the significant expense and the sensation felt by development of themaggots.

- Its inconvenience incorporate apoplexy at anastomosis locales and the careful gamble related with the gadget implantation and reterieval.
- Hydrogels are nonadherent; they might should be gotten by an optional dressing.
- Hindrances of hydrogel in contact focal points are focal point statement, hypoxia, parchedness and red eye responses.

Applications of Hydrogel:

Utilizations of hydrogels in drug conveyance various procedures have been proposed to accomplish drug conveyance frameworks for productive treatment. Among them, hydrogels extensive stand out pulled in as great contender for controlled discharge gadgets, bioadhesive gadgets, or targetable gadgets of remedial specialists **(Figure 3)**. Hydrogel-based conveyance gadgets can be utilized for oral, rectal, visual, epidermal and subcutaneous application.

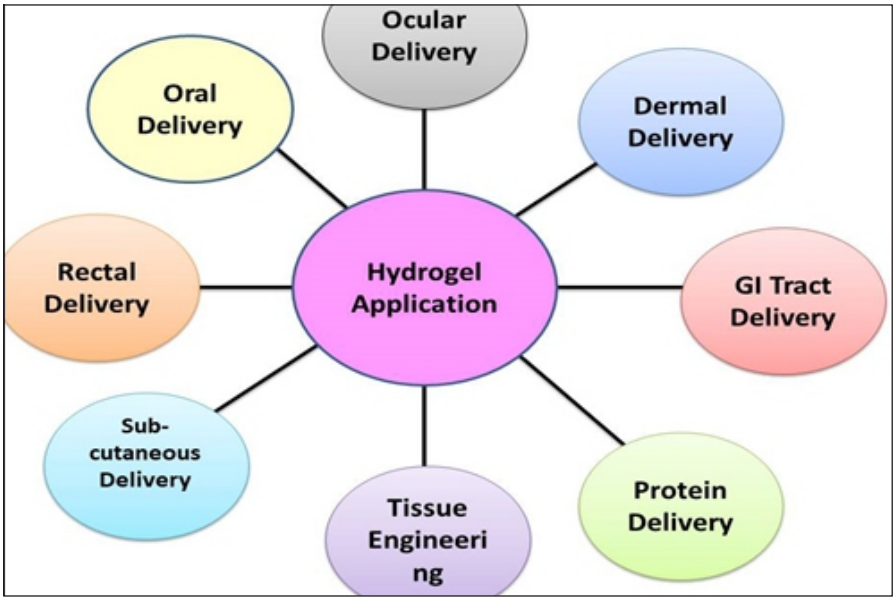

Fig. 3: Application hydrogel system

Peroral drug conveyance:

Medication conveyance through the oral course has been the most widely recognized strategy in the drug utilizations of hydrogels. In peroral organization, hydrogels can convey medications to four significant explicit destinations; mouth, stomach, small digestive system and colon. By controlling their expanding properties or bioadhesive qualities within the sight of a natural fuid, hydrogels can be a valuable gadget for delivering drugs in a controlled way at these ideal destinations. Moreover, they can likewise stick to specific explicit districts in the oral pathway, prompting a privately expanded drug fixation, and subsequently, improving the medication retention at the delivery site.

Drug delivery in oral cavity:

Medication conveyance to the oral pit can have flexible applications in neighborhood therapy of illnesses of the mouth, like periodontal sickness, stomatitis, contagious and viral diseases, and oral pit tumors. Long haul attachment of the medication containing hydrogel against plentiful salivary stream, which washes the oral depression mucosa, is expected to accomplish this nearby medication conveyance. For this reason, many sorts of bioadhesive hydrogel frameworks have been contrived since the mid 1980s. A portion of these are as of now available. For instance, a bioadhesive tablet created by Nagai et al. is industrially accessible under the brand name Aftachw. This item is made out of a twofold layer, with a bioadhesive layer made of hydroxypropyl cellulose and poly(acrylic corrosive) and a lactose non glue backing layer. It is a nearby conveyance arrangement of triamcinolone acetonide for the treatment of aphthous ulcers. A hydrogel-based salve can likewise be used for the skin treatment of specific illnesses in the oral cavity. It tends to be utilized as a medication conveyance gadget, yet additionally as a liposome conveyance vehicle.

The conceivable benefit of liposome conveyance with this treatment is that the utilization of liposomal plans with exemplified medication can prompt an increment of neighborhood, and a diminishing fixation, of fundamental, in view of medication the exemplification of medications with phospholipids. This might give more positive properties to skin use, like decrease of uncontrolled arrival of medications into the blood course and certain unwanted aftereffects, contrasted and the regular salve drug details. Drug execution of three distinct hydrogel-based balms as potential vehicles for liposome conveyance into the oral depression tissues by electron paramagnetic reverberation (EPR). The vehicles utilized were Orabasew (a sodium carboxy methylcellulose, gelatin and gelatin mix in a polyethylene - paraffin base), Carbopol 934Pw and killed poly(MAA-co-methyl methacrylate (MMA)). Liposome containing mucoadhesive balms were ready by just blending multilamellar liposomes with every treatment prediluted with phosphate-cushioned saline of pH 7.4 in the volume proportion of 1:4. An EPR study showed that P(MAA-co-MMA) was the most proper treatment as far as liposomal steadiness in the salve, transport of liposome ensnared atoms from the balm into the oral delicate tissues, and washingout time from oral mucosa or gingvia.

The oral hole can likewise give a valuable area as a vehicle course for vigorously used drugs, since the medications retained from this course sidestep first-pass hepatic digestion. A hydrogel salve containing ingestion enhancers for the buccal conveyance of 17 b-estradiol (E2) to treat osteoporosis. It is notable that the oral organization of E2 brings about extremely low accessibility because of its high first pass impact. Ethanol arrangement containing E2, and glyceryl monolaurate as a retention enhancer, and a watery arrangement of a business carboxyvinyl polymer (Hiviswako 103) and triethanolamine were combined as one to create the hydrogel treatment. In-vivo examinations utilizing hamsters showed that the buccal organization of E2 with this detailing permitted the upkeep of the E2 plasma level at more than 300 ng/ml per cm3 for 7 h, while no essential morphological difference in buccal layer was noticed 7 h after application. New buccal bilayered tablets containing nifedipine and propranolol hydrochloride planned for foundational drug organization. The tablets, including two layers, a medication containing mucoadhesive layer of chitosan with polycarbophil and a support layer of ethylcellulose, were gotten by direct pressure.

The twofold layered structure configuration gave a unidirectional medication conveyance towards the mucosa, and stayed away from a deficiency of medication coming about because of wash-out with spit stream. The striking element of this gadget would be the usage of an in-situ crosslinking response between cationic chitosan and anionic polycarbophil, which advanced upon entrance of the watery medium into the tablet. Because of the crosslinking impact, the tablets showed controlled expanding and delayed drug discharge, and a satisfactory adhesiveness could be acquired.

Drug conveyance in the GI tract:

The GI lot is certainly the most famous course of medication conveyance due to the office of organization of medications for agreeable treatment, and its enormous surface region for foundational retention. It is, notwithstanding, the most complicated course, so flexible methodologies are expected to convey drugs for successful treatment. Like buccal conveyance, hydrogel-based gadgets can be intended to convey medicates locally to the particular destinations in the GI plot. For instance, stomach-explicit anti-infection drug conveyance frameworks for the treatment of Helicobacter pylori contamination in peptic ulcer sickness. For confined anti-infection conveyance in the acidic climate of the stomach, they created cationic hydrogels with pH-delicate expanding and drug discharge properties.

The hydrogels were made out of freeze-dried chitosan-poly (ethylene oxide) (PEO) IPN. pH-subordinate expanding properties and the arrival of two normal anti-microbials, amoxicillin and metronidazole, ensnared in the chitosan-PEO semi-IPN were assessed in compound free recreated gastric liquid (SGF; pH 1.2) and reenacted gastrointestinal liquid (SIF; pH 7.2). The enlarging proportion of the hydrogels after 1 h in SGF was viewed as 16.1, while that in SIF was just 8.60. Moreover, the freeze-dried chitosan-PEO semi-IPN showed quick arrival of the ensnared anti-toxins in SGF due to its profoundly permeable framework structure coming about because of freezedrying. More than 65 and 59% of the ensnared amoxicillin and metronidazole, separately were let out of the hydrogels after 2 h in SGF.

The quick expanding and drug discharge exhibited by these hydrogel plans might be gainful for site-explicit anti-microbial conveyance in the stomach, due to the impediments of the gastric exhausting time. Enzymatically degradable gelatin-PEO semi-IPN with pH-touchy expanding properties for oral medication conveyance. For this situation, the fuse of gelatin in the IPN made it conceivable to enlarge in the acidic pH of the gastric liquid, because of the ionization of the essential amino corrosive deposits of gelatin. The IPN was viewed as corrupted by proteolytic catalysts, like pepsin and pancreatin. Be that as it may, there are many obstacles, remembering protein inactivation by stomach related compounds for the GI parcel, and poor epithelial porousness of these medications.

Notwithstanding, certain hydrogels might conquer a portion of these issues by suitable sub-atomic plan or detailing draws near. For instance, novel peroral measurement types of hydrogel plans with protease inhibitory exercises utilizing Carbopolw (C934P), a poly(acrylic corrosive) item, which has been displayed to inhibitorily affect the hydrolytic movement of trypsin, and its killed freeze-dried change (FNaC934P). They exhibited that two-stage definitions, comprising of the quick gel-shaping FNaC934P and the eficient chemical restraining, however more leisurely expanding, C934P, affected trypsin movement restraint. As of late, oral insulin conveyance utilizing pH responsive complexation hydrogels was accounted for by Lowman *et al*.

The hydrogels used to safeguard the insulin in the cruel, acidic climate of the stomach prior to delivering the medication in the small digestive system were crosslinked copolymers of PMAA with join chains of polyethylene glycol (P(MAAg-EG)). The insulin-containing P(MAA-g-EG) microparticles exhibited solid portion subordinate hypoglycemic impacts in-vivo oral organization concentrates on utilizing both sound and diabetic rodents. The blood glucose levels in these creatures were diminished essentially for something like 8 h because of the assimilation of insulin in the GI parcel. It is actually important that these impacts were seen without the expansion of added substances,

like ingestion enhancers or protease inhibitors. Because of a lower proteolytic action in contrast with that in the small digestive tract, the colonic locale has likewise been considered as a potential retention site for orally managed peptides and proteins.

A few hydrogels are right now being researched as likely gadgets for colon-explicit medication conveyance. These incorporate artificially or truly crosslinked polysaccharides, for example, dextran , amidated gelatin , guar gum and inulin, and azocross-connected poly(acrylic corrosive) . They are intended to be profoundly enlarged or debased within the sight of colonic chemicals or microflora, giving colon explicitness in drug conveyance.

Rectal conveyance:

The rectal course has been utilized to convey many kinds of medications, albeit patient adequacy is variable because of the distress emerging from managed measurements structures. Its essential applications have been for nearby treatment of illnesses related with the rectum, like hemorrhoids. Also, it is notable that medications retained from the lower a piece of the rectum channel into the fundamental dissemination straightforwardly.

Subsequently, the rectal course is a valuable organization course for drugs experiencing weighty first-pass digestion. Traditional suppositories up until recently adjusted as dose structures for rectal organization are solids room temperature, and liquefy or relax at internal heat level. An issue related with rectal organization utilizing regular suppositories is that medications diffusing out of the suppositories in an uncontrolled way can't be adequately held at a particular situation in the rectum, and at times relocate upwards to the colon.

This frequently prompts a variety of the bioavailability of specific medications, specifically, for drugs that go through broad first-pass end. In this unique circumstance, hydrogels might offer a significant method for conquering the issue in regular suppositories, given that they are intended to show an adequate bioadhesive property following their rectal organization. For instance, Ryu *et al.* announced that expanded bioavailability of propranolol subject to broad first-pass digestion was seen by adding specific mucoadhesive polymeric mixtures to poloxamer-based thermally gelling suppositories. Among the mucoadhesive polymeric mixtures tried, polycarbophil and sodium alginate gave the biggest mucoadhesive power and the littlest intrarectal movement to the suppositories, bringing about the biggest bioavailability of propranolol (82.3 and 84.7%, separately).

Explored the likely utilization of xyloglucan gels with a warm gelling property as vehicles for rectal medication conveyance. Xyloglucan handled by the specialists has the sol gel change temperature of around 22 278 °C, and hence, it very well may be a gel at internal heat level; then again, it tends to be handily controlled since it can act as a fluid at room temperature. *In-vivo* rectal organization of xyloglucan gels containing indomethacin utilizing hares showed a wellcontrolled drug plasma focus time profile without diminished bioavailability, when contrasted with business indomethacin suppositories. Keeping away from rectal aggravation brought about by vehicles is one more significant issue in rectal medication conveyance. Both xyloglucan, propranolol gels items, portrayed above, uncovered no proof of mucosal aggravation after rectal organization. An essentially diminished bothering by rectal hydrogels arranged with water-dissolvable dietary strands, thickener and beetle bean gum, was likewise revealed by Watanabe *et al*.

Ocular Delivery:

In visual medication conveyance, numerous physiological limitations forestall a fruitful medication conveyance to the eye because of its defensive systems, like successful tear seepage, squinting and low penetrability of the cornea. Consequently, ordinary eye drops containing a medication arrangement will more often than not be dispensed with quickly from the eye, and the medications managed display restricted ingestion, prompting poor ophthalmic bioavailability. Furthermore, their momentary maintenance frequently brings about an incessant dosing routine to accomplish the remedial viability for an adequately lengthy span.

These provokes have inspired specialists to foster medication conveyance frameworks that give a drawn out visual home season of medications. Certain dose structures, like suspensions and balms, can be held in the eye, albeit these occasionally give patients an unsavory inclination as a result of the qualities of solids and semi-solids. Because of their flexible properties, hydrogels can likewise address a visual seepage safe gadget. Moreover, they might offer better inclination, with to a lesser degree a dirty sensation to patients. Specifically, in-situ framing hydrogels are appealing as a visual medication conveyance framework due to their office in dosing as a fluid, and their drawn out maintenance property as a gel subsequent to dosing. Cohen et al. fostered an in-situ gelling arrangement of alginate with high guluronic corrosive items for the ophthalmic conveyance of pilocarpine.

This framework fundamentally broadened the length of the tension decreasing impact of pilocarpine to 10 h, contrasted with 3 h when pilocarpine nitrate was dosed as an answer. Rheological assessment of Gelritew, deacetylated gellan gum which gels upon instillation in the eye because of the presence of cations. Their review showed that a high pace of the sol/gel progress of Gelritew in-situ gels results in lengthy precorneal contact times. Silicone elastic/hydrogel composite ophthalmicinserts. Poly(acrylic corrosive) or poly (MAA) IPN was joined on the outer layer of the supplements to accomplish a mucoadhesive property. The visual maintenance of IPN united embeds was fundamentally higher as for ungrafted ones. An in-vivo concentrate on utilizing bunnies showed a drawn out arrival of oxytetracycline from the supplements for a few days.

Transdermal conveyance Medication conveyance to the skin has been generally led for skin utilization of dermatological medications to treat skin illnesses, or for sterilization of the actual skin. Lately, a transdermal course has been considered as a potential site for the fundamental conveyance of medications. The potential advantages of transdermal medication conveyance incorporate that medications can be conveyed for a long term at a steady rate, that drug conveyance can be effectively hindered on request by basically eliminating the gadgets, and that medications can sidestep hepatic ®rst-pass digestion. Moreover, due to their high water content, enlarged hydrogels can give a superior inclination to the skin in contrast with traditional balms and patches. Adaptable hydrogel-based gadgets for transdermal conveyance have been proposed up until this point. Sun *et al*. conceived composite layers containing cross connected PHEMA with a nonwoven polyester support.

Contingent upon the planning conditions, the composite films can be customized to give a penetration transition going from 4 to 68 mg/cm2 per h for dynamite. A Carbopol 934w-based detailing containing phosphatidylcholine liposomes (liposome-gel) was ready by Kim et al.. In their review, the skin assimilation conduct of hydrocortisone containing liposome-gel was surveyed. Gayet and Fortier [announced hydrogels acquired from the copolymerization of cow-like serum egg whites (BSA) and Stake. Because of their high water content more than 96%, permitting the arrival of hydrophilic and hydrophobic medications, their utilization as controlled discharge gadgets in the field of wound dressing was proposed as the likely use of the BSA-Stake hydrogels. Extensive examinations on in-situ photopolymerizable hydrogels produced using terminally diacrylated ABA block copolymers of lactic corrosive oligomers (A) and Stake (B) for obstructions and neighborhood drug conveyance in the control of wound mending have been done by Hubbell.

Late examination patterns in transdermal applications are zeroing in on electrically helped conveyance, utilizing iontophoresis and electroporation. A few hydrogel-based plans are being explored as vehicles for transdermal iontophoresis to get the upgraded pervasion of luteinizing chemical delivering chemical, sodium nonivamide acetic acid derivation, nicotine and enoxacin. Then again, a methyl cellulose-based hydrogel was utilized as a gooey ultrasonic coupling mechanism for transdermal sonophoresis helped with an air conditioner current, bringing about an upgraded saturation of insulin and vasopressin across human skin in vitro.

Subcutaneous conveyance:

As depicted through Segments 1-4, hydrogels have a wide assortment of conceivable drug applications. Among them, their significant application might be tracked down in implantable Subcutaneously embedded therapeutics. Exogenous materials may pretty much inspire possibly bothersome body reactions, like irritation, carcinogenecity and immunogenecity. The fact that makes materials implantable makes in this manner, biocompatibility an essential. Because of their high water content, hydrogels are by and large viewed as biocompatible materials. They additionally give a few promising properties: mechanical bothering , upon negligible in-vivo implantation, because of their delicate, flexible properties;, counteraction of protein adsorption and cell bond emerging from the low interfacial pressure among water and hydrogels; expansive worthiness for individual medications with various hydrophilicities and sub-atomic sizes; and exceptional conceivable outcomes (crosslinking thickness and enlarging) to control the arrival of consolidated drugs. A portion of these may offer a benefit for the conveyance of specific sensitive medications, like peptides and proteins.

Giammona *et al*. grown new hydrogels beginning from the synthetic reticulation polyasparthydrazide of (PAHy) glutaraldehyde. a,b by PAHy is a new watersoluble macromolecule, orchestrated from a polysuccinimide by response with hydrazine. Histological investigation uncovered that this hydrogel was latent when embedded subcutaneously into rodents. A few hydrogel definitions for the subcutaneous conveyance of anticancer medications have been likewise proposed. For instance, crosslinked PHEMA with great biocompatibility was applied to cystabine (Ara-C) and methotrexate. Poly(AAm-co monomethyl or monopropyl itaconate) created by Blanco's gathering was utilized for the controlled arrival of Ara-C and 5-fluorouracil.

Current examinations on implantable hydrogels have been coordinated towards the advancement of biodegradable frameworks requiring no subsequent careful expulsion once the medication supply is drained. A bioerodible hydrogel in light of a semi-IPN structure made out of a poly(1-caprolactone) and Stake macromer ended with acrylate bunches was conceived by Cho *et al*.. Long haul consistent delivery north of 45 days of clonazepam ensnared in the semi-IPN was accomplished *in vivo.*

As of late, two sorts of novel degradable Stake hydrogels for the controlled arrival of proteins were created by Zhao and Harris. One sort is ready by a polycondensation response between difunctional Stake acids and expanded Stake polyols. Endless supply of the subsequent ester linkages, these gels corrupt into just Endlessly stake subordinates. The other is Stake based hydrogels having utilitarian gatherings in which protein medications can be covalently appended to the gel network through ester linkage. Consequently, the arrival of the protein drugs immobilized would be constrained by the hydrolysis of the ester linkage between the gel and the protein, trailed by the dissemination of the protein out of the gel, and by the debasement of the gel. Broad exploration endeavors on degradable dextran hydrogels have been completed by Hennink and his colleagues. These hydrogels depend on acrylate subordinates of dextran. In their examinations, the use of the hydrogels to the controlled arrival of protein was entirely explored. Biodegradable crosslinked dextran hydrogels containing Stake (Stake Dex) were accounted for by Moriyama and Yui. Insulin discharge from these hydrogels was managed by the surface corruption microdomain-organized of Stake Dex.

Tissue Engineering:

The micronized hydrogels (microgels) have been utilized to convey macromolecules like phagosomes into cytoplasm of antigen-introducing cells. The delivery is a result of acidic circumstances. Such hydrogels form themselves to the example of films of the tissues and have adequate mechanical strength. This property of hydrogels is additionally utilized in ligament fixing.

Dermal Delivery:

Hydrogels have been utilized to convey dynamic part like Desonide which is a manufactured corticosteroid generally utilized as a calming. Rather than ordinary creams, the hydrogels have been figured out for better quiet consistence. These hydrogels have saturating properties hence scaling and dryness isn't normal with this medication conveyance framework. Antifungal definitions like cotrimazole has been created as hydrogel formuhydrlation for vaginitis. It has shown preferred assimilation over regular cream plans.

Protein drug conveyance:

Interleukins which are traditionally given as infusion are presently given as hydrogels. These hydrogels have shown better understanding consistence. The hydrogels structure insitu polymeric organization and delivery proteins gradually. These are biodegradable and biocompatible too. (28-80)

Utilization of hydrogels to fix bone substitutions:

Given are muscular clasp and substitutions like nails, screws, pins, hip and knee substitutions, and so on, covered with hydrogels and biocompatible/biodegradable different materials which extend within the sight of fluids. Valuable covering materials incorporate methacrylate, hyaluronic corrosive esters, and crosslinked esters of hyaluronic corrosive coming about because of the esterification of hyaluronic corrosive with polyhydric alcohols Substitutions can be subsequently covered, even those made of hardened steel, metal amalgams, titanium, or cobaltchromium, treatment of the surfaces to further develop metal-polymer adhesion. (81-83) Hydrogels are polymeric organizations that assimilate enormous amounts of water while staying insoluble in fluid arrangements because of compound or physical crosslinking of individual polymer chains. They look like normal living tissue more than some other class of engineered biomaterials because of their high water content; besides, the high water content of the materials adds to their biocompatibility.

Hydrogels show negligible propensity to adsorb proteins from body liquids in light of their low interfacial pressure. Further, the capacity of particles of various sizes to diffuse into (drug stacking) and out of (drug discharge) hydrogels permits the conceivable utilization of dry or enlarged polymeric organizations as medication conveyance frameworks for oral, nasal, buccal, rectal, vaginal, visual and parenteral courses of organization. Basic gooey arrangements which go through no alterations after organization.

The utilization of preformed hydrogels actually has disadvantages that can restrict their advantage for ophthalmic medication conveyance or as tear substitutes. They don't permit precise and reproducible organization of amounts of medications and, after organization; they frequently produce obscured vision, crusting of eyelids, and lachrymation. These are polymers blessed with a capacity to grow in water or fluid solvents and prompt a fluid gel change.

At present; two gatherings of hydrogels are recognized, specifically preformed and in situ framing gels. Preformed hydrogels can be characterized as consequently in situ hydrogels can be imparted as eye drops and go through a quick gelation when in touch with the eye. In situ-framing hydrogels are fluid upon instillation and go through gradually ease progress in the visual circular drive to shape viscoelastic gel and this gives a reaction to ecological changes. Three techniques have been utilized to cause stage progress on a superficial level: change in temperature, pH, and electrolyte structure.

Expansion in arrangement thickness by utilizing polymers further develops maintenance of item on the corneal surface. All the more as of late, the way to deal with improve precorneal maintenance depends on the utilization of mucoadhesive polymers. The guideline for utilization of bioadhesive vehicles depends on their capacity to interface with the mucin covering layer present at the eye surface. The polymers decided to plan ophthalmic hydrogels ought to meet a few explicit rheological qualities. It is by and large very much acknowledged that the instillation of a definition ought to impact tear conduct as little as could be expected. Since tears gave a pseudoplastic conduct, pseudoplastic vehicles would be more

reasonable as contrast with Newtonian definitions, which have a consistent thickness free of the shear rate, while pseudoplastic arrangement display diminished consistency with expanding shear rate, in this manner offering brought down thickness during squinting and steadiness of the tear film during obsession.

Drug discharge from hydrogels:

As examined in the past segments, hydrogels have a one of a kind blend of qualities that make them valuable in drug conveyance applications. Because of their hydrophilicity, hydrogels can soak up a lot of water. Consequently, the atom discharge systems from hydrogels are totally different from hydrophobic polymers. Both straightforward and modern models have been recently evolved to foresee the arrival of a functioning specialist from a hydrogel gadget as a component of time. These models depend on the rate restricting step for controlled discharge and are subsequently ordered enlarging as dissemination, and artificially controlled system.

Smart hydrogels:

"Shrewd" hydrogels, or boosts touchy hydrogels, are totally different from idle hydrogels in that they would be able "sense" changes in ecological properties like pH and temperature and answer by expanding or diminishing their level of enlarging. The volume-changing way of behaving of "shrewd" hydrogels is especially valuable in drug conveyance applications as medication delivery can be set off upon ecological changes. These intelligent or smart polymers assume significant part in drug conveyance since they might direct where a medication is conveyed, yet additionally when and with which stretch it is delivered. The improvements that actuate different reactions of the hydrogel frameworks incorporate physical (temperature) or synthetic (pH, particles) ones. In this, polymers might go through work progress in presence of different particles. Gellan gum monetarily accessible as Gelrite® is an anionic polysaccharide that goes through in situ gelling within the sight of mono-and divalent cations, including Ca^{2+}, Mg^{2+}, K^{+} and Na^{+}. Gelation of the low-methoxy gelatins can be brought about by divalent cations, particularly Ca^{2+}. System and instances of boosts delicate hydrogels are given in **Table** (84-91).

Oral mucoadhesive conveyance frameworks:

Mucoadhesion can be characterized as a state in which two parts, of which one is of organic beginning are kept intact for expanded timeframes by the assistance of interfacial powers. For the most part, bioadhesion is a term which comprehensively incorporates glue communications with any natural or organically inferred substance, and mucoadhesion is utilized when the security is framed with a mucosal surface. (92)

Polymers utilized for oral mucoadhesive medication conveyance

1. Hydrogels:

These swell when in touch with water and stick to tne bodily fluid film. These are additionally grouped by their charge

Anionic polymers-carbopol, polyacrylates

Cationic polymers-chitosan

Brain/nonionic polymers-eudragit analogues. (93-96)

1.1. Chitosan:

It is a cationic polymer(polysaccharide),it is delivered by the deacetylation of chitin. Chitosan is acquiring significance in the improvement of mucoadhesive medication conveyance framework due to its great biocompatibility, biodegradability and non poisonous nature. It ties to the mucosa by means of ionic connections between the amino gathering and sialic corrosive deposits. Chitosan being direct gives more noteworthy polymer chain adaptability. Chitosan and its metaboloized subsidiaries are immediately dispensed with by the kidney. (97 98).

Mechanism of mucoadhesion:

As expressed, mucoadhesion is the attachement of the medication alongside a reasonable transporter to the mucous film. Mucoadhesion is a complicated peculiarity which includes wetting, adsorption and interpenetration of Mucoadhesion has polymer chains. The accompanying system

1. Private contact between a bioadhesive and a film (wetting or enlarging peculiarity)

2. Entrance of the bioadhesive into the tissue or into the outer layer of the mucous membrane (interpenetration). Home time for most mucosal courses is under an hour and regularly in minutes; it very well may be expanded by the expansion of a cement specialist in the conveyance framework which is helpful to limit the conveyance framework and builds the contact time at the site of absorption. (5) The specific component of mucoadhesion isn't known however an acknowledged hypothesis expresses that a nearby contact between the mucoadhesive polymer and mucin happens which is trailed by the interpenetration of polymer and mucin. The attachment is drawn out because of the arrangement of van der vaals powers, hydrogen bonds and electrostatic bonds. (99-102)

Conclusion:

Hydrogels are crosslinked polymer networks that retain significant measures of fluid arrangements. Because of their high water content, these gels look like normal living tissue more than some other kind of manufactured biomaterial. Hydrogels have a novel blend of qualities that make them helpful in drug conveyance applications. Because of their hydrophilicity, hydrogels can soak up a lot of water. In this manner, the particle discharge components from hydrogels are altogether different from hydrophobic polymers.

Hydrogels have been utilized to convey dynamic part like Desonide which is an engineered corticosteroid typically utilized as a mitigating. Rather than traditional creams, the hydrogels have been formed for better understanding consistence. These hydrogels have saturating properties thusly scaling and dryness isn't normal with this medication conveyance framework.

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References:

1. Kaetsu I, Uchida K, Morita Y, Okubo M. Synthesis of electro-responsive hydrogels by radiation polymerization of sodium acrylate. Int. J. Radiat. Appl. Instrum. C Radiat. Phys. Chem. 40(2), 157–160 (1992).
2. Mamada A, Tanaka T, Kungwatchakun D, Irie M .Photoinduced phase transition of gels. Macromolecules 23(5), 1517–1519 (1990).
3. Suzuki A, Ishii T, Maruyama Y. Optical switching in polymer gels. J. Appl. Phys. 80(1), 131–136 (1996).
4. Masteikova R, Chalupova Z, Sklubalova Z. Stimuli-sensitive hydrogels in controlled and sustained drug delivery. Med. Lith. 39(2), 19–24 (2003).
5. Suzuki A, Tanaka T. Phase transition in polymer gels induced by visible light. Nature 346(6282), 345 (1990).
6. Kulkarni RV, Sa B. Enteric delivery of ketoprofen through functionally modified poly (acrylamide-grafted-xanthan)-based pH-sensitive hydrogel beads: preparation, in vitro and in vivo evaluation. Journal of drug targeting. 16(2), 167–77 (2008).
7. Ghasemi Tahrir F, Ganji F, Mani AR, Khodaverdi E. In vitro and in vivo evaluation of thermosensitive chitosan hydrogel for sustained release of insulin. Drug Delivery 23(3), 1028–36 (2016).
8. Shantha K, Harding D. Synthesis, characterisation and evaluation of poly [lactose acrylate-N-vinyl-2-pyrrolidinone] hydrogels for drug delivery. Eur. Polym. J. 39(1), 63–8 (2003).
9. Altinisik A, Yurdakoc K. Chitosan/poly (vinyl alcohol) hydrogels for amoxicillin release. Polymer Bulletin

71(3), 759–74 (2014).

10. Khade S, Behera B, Sagiri S, Singh V, Thirugnanam A, Pal K et al. Gelatin–PEG based metronidazole-loaded vaginal delivery systems: preparation, characterization and in vitro antimicrobial efficiency. Iranian Polymer J. 23(3), 171–84 (2014).
11. Abd El-Hady A, Abd El-Rehim HA. Production of prednisolone by Pseudomonas oleovorans cells incorporated into PVP/PEO radiation crosslinked hydrogels. BioMed Res. Int. 2004(4), 219–26 (2004).
12. Rao KM, Mallikarjuna B, Krishna Rao K, Sudhakar K, Rao KC, Subha M. Synthesis and characterization of pH sensitive poly (hydroxy ethyl methacrylate-co-acrylamidoglycolic acid) based hydrogels for controlled release studies of 5-fluorouracil. Int. J. Polymeric Mat.Polymeric Biomat. 62(11), 565–71 (2013).
13. Kamei N, Morishita M, Chiba H, Kavimandan NJ, Peppas NA, Takayama K. Complexation hydrogels for intestinal delivery of interferon β and calcitonin. J. Control. Rel. 134(2), 98–102 (2009).
14. El-Ghaffar MA, Hashem M, El-Awady M, Rabie A. pH-sensitive sodium alginate hydrogels for riboflavin controlled release. Carbohydrate Polymers 89(2), 667–75 (2012).
15. Hamidi M, Azadi A, Rafiei P. Hydrogel nanoparticles in drug delivery. Adv. Drug Deliv. Rev. 60(15), 1638–1649 (2008).
16. Cruise GM, Scharp DS, Hubbell JA. Characterization of permeability and network structure of interfacially photopolymerized poly (ethylene glycol) diacrylate hydrogels. Biomaterials 19(14), 1287–1294 (1998).
17. Mason MN, Metters AT, Bowman CN, Anseth KS .Predicting controlled-release behavior of degradable PLA-b-PEG-b-PLA hydrogels. Macromolecules 34(13), 4630–4635 (2001).
18. Ferreira JA, de Oliveira P, Grassi M, Romanazzi G. Drug release from viscoelastic swelling polymeric platforms. SIAM J. Appl. Math. 78(3), 1378–1401 (2018).
19. Caccavo D. An overview on the mathematical modeling of hydrogels' behavior for drug delivery systems. Int. J. Pharm. 560, 175–190 (2019).
20. Lacey RE, Tanquary AC. Controlled Release of Biologically Active Agents. Springer, (1974).
21. Siepmann J, Peppas N. Hydrophilic matrices for controlled drug delivery: an improved mathematical model to predict the resulting drug release kinetics (the "sequential layer" model). Pharm Res. 17(10), 1290–1298 (2000).
22. Lee KY, Mooney DJ. Alginate: properties and biomedical applications. Prog. Polym. Sci. 37(1), 106–126 (2012).
23. Salehi A, Zhao J, Cabelka TD, Larson RG. A unified multicomponent stress-diffusion model of drug release from non-biodegradable polymeric matrix tablets. J. Control. Rel. 224, 43–58 (2016).
24. Hong X, Wu Z, Chen L *et al*. Hydrogel microneedle arrays for transdermal drug delivery. Nano-Micro Lett. 6(3), 191–199 (2014).
25. Harrison IP, Spada F. Hydrogels for atopic dermatitis and wound management: a superior drug delivery vehicle. Pharmaceutics. 10(2), 71 (2018).
26. Zhai J, Mantaj J, Vllasaliu D. Ascorbyl palmitate hydrogel for local, intestinal delivery of macromolecules. Pharmaceutics. 10(4), 188 (2018).
27. Zag´ orska-Dziok M, Sobczak M. Hydrogel-based active substance release systems for cosmetology and dermatology application: a review. 12(5), 396 (2020).
28. Li J, Wu C, Chu PK, Gelinsky M. 3D printing of hydrogels: rational design strategies and emerging biomedical applications. Mater. Sci. Eng. R. Rep. 140, 100543 (2020).
29. Singh B, Sharma N, Chauhan N. Synthesis, characterization and swelling studies of pH responsive psyllium and

methacrylamide based hydrogels for the use in colon specific drug delivery. Carbohydr. Polym. 69(4), 631–643 (2007).

30. Das A, Wadhwa S, Srivastava A. Cross-linked guar gum hydrogel discs for colon-specific delivery of ibuprofen: formulation and in vitro evaluation. Drug Deliv. 13(2), 139–142 (2006).
31. Van Tomme SR, Storm G, Hennink WE. In situ gelling hydrogels for pharmaceutical and biomedical applications. Int. J. Pharm. 355(1–2), 1–18 (2008).
32. Hiemstra C, Zhong Z, Van Tomme SR *et al*. *In vitro* and *in vivo* protein delivery from in situ forming poly (ethylene glycol)–poly (lactide) hydrogels. J. Control. Rel. 119(3), 320–327 (2007).
33. Cooper RC, Yang H. Hydrogel-based ocular drug delivery systems: emerging fabrication strategies, applications, and bench-to-bedside manufacturing considerations. J. Control. Rel. 306, 29–39 (2019).
34. Torres-Luna C, Fan X, Domszy R *et al*. Hydrogel-based ocular drug delivery systems for hydrophobic drugs. Eur. J. Pharm. Sci. 154, 105503 (2020).
35. Lynch CR, Kondiah PP, Choonara YE et al. Hydrogel biomaterials for application in ocular drug delivery. Front. Bioeng. Biotechnol. 8, 228 (2020).
36. Miyazaki S, Suzuki S, Kawasaki N *et al*. In situ gelling xyloglucan formulations for sustained release ocular delivery of pilocarpine hydrochloride. Int. J. Pharm. 229(1–2), 29–36 (2001).
37. Burgalassi S, Chetoni P, Panichi L *et al*. Xyloglucan as a novel vehicle for timolol: pharmacokinetics and pressure lowering activity in rabbits. J. Ocul. Pharmacol. Ther. 16(6), 497–509 (2000).
38. Xinming L, Yingde C, Lloyd AW *et al.* Polymeric hydrogels for novel contact lens-based ophthalmic drug delivery systems: a review. Contact Lens Anterio. 31(2), 57–64 (2008).
39. Wang Y, Xu H, Wang J *et al*. Development of a thermally responsive nanogel based on chitosan–poly (N-isopropylacrylamide-co-acrylamide) for paclitaxel delivery. J. Pharm. Sci. 103(7), 2012–2021 (2014).
40. Subramanian B, Agarwal T, Roy A *et al*. Synthesis and characterization of PCL-DA: PEG-DA based polymeric blends grafted with SMA hydrogel as bio-degradable intrauterine contraceptive implant. Mater.Sci. Engin. C. 116, 111159 (2020).
41. Mennini N, Casella G, Cirri M *et al*. Development of cyclodextrin hydrogels for vaginal delivery of dehydroepiandrosterone. J. Pharm. Pharmacol. 68(6), 762–771 (2016).
42. Wang X, Wang J, Wu W, Li H. Vaginal delivery of carboplatin-loaded thermosensitive hydrogel to prevent local cervical cancer recurrence in mice. Drug Deliv. 23(9), 3544–3551 (2016).
43. Vani´ c ˇ Z, Hurler J, Ferderber K *et al*. Novel vaginal drug delivery system: deformable propylene glycol liposomes-in-hydrogel. J. Liposome Res. 24(1), 27–36 (2014).
44. Chang JY, Oh Y-K, Kong HS *et al.* Prolonged antifungal effects of clotrimazole-containing mucoadhesive thermosensitive gels on vaginitis. J. Control. Release. 82(1), 39–50 (2002).
45. Adams TS, Crook T, Cadier MA. A late complication following the insertion of hydrogel breast implants. J. Plast. Reconstr. Aesthet. 60(2), 210–212 (2007).
46. Brunner CA, Gr¨ oner RW. Carboxy-methyl-cellulose hydrogel-filled breast implants– an ideal alternative? A report of five years' experience with this device. Can. J. Plast. Surg. 14(3), 151–154 (2006).
47. Cascone S, Lamberti G. Hydrogel-based commercial products for biomedical applications: a review. Int. J. Pharm. 573, 118803 (2020).
48. Lee SC, Kwon IK, Park K. Hydrogels for delivery of bioactive agents: a historical perspective. Adv. Drug Deliv. Rev. 65(1), 17–20 (2013).

49. Bajpai S, Saggu SS. Insulin release behavior of poly (methacrylamide-co-N-vinyl-2-pyrrolidone-co-itaconic acid) hydrogel: an interesting probe. Part II. J MACROMOL SCI A. 44(2), 153–157 (2007).
50. Ajji Z, Othman I, Rosiak J. Production of hydrogel wound dressings using gamma radiation. Nucl. Instrum. Meth. B. 229(3–4), 375–380 (2005).
51. Gupta A, Kowalczuk M, Heaselgrave W et al. The production and application of hydrogels for wound management: a review. Eur. Polym. J. 111, 134–151 (2019).
52. Ganji F, Vasheghani-Farahani E. Hydrogels in controlled drug delivery systems. Iran Polym. J. 18(1), 63–88 (2009).
53. Khan S, Ullah A, Ullah K, Rehman N-u. Insight into hydrogels. Des. Monomers Polym. 19(5), 456–478 (2016).
54. Sandeep C, Harikumar S, Kanupriy A. Hydrogels: a smart drug delivery system. Int. J. Res. Pharm. Chem. 2, 603–614 (2012).
55. ManthaS, Pillai S, Khayambashi P *et al*. Smart hydrogels in tissue engineering and regenerative medicine. Materials. 12(20), 3323 (2019).
56. Shoukat H, Pervaiz F, Noreen S et al. Fabrication and evaluation studies of novel polyvinylpyrrolidone and 2-acrylamido-2-methylpropane sulphonic acid-based crosslinked matrices for controlled release of acyclovir. Polym Bull. 1–23 (2019).
57. Lin C-C, Metters AT. Hydrogels in controlled release formulations: network design and mathematical modeling. Adv. Drug Deliv. Rev. 58(12–13), 1379–1408 (2006).
58. Hoffman AS. Hydrogels for biomedical applications. Ann. N Y Acad. Sci. 944(1), 62–73 (2001).
59. Garud A, Singh D, Garud N. Solid lipid nanoparticles (SLN): method, characterization and applications. Int. Curr. Pharm. 1(11), 384–393 (2012).
60. Sionkowska A. Current research on the blends of natural and synthetic polymers as new biomaterials. Prog. Polym. Sci. 36(9), 1254–1276 (2011).
61. Slaughter BV, Khurshid SS, and Fisher OZ *et al.* Hydrogels in regenerative medicine. Adv Mater. 21(32–33), 3307–3329 (2009).
62. Deligkaris K, Tadele TS, Olthuis W, van den Berg A. Hydrogel-based devices for biomedical applications. Sensor. Actuat B–Chem.147 (2), 765–774 (2010).
63. Hoffman AS. Hydrogels for biomedical applications. Adv. Drug Deliv. Rev. 64, 18–23 (2012).
64. Gulrez SK, Al-Assaf S, Phillips GO. Hydrogels: methods of preparation, characterisation and applications. Progress in Molecular and Environmental Bioengineering– From Analysis and Modeling to Technology Applications. InTech (2011).
65. Ali A, Ahmed S. Recent advances in edible polymer based hydrogels as a sustainable alternative to conventional polymers. J. Agric. Food Chem. 66(27), 6940–6967 (2018).
66. Zhao QS, Ji QX, Xing K et al. Preparation and characteristics of novel porous hydrogel films based on chitosan and glycerophosphate. Carbohydr. Polym. 76(3), 410–416 (2009).
67. Ebara M, Kotsuchibashi Y, Uto K et al. Smart hydrogels. Smart Biomaterials. Springer, 9–65 (2014).
68. Watanabe T, Ohtsuka A, Murase N, Barth P, Gersonde K. NMR studies on water and polymer diffusion in dextran gels. Influence of potassium ions on microstructure formation and gelation mechanism. Magn Reson Med. 35(5), 697–705 (1996).
69. Lalev´ ee G, David L, Montembault A et al. Highly stretchable hydrogels from complex coacervation of natural polyelectrolytes. Soft Matter. 13(37), 6594–6605 (2017).

70. WangJ, Sun S, Wu B *et al*. Processable and luminescent supramolecular hydrogels from complex coacervation of polycations with lanthanide coordination polyanions. Macromolecules. 52(22), 8643–8650 (2019).
71. Liu T, Jiao C, Peng X et al. Super-strong and tough poly (vinyl alcohol)/poly (acrylic acid) hydrogels reinforced by hydrogen bonding. J. Mater. Chem. B. 6(48), 8105–8114 (2018).
72. Song G, Zhang L, He C et al. Facile fabrication of tough hydrogels physically cross-linked by strong cooperative hydrogen bonding. Macromolecules. 46(18), 7423–7435 (2013).
73. Jayaramudu T, Raghavendra GM, Varaprasad K et al. 5-Fluorouracil encapsulated magnetic nanohydrogels for drug-delivery applications. J. Appl. Polym. 133(37), (2016).
74. Plieva FM, Karlsson M, Aguilar MR et al. Pore structure of macroporous monolithic cryogels prepared from poly (vinyl alcohol). J. Appl. Polym. 100(2), 1057–1066 (2006).
75. Hassan CM, Peppas NA. Structure and applications of poly (vinyl alcohol) hydrogels produced by conventional crosslinking or by freezing/thawing methods. Biopolymers· PVA Hydrogels, Anionic Polymerisation Nanocomposites. Springer, 37–65 (2000).
76. Yu Z, Li Y, Feng Z et al. Cu+-containing physically crosslinked chitosan hydrogels with shape memory. Express Polymer. Lett. 13(9), 785–793 (2019).
77. Chang C, Zhang L, Zhou J, et al. Structure and properties of hydrogels prepared from cellulose in NaOH/urea aqueous solutions. Carbohydr Polym. 82(1), 122–127 (2010).
78. Chang C, Zhang L. Cellulose-based hydrogels: present status and application prospects. Carbohydr. Polym. 84(1), 40–53 (2011).
79. Varaprasad K, Raghavendra GM, Jayaramudu T et al. A mini review on hydrogels classification and recent developments in miscellaneous applications. Mater. Sci. Eng. C. 79, 958–971 (2017).
80. Varaprasad K, Mohan YM, Ravindra S et al. Hydrogel–silver nanoparticle composites: a new generation of antimicrobials. J. Appl. Polym. 115(2), 1199–1207 (2010).
81. Jayaramudu T, Raghavendra GM, and Varaprasad K *et al*. Development of novel biodegradable Au nanocomposite hydrogels based on wheat: for inactivation of bacteria. Carbohydr. Polym. 92(2), 2193–2200 (2013).
82. Wang M, Fang Y, Hu D. Preparation and properties of chitosan-poly (N-isopropylacrylamide) full-IPN hydrogels. React. Funct. Polym. 48(1–3), 215–221 (2001).
83. Maitra J, Shukla VK. Cross-linking in hydrogels-a review. Am.J.Polym.Sci.4 (2), 25–31 (2014).
84. Sperinde JJ, Griffith LG. Synthesis and characterization of enzymatically-cross-linked poly (ethylene glycol) hydrogels. Macromolecules. 30(18), 5255–5264 (1997).
85. Iftime M-M, Morariu S, Marin L. Salicyl-imine-chitosan hydrogels: supramolecular architecturing as a crosslinking method toward multifunctional hydrogels. Carbohydr. polym. 165, 39–50 (2017).
86. Ailincai D, Tartau Mititelu L,Marin L. Drug delivery systems based on biocompatible imino-chitosan hydrogels for local anticancer therapy. Drug Deliv. 25(1), 1080–1090 (2018).
87. Iftime MM. Marin L. Chiral betulin-imino-chitosan hydrogels by dynamic covalent sonochemistry. Ultrason. Sonochem. 45, 238–247 (2018).
88. Iftime M-M, Tartau LM, Marin L. New formulations based on salicyl-imine-chitosan hydrogels for prolonged drug release. Int. J. Biol. Macromol. 160, 398–408 (2020).
89. Ailincai D, Mititelu-Tartau L, Marin L. Citryl-imine-PEG-ylated chitosan hydrogels– promising materials for drug delivery applications. Int. J. Biol. Macromol. 162, 1323–1337 (2020).

90. Zhang J, XiaoH, Li N *et al*. Synthesis and characterization of super-absorbent hydrogels based on hemicellulose. J. Appl. Polym. 132(34), (2015).
91. NiuH, Wang F, Weiss R. Hydrophobic/hydrophilic triblock copolymers: synthesis and properties of physically cross-linked hydrogels. Macromolecules. 48(3), 645–654 (2015).
92. Mahdavinia GR, Etemadi H, Soleymani F. Magnetic/pH-responsive beads based on caboxymethyl chitosan and κ-carrageenan and controlled drug release. Carbohydr Polym. 128, 112–121 (2015).
93. Traitel T, Cohen Y, Kost J. Characterization of glucose-sensitive insulin release systems in simulated in vivo conditions. Biomaterials. 21(16), 1679–1687 (2000).
94. Pluta J, Karolewicz B. Hydrogels: properties and application in the technology of drug form. I. The characteristic hydrogels. Polim. Med. 34(2), 3–19 (2004).
95. Lee Y-J, Pruzinsky SA. Braun PV. Glucose-sensitive inverse opal hydrogels: analysis of optical diffraction response. Langmuir. 20(8), 3096–3106 (2004).
96. Yetisen AK, Jiang N, Fallahi A et al. Glucose-sensitive hydrogel optical fibers functionalized with phenylboronic acid. Adv Mater. 29(15), 1606380 (2017).
97. Zhang R, Tang M, Bowyer A et al. Synthesis and characterization of a D-glucose sensitive hydrogel based on CM-dextran and concanavalin A. React. Funct. Polym. 66(7), 757–767 (2006).
98. Prabaharan M, Mano JF. Stimuli-responsive hydrogels based on polysaccharides incorporated with thermo-responsive polymers as novel biomaterials. Macromol. Biosci. 6(12), 991–1008 (2006).
99. Ramanan RMK, Chellamuthu P, Tang L, Nguyen KT. Development of a temperature-sensitive composite hydrogel for drug delivery applications. Biotechnol. Prog. 22(1), 118–125 (2006).
100. Shim WS, KimSW, Lee DS. Sulfonamide-based pH-and temperature-sensitive biodegradable block copolymer hydrogels. Biomacromolecules. 7(6), 1935–1941 (2006).
101. Miyata T, Asami N, Uragami T. Preparation of an antigen-sensitive hydrogel using antigen−antibody bindings. Macromolecules. 32(6), 2082–2084 (1999).
102. LuZR, Kopeˇ ckov´aP, Kopeˇ cek J. Antigen responsive hydrogels based on polymerizable antibody Fab fragment. Macromol. Biosci. 3(6), 296–300 (2003).

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A Review on Anthelmintics and Heterocyclic moieties

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Abstract:
Parasites have been of concern to the medical field for centuries and the helminthes considerable problems for human being and animals. A large number of medicinal plants are claimedto possess anthelmintic property in traditional systems of medicine and are also utilized by ethnic. Anthelmintic activity is associated with diverse heterocyclic nucleus such as piperazine, pyrimidine, quinoline, azoles (imidazole, 1, 2, 4 triazole,isoxazole, pyrazole, thiazole, thiadiazole), quinazoline, 1,5-benzodiazepines and benzimidazols.

Key words: Anthelmintic activity, earthworms, tapeworms, hookworms, heterocyclic moieties.

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Heterocyclic moieties-a profile of anthelmintics:

Introduction:

Parasitic nematodes have successfully survived the impressive wave of anthelmintic drugs, which were developed during the last five decades and since then have been used in billions of treatments all over the word.There is no major worm species that can be considered to be eradicated, drspite this systematic over kill. Nevertheless through the strategic use of anthelmintics it has been possible to drastically increase the productivity of grazing livestock and to largely reduce gastro-intestinal infection in companion animals.

Today, anthelmintics play a key role in the control of gastro-intestinal helminthes in livestock and this will most probably remain as such in the foreseeable future. However, increasing problems with populations that have developed resistance against anthelmintics severely threaten the beneficial exploitation of this instrument. A thorough understanding of the mechanisms by which nematodes achieve resistance is essential for better and more sustainable use of the anthelmintics.For example, detection of resistance as early as possible helps to avoid exacerbation of the problem.

However, conventional resistance tests are often labor- and cost-intensive as well as relatively insensitive. Molecular tests, based on the knowledge of genetic resistance markers and resulting from a detailed understanding of the resistance mechanisms, are considered to be a promising solution. [1]

Helminthic infections are among the most common infections in human being, affecting a large proportion of the world's population. In developing countries they pose a large threat to public health and contribute to the prevalence of anaemia, malnutrition, eosinophilia and pneumonia. Although the majority of infections due to worms are generally limited to tropical countries, they can occur to travelers, who have visited those areas and some of them can be developed in the temperature climates. [2] The helminthes which infect the intestine are cestodes e.g. tapeworms (Taenia solium), nematodes e.g. hookworm (Ancylostoma duodenale), round worm (Ascarislumbricoids) and trematodes or flukes (Schistosoma mansoni and Schistosoma hematobolium).

The diseases originated from parasitic infections causing severe morbidity include lymphatic filariasis, onchocerciasis and schistosomiasis. These infections can affect most populations in endemic areas with major economic and social consequences. [3]

Various heterocyclic moieties as anthelmintic agent:

1a. Benzimidazole:

Methyl5(6)-phenylsulfinyl-2-benzimidazolecarbamate(1a)was synthesized by Beard *et al*. [4] It was effective at a dose of 10 mg/kg against gastrointestinal nematodes and lung worms and cattle,sheep,and swine.Compound (1a)was found to be most potent against a variety of parasites in laboratory and domestic animals.

1b.Benzimidazole:

2-(Trifluoromethyl) benzimidazole derivatives substituted at the 1-,5-, and 6-positions have been synthesized by Gabriel Navaarrete-V'azquez. Result indicates that all the compounds tested are more active as antiprotozoal agents than Albendazole and metronidazole.one compound (1b) was as active albendazole against T. spiralis. These compounds were also tested for their effect on tubulin polymerization and none inhibited tubulin polymerization.

1c. Benzimidazole:

The synthesis of alkyl 5(6)-(benzimidazol-2-carbamates) and (6,7), and alkyl 5(6)-(4- substituted piperazin-1-yl)benzimidazole-2-carbamates synthesized by Rashmi Dubey.When the Compounds were tested for their anthelmintic activity against Ancyclostoma ceylanicum in hamsters, hymenolepis nanain rats, Litomosoides cariniiin cotton rats, and Dipetalonema viteae in Mastomys natalensis.

2. Triazine:

Anumberof1-aryl-diamino-1,2-dihydro-s-triazines (2) was synthesized by Roth *et al*. [5]. By condensation of biguanides with ketones or aldehydes, or by an one step reaction in which aromatic amines are heated with dicyandimide in the presence of ketones or aldehydes. Such compounds have been found to have high anthelmintic activity against intestinal parasites and negligible microbiological activity. Accordingly, they were screened against Syphaciaobvelata infestationin mice, and it was found that at oral dosages of 300mg/kg/day for 3 days, over 90% of the worms were cleared, with no apparentad verse effects on the mice.

3. Pyrantel and Morantel:

The anthelmintic activity in sheep of pyrantel, morantel, and other cyclic amidines, of a series of thiazoline and dihydrothiazine analogs of pyrantel, and a related series of 1-(2- arylvinyl) pyridinium compounds by Austin *et al.* [6] The rodent screen was shown to be a good early indicator for activity against the gastrointestinal nematodes of sheep for these classes of compounds, although it become clear subsequently that for some species, Trichostrongylus colubriformis. Pyrantel (3) and morantel (4) are the most active against the major nematodes infections of sheep and there commended therapeutic dosages are 25mg/kg and 10 mg/ kg respectively.

4. Indazole:

Compound (5) was highly activeagainstboth theenteralphaseof Trichinella spiralis in mice and a broad spectrum of intestinal nematodesin sheep by Kings bury *et al*. [7] Several Indazoles showed some activity against T. spiralis in mice. The available data the indicated that the indazole nucleus be less attractive than the benzimidazole nucleus for the preparation of anthelmintic.

5. Benzothiazole:

A new series of anthelmintic agent benzthiazoles were synthesized by novel 8-fluoro- 9- substituted(1,3) benzothiazole (5, 1-b)-1,3,4- triazole Siddiqui *et al*. [8] All these compounds were studied for their anthelmintic activity against earthworms, Pheritima posithuma. The compound (6) with R= O- nitroanilino substituent was possess higher anthelmintic activity.

6. Pyrazoline:

Somenew1-(2',4'-dinitrophenyl),3-methyl,4-(arylhydrazono)-2-pyrazolin-5-one(7) were prepared by reacting with different ethyl2-arylhydrazono-3-oxybutyrate derivative with 2, 4-DNP. The products were screened for their antimicrobial and anthelmintic activities by Rao *et al*. [9] The compounds were also tested for anthelmintic activity against earthworms using piperazine hydrochlorideas reference anthelmintic. All the compounds 7b - 7f showed greater activity than of standard drug against earthworm.

7a. Oxadiazole:

5-(4-isothiocyanatophenyl)-1,2,4-oxadiazoleand3(4-isothiocyanatophenyl)-1,2,4- oxadiazole was synthesized by Haugwitz *et al*. [10] The compound (8a) showed100% nematocidal activity and 3-(2-furanyl)-5-(4-isothiocyanatophenyl) - 1, 2, 4-oxadiazole (8b), 3- (2-furanyl)-5-(2-chloro-4-iso thiocyanotophenyl)- 1, 2, 4-oxadiazole(8c), and 3 - (2furanyl) -5- (4-chloro-3-isothiocyanato phenyl) -1, 2, 4-oxadiazole (8d) showed 100% taeniacidal activity when administered orally to mice. The two most active members of this series, 37 and 38, were active against the gastrointestinal nematodes of sheep at100mg/kg.The compound (8a) was 100% against Hymenolepis nana when administered subcutaneously and 100% active against Nemato spirodesdubius with some taeniacidal activity as indicated by destrobilization.

7b.Oxadiazole:

Substituted 1,2,4-oxadiazoles were screened for anthelmintic activity in mice experimentally infected with Nematospiroides dubius. 3-Alkyl- and 3-aryl-1, 2, 4-oxadiazoles without substituents at the 5 position were effective

when administered orally at 500mg/kg or by subcutaneous injection at 100mg/kg, whereas the 5-substituted 3-alkyl- and 3-aryl-1,2,4- oxadiazoles tested were inactive. These compounds were synthesized by C. Ainsworth *et al*.

8: Isothiocyanate:

An efficient, mild, chemoselective and convenient protocol for novel synthesis of anthelmintic drug 4-isothiocyanato-4'-nitrodiphenyl ether compound (9) by Modhaveetal [11] have exhibited antifungal and anthelmintic activities. Isothiocynates derivatives were synthesized by Amine, carbon disulfide, and acetone was stirred at room temperature to form dithiocarbamate salt,which was subsequently treated with triethyl amine and ferrous sulfate to secureisothiocyanates.This reaction couldnot be completed without ferrous sulfate; therefore it acts as a catalyst.

9: 1, 5-Benzodiazepine:

1,5-benzadiazipine derivative was synthesized by Kumar *et al.* [12] anthelmintic active compound (10) was carried out on Pheritima by technique a with slight modification. Piperazine citrate was used as the standard drug.

10: Avermectin:

13-epi-Avermectin analogs retain the fulla nthelmintic activity of the natural compounds. Chemical conversion of the potent anthelmintic natural products avermectin B1 (A) and avermectin bB2(B) to corresponding13-epianalogs(11aand11b) were synthesized by Blizzard *et al*. [13] Compound 11a and 11b retain excellent antiparasitic active.

11: Thiadiazole:

The compound have been synthesized and screened for their anthelmintic activity against Hymenolepsis nana infection in mice.The compounds have also been tested for their *in vivo* and *in vitro* activity against tobacco mosaic virus (TMV) and cucumber green mottel mosaic virus (CGMMV). The compounds (12a-12j) have been prepared by the reaction of compounds (C) with secondary amine in presence of formaline (i.e. Mannich reaction). The compounds (12a-12j) were synthesized by Fadayan *et al*. [14]

12: Quinazoline:

The most active compounds were those bearing a hydroxyl alkyl amino substituent in the 4 position. The most active compound (13) against the two helmintic parasites Ascaris suum and Syphacia obvelata and also against the tapeworm Hymenolepsis nana. Compound 13 was synthesized by Alaimo *et al.* [15]

13: Benzazepine:

The compound 14 was found to possess high cestocidal activity. The cyclohexanoyl derivative (14) was synthesized by Dorgan *et al.* [16]

14: Piperazine:

Piperazine has been shown to possess anthelmintic activity. The 15a and 15b most potent because Oragano phosphates exhibiting potent antiacetyl cholinesterase activity. The compound 15a and 15b synthesized by Mehra *et al*. [17]

15: Pyridine:

Methyl imidazo [1, 2-a] pyridine-2-carbamates was synthesized by Bochis *et al*. [18] The mos tpotent compound,6-(phenylsulfinyl)-imidazo[1,2-a] pyridine - 2 - carbamate (16), was orally effective against a broad range of helminthes in sheep and cattle, at dosage of 2.5mg/kg. At 2.5 mg/kg, the compound was more than 98% effective against Haemonchus contortus, Ostertagia circumcincta, Trichostrongylus axei.

16: Imidazole:

A series of 1-(substituted cinnamamido)-2, 4-imidazolidinediones (17) has prepared from the corresponding cinnamoyl chloride and 1-amino-2, 4 imidazolididinedione hydrochloride in pyridine by Alaimo *et al*. [19] These compounds possess a significant degree of anthelmintic activity against the pinworm Syphacia obvelata. The most active compounds are those with halogen or cyano groups.

17: Furan:

2, 9-Disubsituted Naphtho [2, 1-b] Furan synthesized by Vaidya *et al*. [20] The compounds (18a-18c) were obtained from 1-formyl-2 naphthyl benzoates via Fries rearrangement.The compounds 18c were found to be exhibit significant anthelmintic activity. Anthelmintic activity was evaluated by using earthworm Pheritimaposthuma (class-Annelida and order- Order-oligichaeta).

18: Thiazole:

Thiazoles with substituted piperonylidenehydrazine substitutedatthe2nd position and an aryl sydnone at the position 4 were synthesized byKalluraya et al. [21] Compounds (19h) showed significant activity. The anthelmintic activity studies were carried out against earthworms (Portoscoplex corethrusus) according to the method of Garg and *et al.*

19: Thiadiazine:

The compounds were screened for anthelmintic activity against third stage larvae of hookworms, Anchylostoma caninum. Compound (20) was found to be the most active. This compound synthesized by Shirodkar *et al*. [22]

20: Quinoline:

The most active compounds 21a and 21b. All compounds are unsubstituted 2-aryl derivatives. Addition of a methyl group at position 8 (21b) result in a decrease in activity.The most potent compound was found to be (21a), 2-furyl analogue. These compounds were synthesized by Alaimo *et al*. [23] Compounds were tested against the mouse tapeworm Hymenolepsis nana.

21: Coumarin:

Aseries of 4-substituted coumarins (22a-c) was synthesized from condensation of various phenols with β ketoesters. Phosphotungstic acid is commercially available and environmentally benign catalyst to promote the condensation of various phenols with β ketoesters. These compounds were synthesized by Raju *et al.* [24]

22: Benzoxazole:

A series of 2-(aryloxymethyl)-5-(2'-mercapto acetylamino benzoxazol-2'-yl)-1,3,4- thiadiazole (23a-j) have been synthesized and screened for their cestodicidal activity against hymenolepis nana infections in rat. Compounds 5b and 5c have been found to be the most active member of the series. These compounds were synthesized by saksena *et al*. [25]

23: Isoxazole:

Aseries of 3-aryl-5-halomethyl isoxazole (24a-o)were synthesized by Senetal.[26]

24a: cyclopeptides:

The class of cyclooctadepsipeptides has entered the scene of anthelmintic research in thee arly 1960s by Harder *et al*. [27] PF1022A (25), the first anthelmintically active member, is the natural compound from the fungus Myceliasterilia that belongs to the microflora of the leaves of the Camellia japonica.

24b: Cyclopeptides:

The anthelmintic activity was carried out against the three earthworm species Megascoplex konkanensis (ICARBC 211), Pontoscotex corethruses (ICARBC 408) and Eudrilus sp. (ICARBC042) by Gargand A talmethod at concentrationof 2mg/ml using mebendazoleas standard drug. Almost all newely synthesized benzimidazolopeptides have shown moderate to good anthelmintic activity. These entire derivatives were synthesized by Rajiv Dahiya *et al*.

25: Pyrazole:

Aseries of N'-substituted aryl sulfonyl-3,5-dimethyl-4-arylazopyrazoles(26)was synthesized by Garg *et al*. [28] These compound displayed anthelmintic activity.

26: Benzoxazine:

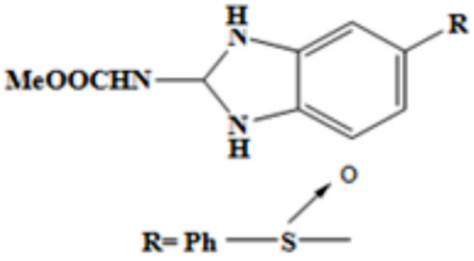
A series of 8-isothiocynato-4H-imidazo (2,1-c) (1,4) benzoxazines (27a-e & 28a-e) have been synthesized and screened for their anthelmintic activity against Ancylostoma ceylanicum in hamsters and Hylenolepis nana in mice by Rao *et al.* [29-35]

27a: Quaternary salt:

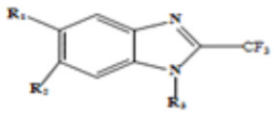
The synthesis and anthelmintic activity of a group of amino pentadiene ammonium salt is described by D.L. Garmaise *et al*. The compounds were tested first against infections of Nemato spiroidesdubius and a scarissuum in mice, and most of the members of the series were subsequently evaluated for effectiveness against A.suumins wine and a group of six gastrointestinal nematodes in sheep.

27b: Quaternary salt:

Comparison of the activities of analogs of dithiazinine (iii) against gastrointestinal nematodes of sheep showed that the pentamethine chainis essential. Activity may be retainedwhen the 6 position is substituted with alkyl or alkoky groups or alkoky groups, but substitution with electron-withdrawing groups produces inactive compounds. Two members of a series of hemithiacyanines containing the 4-dimethylamino-1,3-butadienyl group were very active in inhibiting Ascaris suum larval migration in mice and in swine and more effective than dithiazinine in preventing liver pathology due to migratory ascariasis.These compounds were synthesized by D.L. Garmaise *et al*.

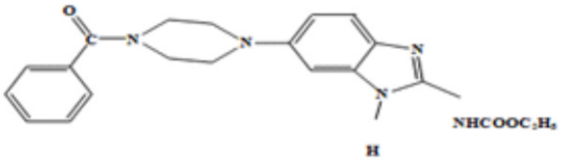


(1a)

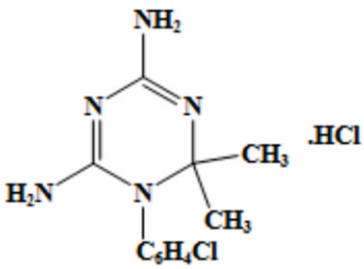


(1b)

Compound	R^1	R^2	R^3
1b	H	H	H
1c	Cl	H	H
1d	Cl	Cl	H
1e	H	H	CH_3



(1C)



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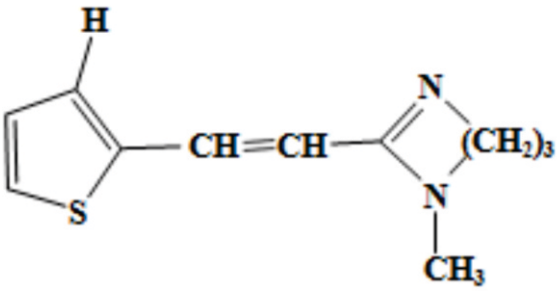
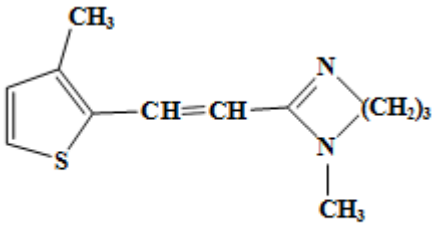


(3)



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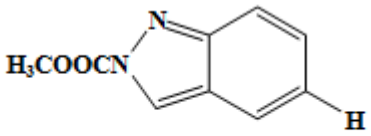
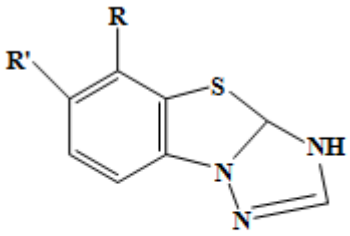


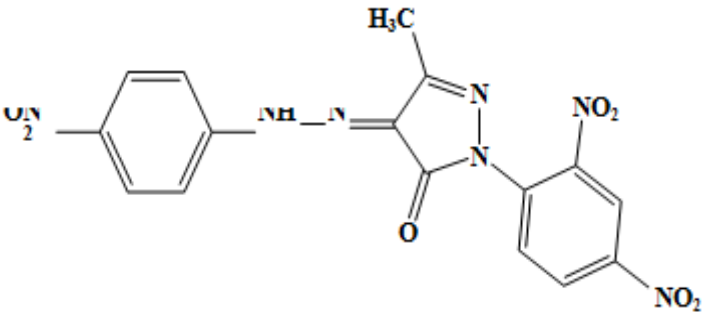
(5)



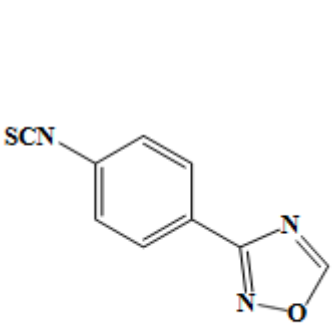
R=o-nitroanilino R'

= Br.

(6)



(7)



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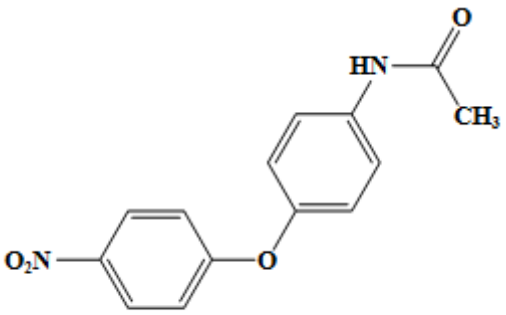

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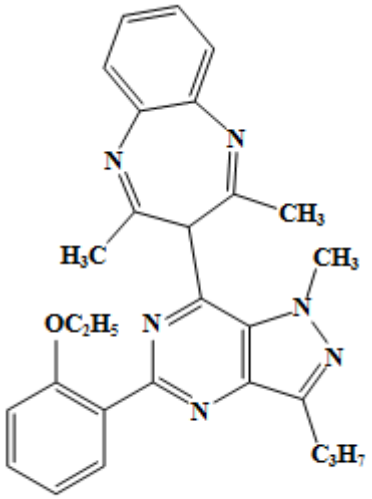

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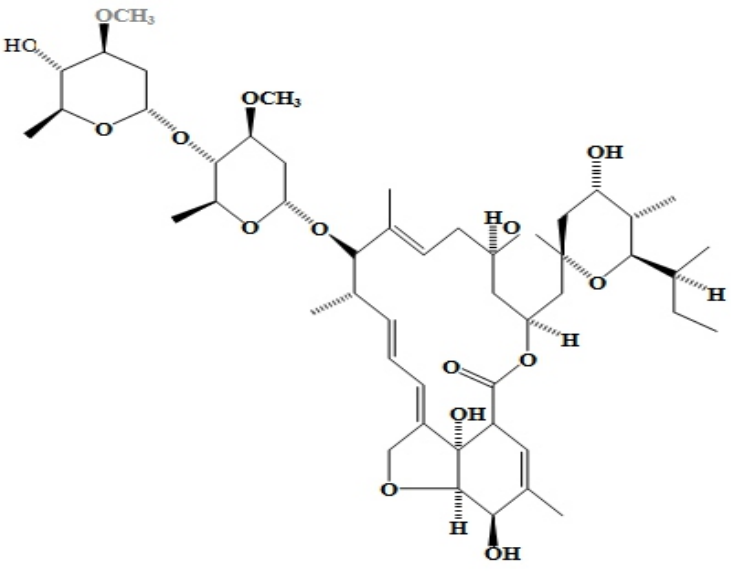
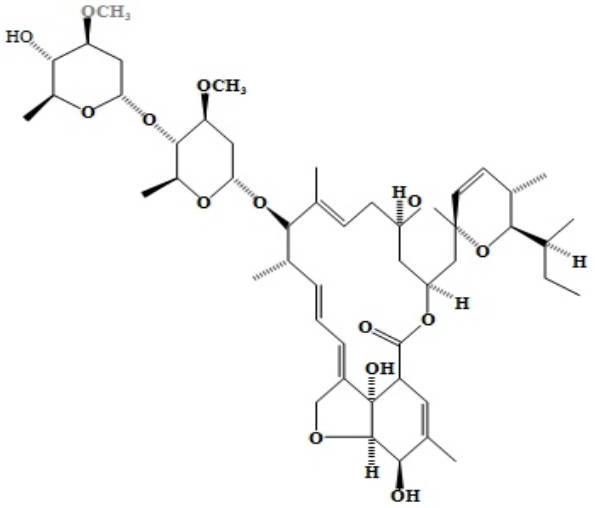
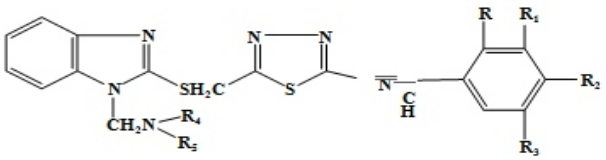


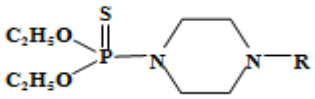
(11a)



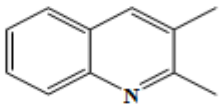
(11b)



(12a-j)

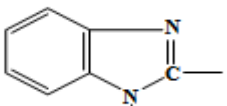


R=

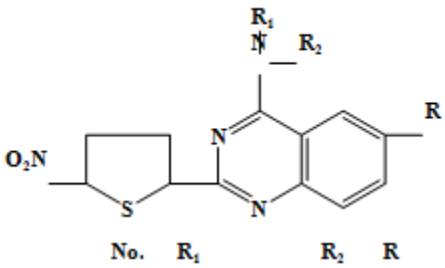


(15a)

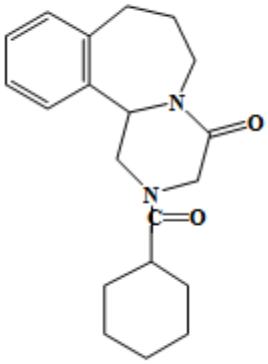
R =



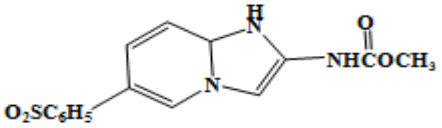
(15b)



No.	R_1	R_2	R
13	$HOCH_2CH_2$	H	H



(14)



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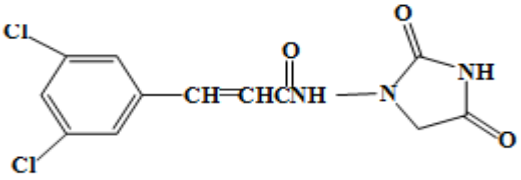
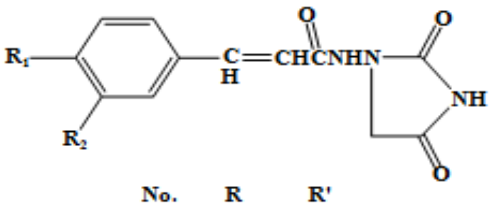
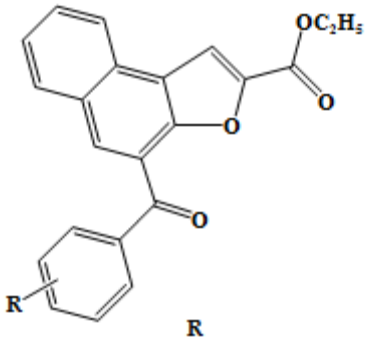


(17)

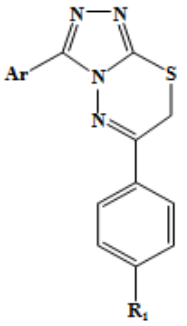


No.	R	R'
19a	Cl	Cl
19b	H	H
19c	CH_3	Cl
19d	Cl	H
19e	O—C(H2)—O	
19f	Cl	CF_3
19g	F	H
19h	CN	H
19i	H	F
19j	F	Cl
19k	C_2H_5	Cl
19l	Br	CH_3



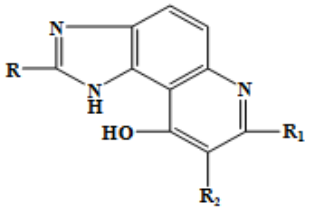
R

18a-H
18b-2-Cl
18c-4-NO_2

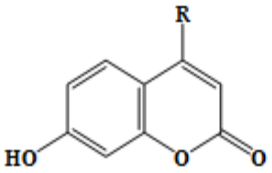


Ar=3-5-dinitrophenyl R_1 =H

(20)

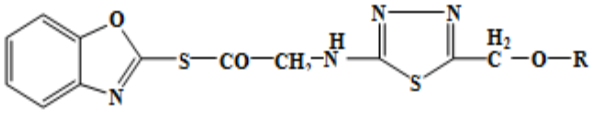


No.	R	R_1	R_2
21a	2-Furyl	CH_3	H
21b	Ph	CH_3	CH_3



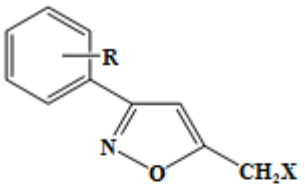
R=CH_3,CH_2Cl,Ph

(22)

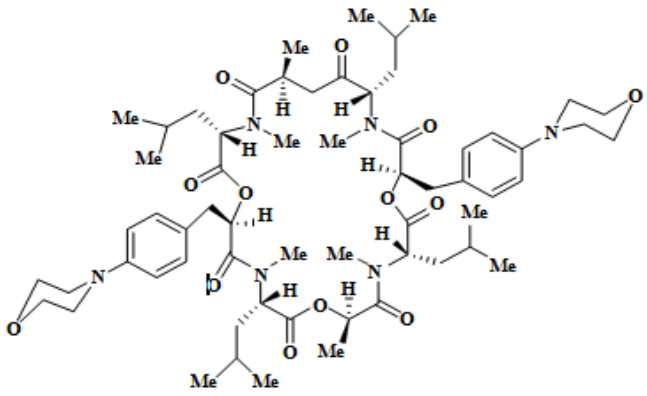


(23a-j)

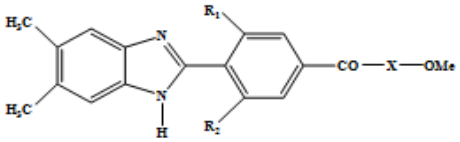
R=C_6H_5,4-$NO_2C_6H_4$,2-$NO_2C_6H_4$,2-$CH_3C_6H_4$,3-$CH_3C_6H_4$,4-$CH_3C_6H_4$,
2-ClC6H4,4-ClC6H4,1-Napthoxy,2-Napthoxy



Compdno.	R	X
24a	4-Cl	Br
24b	3,4-Cl_2	I
24c	H	Br
24d	3-NO_2	I
24e	3,4-Cl_2	Br
24f	4-Cl-3-NO_2	Br
24g	4-Cl	I
24h	3,4-Cl_2-5-NO_2	Br
24i	3,4-Cl_2	Cl
24j	4-Br	Br
24k	2,4-Cl_2	Br
24l	3-F	Br
24m	4-Cl	Cl
24n	3-NO_2	Br
24o	4-F	Br

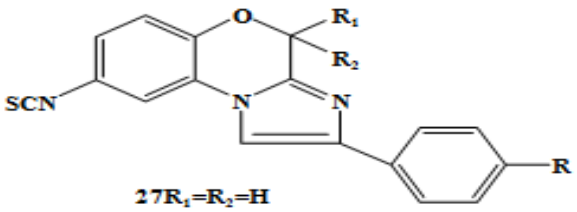


(25)



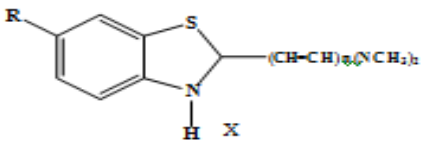
(26 b)

Compound	R_1	R_2	X
26 b	H	H	Pro
26 c	H	H	Nitro(Arg)
26 d	H	H	Leu-Gly
26 e	H	H	His-Tyr



27 R_1=R_2=H
28 R_1=R_2=CH_3

R=a) H
b) F
c) Cl
d) Br
e) OCH_3



(29)

No.	R	n	X
XV	H	1	I
XVI	CH_3	2	I
XVII	CH_3	2	Cl

Conclusion:

It has been concluded that in most of the drugs used in the treatment of Helminths,heterocyclic nucleus is present Any structural changes on the moiety provide better drug for the chemotherapy.From there view it was known those heterocyclic nucleuses are potential targets for drug discovery of anthelmintic drugs. These all nucleus containing compounds represent new pharmacophore for the development of novel anthelmintic drugs.

References:

1. GS Himmelsyjena, Mechanisms of Resistance to Anthelmintics in Nematodes, University of Veterinary Medicine, Germony.
2. GN Vazquez; RCedillo;AH Campos; LYepez; FHLuis; J Valdez; R Morales; R Cortes; M Hernandez; R Castillo. Bioorg. Med. Chem. Lett., 2001, 11,187-190.
3. R Dubey; S. Abuzar; S Sharma; RK Chatterjee; JC Katiyar. J.Med.Chem. 1985, 28, 1748- 1750.
4. DAP Bundy, Trans Royal Soc Trop Med Hygiene, 1994, 8, 259-261.
5. GV Satyavati, Use of Plant drugs in Indian traditional system of Medicine and their relevance to primary healthcare, In: Economic and Medicinal Plan tresearchby Farmworth NR and Wagner H (Eds), Academic Press Ltd, London, 1990; 190-210.
6. A Eugene; CC Beared; AE John; HF John; GK John, AS Richard; PKT heodore; JH Drudge; MC Robert. J. Med. Chem., 1975, 18, 1164-1166.
7. B Roth; RB Burrows; GHHitchings. The Wellcome Research Laboratories, Burroughs Wellcome & Co., Tuckahoe, New Tork, 1963, 6, 370-378.
8. WC Austin; RLCornwell; RM Jones; M Robinson. J. Med. Chem., 1972, 15, 281-285.
9. WD Kingsbury; J G Robert; JT Vassillos; GJ Gregory. J. Med. Chem., 1976, 19,839-840.
10. C Ainsworth; WE Buting; J Davenport; ME Callender; MC McCowen. The Lilly Research Laboratories, Indianapolis, Indiana. 1966, 208-211.
11. A Rana; N Siddiqui; SA Khan. Indian J. Phar. Sci., 2009, 10, 10-17.
12. EOPrakash; ES Devi; JT Rao. Asian J.Chem. 2003, 15, 1607-1610.
13. RD Haugwitz; AJ Martinez; J Venalavsky; RG Angel; BV Maurer; GA Jacobs; VL Narayanan; LR Cruthers; J Szanto. J. Med. Chem., 1985, 28, 1234-1241.
14. AC Chaskar; BP Bandgar; RK modhave; AP Patil; S Yewale. Syntheticcomm. 2009; 39, 992-1001.
15. R Kumar; YC Joshi. Arkikovc. 2007, 13, 142-149.
16. TA Blizzard; MM Gaye; M Helmut; LS Wesley; AF Robert; HF Fisher. J. Med. Chem., 1992, 35, 3873-387.
17. MFadayan; YD Kulkarni; ASH Pakdaman. Asian J.Chem. 1993, 5, 282-286.
18. RJ Alaimo; CF Spencer; JB Sheffer; RJ Storrin; CJ Hatton; RE Kohls. J. Med.Chem., 1978, 21, 298-300.
19. MD Brewer; MN Burgess; RJJ Dorgan; RL Elliott; P Mamalis; BRManger; RAB Webster, J. Med. Chem., 1989, 32, 2058-2062.
20. R Mehra; A Mohan; SC Mehra, Indian J. Heterocycl. Chem., 2008, 18,191-192.
21. RJ Bochis; LE Olen; MH Fisher; RA Reamer; G Wilks; JE Taylor; Olson G. J.Med. Chem., 1981, 24, 1483-1487.
22. RJ Alaimo; CJ Hatton.J.Med.Chem., 1976, 19, 349-350.
23. C Chandrashekhar; MN Kumaraswamy; KM Basavaraja; VP Vaidya, Indian J. Heterocycl. Chem, 2007, 16, 341-344.

24. B Kalluraya; AM Rahiman; D Banji; AM Isloor; G Rai, Indian J. Hetrocycl Chem.,2007, 9, 217-222.

25. PY Shirodkar; B Kulkarni. Indian J. Heterocycl.Chem., 1998, 7, 235-236.

26. RJ Alaimo; CJ Hatton. J.Med.Chem. 1976, 15,108-109.

27. BC Raju; TH Babu; JM Rao. Indian J. Chem., 2009, 48B, 120-123.

28. RKSaksena; S Puri; R Prakash. Indian J. Heterocycl.Chem., 2003, 13, 127-130.

29. HG Sen; D Seth; UN Joshi. Notes, 1965, 131.

30. A Harder; HPS Wrede; J Krucken; P Marinovski; F Wunderlich; J Willson; K Amliwala; LH Dye; RWalker. International J. Antimicrobial Agents, 2003, 22, 318-331.

31. HG Garg; Nkaur. J.Med. Chem., 1972, 15, 554-555.

32. KS Rao; CVR Sastry. Indian J. Heterocycl. Chem., 1992, 2, 103-106.

33. DL Garmaise; CH Chambers; J Komlosy; RC McCrae, Department of parasitology, Abbott Laboratories, North Chicago, Illinois, 1967, 891-893.

34. DL Garmaise; GY Paris; J Komlossy; RC McCrae, Abbott Laboratories Ltd., Montreal, Quebec, Canada.1969, 806-81350.

35. R Dahiya; D Pathak, Eur.J.Med.Chem. 2007,772-798. R Dahiya; D Pathak, Eur.J.Med.Chem. 2007,772-798.

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JOHP

A review on study of herbal extract for immunity booster with a focus on *Ocimum sanctum* [Tulsi] leaves

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Abstract:
Tulsi, known as the "queen of herbs," has been used for millennia. Tulsi is a medicinal plant also known as oscimum sanctum. Tulsi has a lot of therapeutic benefits. Tulsi has also been demonstrated in studies to be beneficial for diabetes by lowering blood glucose levels. Tulsi was shown to significantly lower overall cholesterol levels in the same research. According to a different study, tulsi's antioxidant qualities are what provide it a positive impact on blood glucose levels. The most effective treatment for severe acute respiratory syndrome is Rama tulsi. Its leaf juice relieves cough, bronchitis, fever, and colds. Another ear drop that is utilized is tulsi oil. Malaria can be cured with tulsi. It works well for cholera, headaches, sleeplessness, hysteria, and indigestion. Every day, millions of people consume fresh Tulsi leaves.

Keywords: punch tulsi extract immunity booster; medicinal uses.

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Introduction:

Tulsi, also known as holy Basil, is a sacred herb in Hinduism and is highly regarded for its medicinal properties in Ayurvedic medicine. Scientifically known as Ocimum sanctum or Ocimum tenuiflorum, Tulsi is native to the Indian subcontinent and has been cultivated for thousands of years for its spiritual, medicinal, and culinary uses. The organic chemicals found in the kingdom of plants are abundant and have been utilized as agents to combat many infectious and non-infectious ailments In the current investigation, the antibacterial properties of crude tulsi leaf extracts with two solvents methanol, acetone, and water and their polar to non-polar extraction methods cold and hot extractions were assessed against clinically isolated MDR bacterial strains. The discovery of medicinal plants around the globe has implications for the fields of medicine and agriculture as well as for the development of new strategies for the propagation of alternative medicinal crops with greater social and economic benefits. [1]

One of the main sources of medicine is plants, from which many common pharmaceuticals are generated. Plants can be used safely, affordably, and effectively for medicinal purposes, and they are widely available. The plants of tulsi are very significant due to their potential for therapeutic use among the known medicinal value of plants. It is frequently suggested that tulsi has medicinal properties that are used to cure a variety of illnesses. It is anti-cancer, anti-diabetic, analgesic, anti-fertility, antimicrobial, antispasmodic, and adapto genic, among other qualities. [2]

Fig.1: Matured plant of *Ocimum sanctum*

Tulsi is grown for its essential oil as well as for religious and medical purposes. It is well-known in the Indian subcontinent for its medicinal properties and for being a popular herbal tea in Ayurveda. Tulsi leaves are aromatic, alternate, and grow up to five centimeters long. They also have some tooth margins. In close-ups, the flowers are elongated, and the plant variety determines the color of the leaves and flowers. [2-6]

Materials and Method:

Plant leaf collection:

The leaves of *O. sanctum* were collected from botanical herbal garden, leaves were manually separated, cleaned, and air-dried.

Preparation of oil:

- Gather the tulsi leaves using the Clevenger method, following the formula.
- Weigh the leaves and place every leaf inside the flask with a circular bottom.
- Complete the Clevenger cycle, gather the mixture, and cover it in a conical flask.
- Now, pour the entire mixture into a separator funnel and let the water and oil separate for eight hours.
- As of right now, water is within the funnel and the oil layer is pouring out the top.
- Eliminate all the water and gather the oil in a beaker, covering the beaker with silver foil, etc.
- Now gather all five tulsi oils using the same procedure.
- Right now as directed by the formulation, combine all five tulsi oils and take two drops of tweens 20 and mix them to make a final product.

Taxonomy: [7]

Kingdom	:	Plantae
Subkingdom	:	Tracheobionta
Superdivision	:	Spermatophyta
Division	:	Magnoliophyta
Class	:	Magnoliopsida
Subclass	:	Asteridae
Order	:	Lamiales
Family	:	Lamiaceae
Genus	:	*Ocimum*
Species	:	*Ocimum sanctum*

Botanical description: [8-10]

When fully grown, it is a fragrant, upright, heavily branched plant that reaches a height of between 30 and 60 cm. Its aromatic leaves can grow up to 5 cm long and are simple, opposite, elliptic, oblong, obtuse, or acute with entire, sub-serrate, or dentate margins. The tiny, compact clusters of purple to reddish-colored tulsi flowers are borne atop cylindrical spikes.

Mechanisms of action: [11-12]

Modulation of immune response:

Tulsi modulates the immune system, enhancing the body's ability to fight off pathogens while maintaining immune balance.

Reduction of oxidative stress:

By scavenging free radicals and upregulating antioxidant enzymes, Tulsi reduces oxidative stress, which is linked to various chronic diseases.

Regulation of neurotransmitters:

Tulsi influences neurotransmitters like serotonin and dopamine, which play a role in mood regulation and stress response.

Anti-inflammatory pathways:

Tulsi inhibits the production of pro-inflammatory cytokines and enzymes such as COX-2, thereby reducing inflammation.

Traditional uses:

Tulsi is also known as "the elixir of life" since it promotes longevity. Different parts of the plant are used in Ayurveda and Siddha systems of medicine for prevention and cure of many illnesses and everyday ailments like common cold,

headache, cough, influenza, earache, fever, colic pain, sore throat, bronchitis, asthma, hepatic diseases, malarial fever, as an antidote for snake bite and scorpion sting, flatulence, migraine headaches, fatigue, skin diseases, wound, insomnia, arthritis, digestive disorders, night blindness and diarrhoea. The leaves are good for nerves and to sharpen memory.

Pharmacological activity:

A herbal product called punch tulsi drops usually comprises extracts from five different varieties of Tulsi (Holy Basil). Because of the several Tulsi kinds' combined pharmacological activity, this blend is thought to provide a number of health benefits.

Antioxidant activity: Tulsi is rich in antioxidants such as flavonoids, phenols, and polyphenols. These compounds help neutralize free radicals, reducing oxidative stress and protecting cells from damage.

Anti-inflammatory activity: Tulsi contains compounds like eugenol, rosmarinic acid, and ursolic acid, which have anti-inflammatory properties. These compounds help reduce inflammation in the body, making tulsi useful in managing conditions like arthritis and other inflammatory diseases.

Antimicrobial activity: The essential oils in Tulsi have strong antimicrobial properties against a wide range of bacteria, viruses, and fungi. This makes punch tulsi drops beneficial in boosting immunity and preventing infections.

Adaptogenic and anti-stress activity: Tulsi is an adaptogen, which means it helps the body adapt to stress and promotes mental balance. It is known to reduce cortisol levels and improve overall resilience to stress.

Anti-diabetic activity: Tulsi has been shown to help regulate blood sugar levels. Compounds in Tulsi can enhance insulin secretion and improve insulin sensitivity, making it beneficial for managing diabetes.

Gastroprotective activity: Tulsi has been found to protect the stomach lining and reduce the occurrence of ulcers. It promotes overall digestive health and can alleviate symptoms of gastrointestinal disorders.

Conclusion:

Punch tulsi drops harness the combined pharmacological activities of multiple tulsi varieties, offering a potent natural remedy for a wide range of health issues. Regular use can enhance overall health, boost immunity, and provide protection against various diseases, thanks to its diverse bioactive compounds. Even though it's common practice to only use western medicine and adhere to its blindfold, one should consider using a natural resource like the *Ocimum sanctum* plant to strengthen immunity and fend off many illnesses. Numerous research studies have demonstrated the therapeutic and natural properties of *Ocimum sanctum*. These properties stem from the phytochemicals found in the plant, which have been found to be effective in treating a wide range of illnesses, including bacterial diseases, cancer, infertility, colds, and coughs. Additionally, the plant has been shown to boost immunity, preventing various diseases at an early stage. Future research on holy basil, also known as tulsi, ought to be considered in order to prevent a variety of diseases.

References:

1. Naik, L. S., Shyam, P., Marx, K. P., Baskari, S., & Devi, V. R. (2015). Antimicrobial activity and phytochemical analysis of Ocimum tenuiflorum leaf extract. Int. J. PharmTech Res, 8(1), 88-95
2. Satyendra, M. (2020). Phytochemical efficiency of Ocimum sanctum (Tulsi) in health enhancement and disease prevention: A review. IJARESM, 9, 1346-1351.
3. Kumar, V., Chakraborty, A., Kaur, M., Pandey, S., & Jena, M. K. (2018). Comparative study on antimicrobial activity of tulsi (Ocimum sanctum) and neem (Azadirachta indica) methanol extract. Asian journal of pharmaceutical and clinical research, 514-517.
4. Verma, S. (2016). Chemical constituents and pharmacological action of Ocimum sanctum (Indian holy basil-Tulsi). The Journal of phytopharmacology, 5(5), 205-207.

5. Sharma A, Dikshit M, Jhunjhunwala A, Som AK. Extraction process of Haridra & Tulsi essential oil with their medicinal uses. Journal of ayurveda and integrated medical sciences. 2022 Jul 10; 7(5):41-7.
6. Pandey G, Madhuri S. Pharmacological activities of Ocimum sanctum (tulsi): a review. Int J Pharm Sci Rev Res. 2010 Nov; 5(1):61-6.
7. Prakash PA, Gupta N. Therapeutic uses of Ocimum sanctum Linn (Tulsi) with a note on eugenol and its pharmacological actions: a short review. Indian journal of physiology and pharmacology. 2005 Apr 1; 49(2):125.
8. Srinivas N, Sali K, Bajoria AA. Therapeutic aspects of Tulsi unraveled: A review. Journal of Indian academy of oral medicine and radiology. 2016 Jan 1; 28(1):17-23.
9. Sahoo DD, Tabassum Y, Sharma D. Multiple health benefits of Tulsi plants. Journal of Medicinal Plants. 2022; 10(5):95-102.
10. Kaur S, Sabharwal S, Anand N, Singh S, Baghel DS, Mittal A. An overview of Tulsi (Holy basil). European journal of molecular & clinical medicine. 2020; 7(7):2833-9.
11. Gulhane NS, Ghode CD, Jadhao AG, Patil PA. Study of medicinal uses of Ocimum sanctum (Tulsi). Journal of pharmacognosy and phytochemistry. 2021; 10(2):1427-31.
12. Jamshidi N, Cohen MM. The clinical efficacy and safety of tulsi in humans: a systematic review of the literature. Evidence-based complementary and alternative medicine. 2017.

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Manuscripts should be concisely typewritten in double space in A4 sized sheets, only on one side with a 2 cm margin on all sides. The manuscript shall be prepared in

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Abstract: The abstract is limited to 250 words, and should describe the essential aspects of the investigation. In the first sentence, the background for the work should be stated; in the second sentence the specific purpose or hypothesis shall be provided; followed sequentially by summary of methods, results and conclusion. No references should be cited.

Material and Methods: This section may be divided into sub-sections if it facilitates better reading of the paper. The research design, subjects, material used, and statistical methods should be included. Results and discussion shall not be drawn into this section. In human experimentation, ethical guidelines shall be acknowledged.

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Acknowledgments. Acknowledgments should appear on a separate page.

Tables. Each table should be given on a separate page. Each table should have a short, descriptive title and numbered in the order cited in the text. Abbreviations should be defined as footnotes in italics at the bottom of each table. Tables should not duplicate data given in

The text or figure. Only MS word table format should be used for preparing tables. Tables should show lines separating columns with those separating rows. Units of measurement should be abbreviated and placed below the column headings. Column headings or captions should not be in bold face. It is essential that all tables have legends, which explain the contents of the table. Tables should not be very large that they run more than one A4 sized page. If the tables are wide which may not fit in portrait form of A4 size paper, then, it can be prepared in the landscape form. Authors will be asked to revise tables not conforming to this standard before the review process is initiated. Tables should be numbered as Table No.1 Title…., Table No.2 Title…. Etc. Tables inserted in word document should be in tight wrapping style with alignment as center.

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General Guidelines for units and symbols - The use of the International System of Units (SI) is recommended. For meter (m), gram (g), kilogram (kg), second (s), minute (m), hour (h), mole (mol), liter (l), milliliter (ml), microliter (µl). No pluralization of symbols is followed. There shall be one character spacing between number and symbol. A zero has to be used before a decimal. Decimal numbers shall be used instead of fractions.

Biological nomenclature - Names of plants, animals and bacteria should be in italics.

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Spelling- These should be as in the Concise Oxford Dictionary of Current English.

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Experimental Pharmacology Series

What is Experimental Pharmacology (Ex-Pharm) Series

This is a computer assisted learning (CAL) software containing various programs which simulate animal experiments in Pharmacology. These programs can be used to demonstrate effect of drugs on different animals systems. The package is user friendly, highly interactive and full of animated sequences which make simulation appear realistic. The current version of Experimental Pharmacology (Ex-Pharm) Series Software consists of following computer simulated experiments:

Experiments List

01. Experiment on effects of various drugs (Mydriatic, Miotic and Local Anesthetic) on rabbit's eye.
    - Epinephrine
    - Atropine
    - Ephedrine
    - Physostigmine
    - Lignocaine
02. Study of Analgesic activity with the help of "Tail Flick Apparatus" (Analgesiometer).
03. Study of Analgesic activity with the help of "Hot Plate Apparatus" (Analgesiometer).
04. To study Analgesic activity by writhing test.
05. Study of Antihistaminic drugs/Anti allergic drugs by mast cell stabilization method with help of "Histamine Chamber".
06. Study of Muscle Relaxant activity with the help of "Rota-Rod Apparatus".
07. Study of CNS Depressants & Stimulants Using "Actophotometer".
08. Study of Drugs acting on CNS (Including Anxiolytic Activity) using following modules

- Elevated Plus Maze Method
- Pole Climbing Method

09. Study of anticonvulsant activity using "Electro Convulsiometer" (MES Method).
10. To study PTZ induced convulsions in mice
11. Study of effect of hepatic microsomal enzyme inducers on the phenobarbitone sleeping time in mice.
12. To study the action of strychnine/anesthetic on frog neurons (excitability).
13. Simulation of pupil control
    - Simulation of the effects of the physiological stimuli and drugs on the papillary reflexes.
    - Simulation of the control in patient with partial parasympathectomy.
14. Test for pyrogens using rabbits.
15. Effect of drugs on isolated guinea pig ileum (in-vitro).
16. To study respiratory depression effect on rabbit.
17. Study of stereotype and anti-catatonic activity of drugs on mice.
18. Experiments on thyroid and anti-thyroid drugs

- The effect of thyroxin, TSH, propylthiouracil on metabolism.

19. Experiments on blood sugar

- The effect of insulin (hypoglycemic activity) and alloxan on blood glucose.

20. Study of anti-inflammatory activity using carrageenan induced paw oedema method
21. Study of diuretic activity using metabolic cage
22. Experiment on Effect of various drugs on Isolated Frog's Heart. (DRC-Dose Response Curve)
    - Epinephrine
    - Norepinephrine
    - Isoprenaline
    - Calciumchloride
    - Propranolol
    - Acetylcholine
    - Potassiumchloride
    - Atropinesulphate
23. Experiments on effect of different drugs on dog BP & heart rate.
    1. Virtual Practice-Effects of drugs on the dog BP and Heart Rate.
    2. Effects of Vasopressor and Vasodepressor with appropriate blockers.

    a. Virtual Practice-Reversal action of adrenaline on blood pressure and heart rate.

    b. Virtual Practice-Reversal action of acetylcholine on blood pressure and heart rate.
24. Experiments on Lagendorff's Apparatus
    - Effect of coronary vasodilators on isolated heart
    - Effect of parasympathomimetics
25. Experiment on Bioassay of Histamine on the Ileum of Guinea Pig.
26. Bioassay of Acetylcholine on the isolated rectus abdominis muscle of frog
    (a) By Matching Method, (b) By Interpolation Method,
    (c) By 3 Point Method, (d) By 4 Point Method.
27. Bioassay of oxytocin on the isolated rat uterine horn by following methods
    (a) By Matching Method, (b) By Interpolation Method,
    (c) By3 Point Method, (d) By 4 Point Method.
28. Bioassay of serotonin on the isolated rat fundus strip by following methods
    (a) By Matching Method, (b) By Interpolation Method,
    (c) By3 Point Method, (d) By 4 Point Method.
29. To record the DRC and to determine the PD2 value for acetylcholine on frog rectus abdominis muscle.
30. Study of anti-ulcer activity-using pylorus ligation method.
31. Evaluation of effect of acetylcholine (spasmogens) using rabbit jejunum
32. Evaluation of effect of different drugs on ciliary motility.
33. Evaluation of effect of saline purgatives on frog intestine.
34. Determination of acute irritation of a test substance.

- Skin irritation (Including edema formation)
- Eye irritation

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*With the above-mentioned list of Interactive Software Experiments, Modules will also be provided for following

-Different routes of drugs administration in mice/rats.

-Common laboratory techniques of blood withdrawal.

-Different methods of anesthesia and euthanasia.

For whom is the software?

Software is aimed for medical, pharmacy, ayurveda, veterinary and dental science students. The software can also be used by the students of paramedical courses such as nursing, medical laboratory technology and physiotherapy etc.

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