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THERAPEUTIC POTENTIAL OF *RAUWOLFIA SERPENTINA*: PHYTOCHEMICAL CONSTITUENTS, BIOLOGICAL MECHANISMS, AND CLINICAL EVIDENCE

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Keywords:

Rauwolfia serpentina, Sarpagandha, Reserpine, Indole alkaloids, Traditional Indian medicine, Medicinal plants

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ABSTRACT: *Rauwolfia serpentina* is a traditional medicine used by Indians for a long time. Because of its serpentine shape, the drug is known as *Sarpgandha*. Despite having more than 50 alkaloids, the primary alkaloid in *Rauwolfia serpentina* is reserpine. Reserpine, even at lower doses, is an effective antihypertensive. *Rauwolfia serpentina* has a wide variety of medicinal uses, including lowering blood pressure and protecting the liver, but it also has sedative, antipsychotic, antidiarrheal, and anticancer (in breast) effects, among many others. The herb *Rauwolfia serpentina* contains all four of the main indole alkaloids, but we're mainly interested in the root-concentrated active alkaloid reserpine here because of its role in the plant's antihypertensive effects. In order for reserpine to have an antihypertensive effect, it needs to be administered at a much lower level. At higher doses, it can cause serious adverse effects such as drowsiness, depression, anxiety, nausea, bradycardia, bronchospasm, and withdrawal psychosis.

INTRODUCTION: Asthma affects about 300 million people worldwide, or about 7% of the population, and it's a chronic condition that often becomes worse with time. One hundred million more people will reportedly be affected by this by the year 2025. When it comes to proper medical care, almost 80% of the population still uses herbal remedies. The nearly 45,000 species of medicinal plants present in India play an essential role in the treatment of a wide range of diseases [1, 2].

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If you suffer from bronchial asthma, this article will provide you a rundown of the medicinal herbs that may help. Constant symptoms of asthma, an inflammatory disease of the airways, include wheezing, coughing, difficulty breathing, and a feeling of heaviness in the chest. Asthma and other respiratory illnesses share a strong correlation with allergies [3, 4].

Bronchial asthma is characterized by periodic, adjustable narrowing of the airways. It is possible to diagnose bronchial asthma with the use of diagnostic tools including spirometry, chest x-rays, and peak expiratory flow (PEF). Asthma is believed to have both genetic and environmental causes. Substances that trigger asthma attacks are called allergens. The flu, other respiratory illnesses,

second-hand smoke, and smoking are all potential triggers for asthma [6, 7]. A few examples of possible triggers are being cold; allergens (such as dust, pollen, and exercise); air pollution and pollutants; medications; the weather; dietary additives; and mental stress and anxiety. The *Apocynaceae* family counts *Rauwolfia serpentina* (Linn.) Plant Ex Kurz among its members, which are sometimes called devil hot pepper, Indian snake root, *Sarpagandha,* and other names. Of the over a hundred species that fall under the *Rauwolfia umbrella*, the vast majority are native to tropical and subtropical zones. These zones encompass not only Africa and Central and South America but also Australia, Europe, and Asia. *R. serpentina* is an evergreen, smooth shrub that may grow to a height of 60 meters. It is native to damp, deciduous forests in Southeast Asia, including Bangladesh, Burma, Malaysia, India, and Sri Lanka. Many different types of alternative medicine make heavy use of *R. serpentina*, including allopathy, folk medicine, Ayurveda, and Unani. As early as the pre-Vedic period, people were using *R. serpentina* root preparations as laxatives, uterine stimulants, diuretics, antidotes, expectorants, and febrifuges in folk and regional medicine.

Root extracts are used to treat a wide variety of illnesses and disorders, including respiratory infections, asthma, malaria, skin issues, parasites, organ diseases, circulatory difficulties, AIDS, rheumatism, diarrhoea, and dysentery. There are many different kinds of chemical components found in *R. serpentina*. Alkaloids such as *ajmalicine, serpentinine, yohimbine, reserpine, desipramine, indolizine, rescinnamidine, serpentine, serpentine,* and *reserpine* are found in this plant's root. Researchers from around the world in the field of drug development are interested in reserpine, one of the alkaloids. Additionally, it helps lower blood pressure and is effective in treating sedative sleeplessness, anxiety, trauma, schizophrenia, insanity, and psychiatric problems. *Reserpine* lowers blood pressure by decreasing levels of the catecholamine [8, 9]. The actions of reserpine and rescanning are the same. Nonetheless, it reduces plasma angiotensin II levels by inhibiting the angiotensin-converting enzyme (ACE), which converts angiotensin I. The antiarrhythmic action of ajmaline is due to its ability to block the sodium channel.

A potential antipsychotic effect of serpentine is due to its effect on type II topoisomerase activity. High quantities of *R. serpentina* phenols showed significant antimicrobial, hypolipidemic, and antidiabetic actions; yohimbine cures erectile dysfunction by acting as a selective alpha-adrenergic inhibitor in blood vessels [10, 11]. In addition to protecting cells from oxidative stress, the flavonoids found in R. serpentine exhibit anti-inflammatory, anticancer, and antioxidant properties [12]. The presence of saponins in system causes the homolytic impact and binds to the cholesterol characteristic [13].

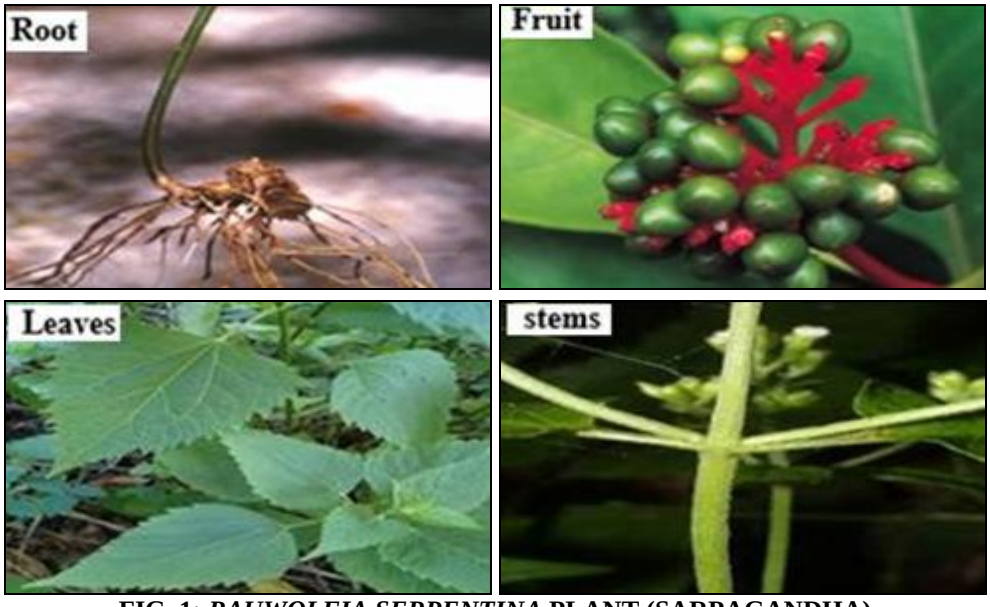

FIG. 1: *RAUWOLFIA SERPENTINA* PLANT (SARPAGANDHA)

Botanical Description:

Synonym's:

TABLE 1: DIFFERENT PLACES THE PLANTIS KNOWN AS DIFFERENT NAMES LIKE

Hindi	Sarpagandha, Chandrabhaga
English	Rauwolfia or Indian snake roots
Latin	*Rauwolfia serpentina*
Kannada	Keramaddinagaddi
Bengali	Chandra
Tamil	Chevanamalpodi
Chinese	Lufumu
Sanskrit	Sarpagandha

TABLE 2: TAXONOMICAL CLASSIFICATION

Kingdome	Plantae
Phylum	Angiosperms
Subphylum	Eudicots
Order	Gentianellas
Family	Apocynaceae
Genus	Rauwolfia
Species	Serpentina

Growing *Rauwolfia serpentina*: The best places to grow this plant are in humid, warm climates with uniform rainfall, which is found in tropical and subtropical regions. Loamy soil that is deep, organically rich, well-drained, and slightly acidic to neutral is ideal for its growth. Although the germination rates are low, the most typical way of multiplication is taking cuttings of seeds, roots, or stems. Seeds are scattered onto nursery beds once the rainy season ends. At the correct intervals after 6 to 8 weeks, healthy plants are transplanted to the field. Consistent drip watering, cultivation, and biodegradable manuring are essential in the early stages of development. It is important to provide shade and prevent water logging for the crop. Upon reaching an alkaloid content sufficient for medicinal usage, which typically takes 18 to 24 months, the roots are harvested, cleaned, and dried.

Rauwolfia Serpentine Collection: When the plant reaches full maturity, which is around 18 to 24 months after planting, and the roots contain the highest concentration of alkaloids, that's when the plant is often harvested. In order to harvest, the plant must be gently uprooted or its roots dug out without damaging it in any way. Before being chopped into appropriate pieces, the gathered roots are cleaned extensively to eliminate dirt and other contaminants. These are allowed to dry in shade or well-ventilated areas. To maintain the active ingredients in well-ventilated spaces.

For medical purposes, the roots are kept in a cold, dry area once they have dried completely and are put in receptacles that do not retain moisture. Components of a Chemical a structural nitrogen ring is present in a wide variety of chemical compounds known as alkaloids. Plants produce an exceptionally diverse array of alkaloids; however, they are produced by a number of other organisms, including bacteria and mammals. It is believed that 10% of plant species include alkaloids as secondary metabolites; they mostly serve as defences against herbivores and diseases. The analgesic, antispasmodic, and antibacterial effects of pure isolated alkaloids and their synthetic derivatives make them useful therapeutic chemicals.

The root extract contains alkaloids that reduce blood pressure by acting directly on the central nervous system, in contrast to other drugs that do the same. *Resederpine,* an indole alkaloid, accounts for around 0.1% of the total alkaloids found in R. serpentina root, which is said to contain 0.7-3.0% of the plant's total alkaloids. Therefore, these plants' stem biomass production may have economic significance. Weak basic dimethyl alkaloids, moderately basic alkaloids, and strong hydronium bases are the three classes of substances distinguished by their structural similarities. **Table 1** lists some of the alkaloids included in the Rauwolfia plant, including ajmaline, *ajmalimine*, *ajmalicine, deserpidineinosine*, *indolizine*, *Reserpine*, *reserpine*, *rescanning*, *rescinnamidine*, *serpentine*, *serpentine,* and *yohimbine*. The principal alkaloid with several medicinal applications is resperine [14-18].

These medications are utilized for the treatment of hypertension and breast cancer alongside *resperine*, *yohimbine*, *snakebite*, *deserpidine*, *ajmalicine*, and *ajmaline* [19, 20]. Purified crystalline mono alkaloid *Reserpine* was first discovered in 1952 from *Rauwolfia* root extract. This weak tertiary base is present in the oleoresin fraction of the roots and is useful in the treatment of hypertension, cardiovascular disease, and neurological problems [21]. *Reserpine* (3,4,5-trimethyl benzoic acid), an indole chemical of the 18-hydroxy yohimbine plant type, is associated with the antihypertensive effects of *Rauwolfia* roots. A natural sedative, this alkaloid is well-known for its many uses [22, 23]. As a result of its antihypertensive effects and its ability to bind to

catecholamine storage vesicles in nerve cells, *reserpine* is currently being used in physiologic investigations of physiological functions and in medicinal research. When catecholamine levels drop, this prevents the proper storage of serotonin and catecholamines. It interferes with the autonomic nervous system by reducing the amount of transmitter material in catecholamine neurons, which might set off the central parasympathetic nervous system [24].

The major focus of these compounds is regulation of cardiac contractions, peripheral resistance, and heart rate. In cases of hypotension brought on by stress or antagonistic nervous system activity, it can also help with sedation and lowering blood pressure. *Reserpine* stimulates the release of 5-hydroxytryptamine (5-HT) from all normally stored tissues and increases urine metabolites. Sacituzumab Siddiqui first isolated ajmaline in 1931 from *serpentine*, the chemical's source. In honour of Hakim Ajmal, the Khan, a prominent Unani practitioner from South Africa, he was given the name ajmaline [25].

Produced from *R. serpentine* pattern roots, this class I antiarrhythmic medicine is useful for detecting Brugada Syndrome (a genetic form of cardiovascular illness) and differentiating between subtypes of affected people [26]. By their method of action, these drugs may be broadly classified into four groups: calcium channel blockers, beta-adrenergic receptor blockers, depolarization delayers, and calcium channel blockers.

One diagnostic tool that shows rapid action when administered intravenously is ajmaline, a calcium channel blocker. One of the many cardiovascular problems that ajmalicine and its derivatives might alleviate is irregular cerebral blood flow. This alkaloid has many other applications as well. An effect on smooth muscle function in lowering blood pressure and preventing strokes. The pharmaceutical industry obtains around 3,500 kg of the chemical each year from *Rauwolfia* or *Catharanthus spp*. for the treatment of circulatory disorders. Starting with geraniol, the synthetic method continues with iridodial smell and industrial loaning synthesis, which, when oxidized, yields serotonin. As a result, serotonin, cat enamine, and strictosamide are able to convert *tryptophan* from *ajmalicine*, the building block of ajmalicine which aids in the development of the *tryptamine* coronate class nucleus. *Yohimbine* is a pharmacologically well-studied alkaloid that acts as a beta-blocker in the blood vessels or as an antagonist of some alpha-adrenergic receptors; it is therefore used to treat erectile dysfunction. As a result of dilating blood vessels and increasing blood flow to the penis, it helps with erectile dysfunction [28, 29]. *Yohimbine* was also studied in animal and human models with α2A-adrenergic receptor gene polymorphisms to see whether it may cure diabetes. By acting antagonistically against one another, these receptors reduce blood pressure and relax smooth muscle. Because it causes the body to produce more of certain chemicals, it widens the pupils of the eyes.

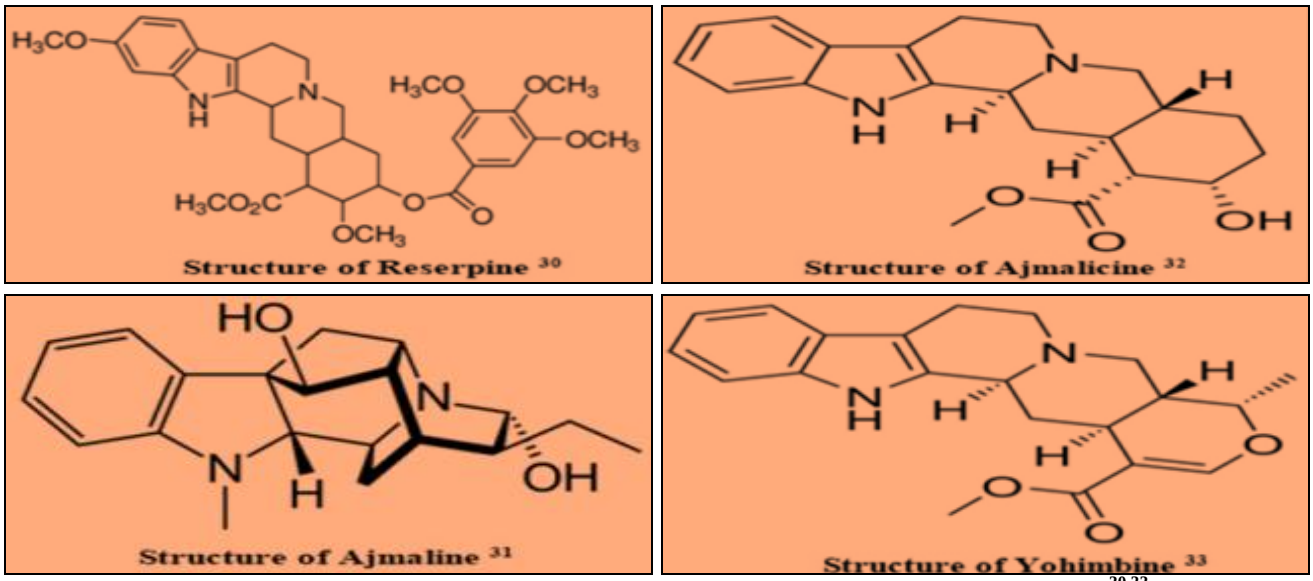

FIG. 2: CHEMICAL CONSTITUENTS OF *RAUWOLFIA SERPENTINA* PLANT [30,33]

Clinical Trial: There are over a hundred different treatments for hypertension that claim to be able to reduce blood pressure, according to a quick search of the literature on the topic. Using several hypotensive therapies, Ayman Ali was able to gather about two hundred testimonials regarding the successful treatment of hyperpiesia in 1930. The optimal strategy is still unclear in light of the persistently high mortality rate associated with hypertension despite the abundance of therapies proposed to address this illness. Evans and Loughnan were forced to admit that all thirteen preparations were worthless following a thorough examination or trial involving seventy cases of increased blood sugar levels (essential hypertension). Little sedatives, in their view, can be just as effective, if not more so, than the flashy, highly priced products that are now on sale. It is not entirely accidental that *R. Serpentine* has been selected for the current study. My decision to launch this inquiry is based on various factors.

Although these tablets have only been available for purchase for a decade, there has been a significant increase in demand in India for the dried roots of the serpentine plant. Serpentina root preparations are so popular for hypertension that nearly every patient in the country, even those without hypertension, has felt their effects. According to reports, a single company has sold more than fifty million capsules of the dried root. As a result, one objective of the ongoing inquiry is to determine whether the enthusiastic reaction to this treatment is justified. In the year 1940, I had previously brought up the topic of *R. serpentina* as a potential therapy for hypertension: Although the indications and case appropriateness of the drug have not been identified, it has been demonstrated that the treatment is effective in a certain percentage of hypertension cases only. Because of this, I have witnessed the effects of this medication in action on several occasions since then [34].

TABLE 3: CLINICALTRIAL DATA

Study/Trial Title	Authors	Indication/ Outcome	Summary	Ref.
A clinical trial of *Rauwolfia serpentina* in essential Hypertension	Rustom Jal Vakil *et al.*, 1949	Hypertension	One of the earliest clinical trials showing *R. serpentina* root extract (containing active alkaloids like reserpine) lowers blood pressure in patients with essential hypertension.	[35]
Rauwolfia serpentina in the control of anxiety	Paul Leninger, *et al*, 1957	Anxiety Control	Compared formulations (reserpine, scleroxcylon, crude root) in anxiety patients, showing equivalent effectiveness for overt anxiety; reported minor toxic symptoms manageable clinically	[36]
Antidiabetic Potential of *R. serpentina (in-vitro &* invivobutnot human clinical)	R. Kavitha, e*t al.*, 2025	Diabetesmodels	Demonstrated inhibition of α- amylase / α-glucosidase and reduced blood glucose in alloxan-induced diabetic rats; suggests potential antidiabetic effects requiring clinical validation.	[37]
Rauwolfia serpentina antioxidant & antidiabetic evaluation (preclinical)	Saveena Chauhan, *et al.* 2017	Antioxidant & antidiabetic assays	Compared wild and cultivated plant extracts *in-vitro* for antioxidant & alpha-amylase inhibition; not a human clinical trial but pharmacological evaluation.	[38]

Pharmacological Activity:

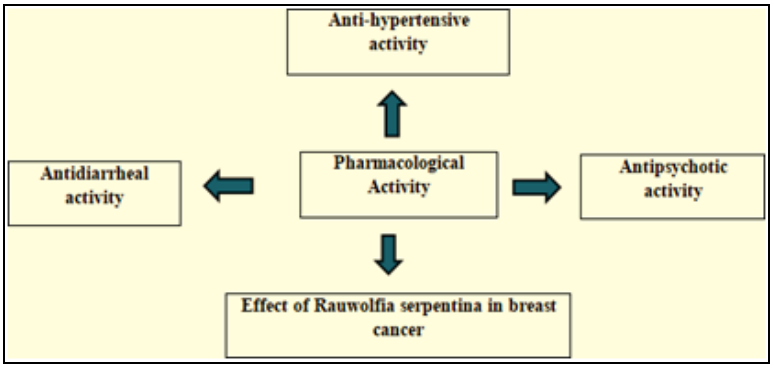

FIG. 3: PHARMACOLOGICAL PARAMETERS OF *RAUWOLFIA SERPENTINA*

Antihypertensive Activity: The alkaloid reserpine, found in *Rauwolfia serpentina*, is probably known to have antihypertensive properties. The root, leaflets, and base of the stem are the primary locations for the alkaloid reserpine. The typical start of the hypotension effect after an injectable treatment is around 1 hour. Approximately four hours following an intramuscular injection, you will feel the full impact of the medicine. The effects will be at their peak two weeks after your last dosage and may continue for up to four weeks thereafter. Typical dosages for the treatment of severe hypertension when used in conjunction with other underweight medications are 100 to 250 mg. Reserpine works by reducing the stores of catecholamine in nerve terminals, which in turn lowers the heart rate. It permits the enzymatic breakdown of neurotransmitter by blocking the reabsorption of both enzymes at their respective storage sites [39]. Reserpine transporters (VMATs) attach to the membranes of organelles that contain presynaptic neurons [40, 41]. The circular norepinephrine transporters VMAT1 and VMAT2, which are H^+ linked, are irreversibly inhibited by reserpine. Many endocrine and brain cells include VMAT1. Neurons have a high VMAT2 level. The neurotransmitters serotonin, dopamine, histamine, and adrenaline are all inhibited in the synaptic vesicles of neurons by the action of reserpine, which also decreases monoamine neurotransmitter

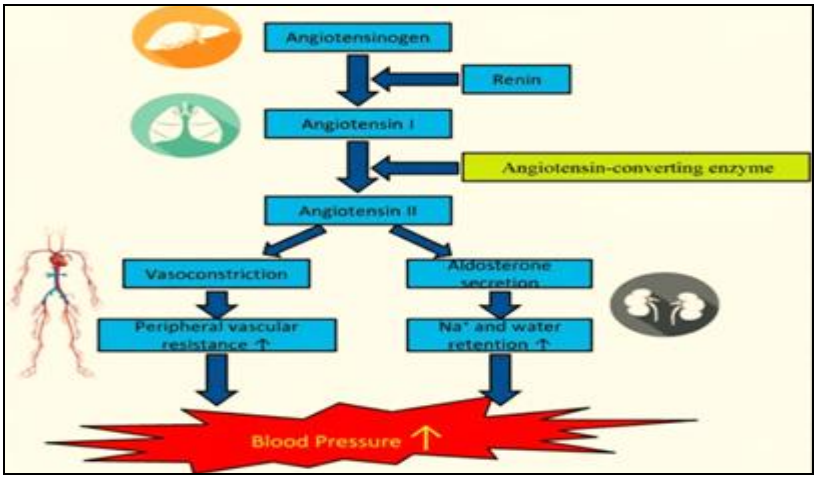

FIG. 4: THE RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM (RAAS) IN THE REGULATION OF BLOOD PRESSURE [42]

Anti-diarrhoeal Activity: In an investigation into the anti-diarrheal properties of a methanolic extract of *Serpentine rauwolfia* leaves in mice with peanut oil-induced diarrhoea, Dr. Ezeigbo, II discovered shows the extracts of its *serpentine* leaves has substantial Anti-diarrhoeal action.

Mechanism of Action: Many alkaloids in the plant (particularly rescindment, ajmaline, serpentine) inhibit calcium influx into smooth muscle cells. Reduced intracellular Ca^{2+} → decreased muscle contraction → slowed intestinal transit.

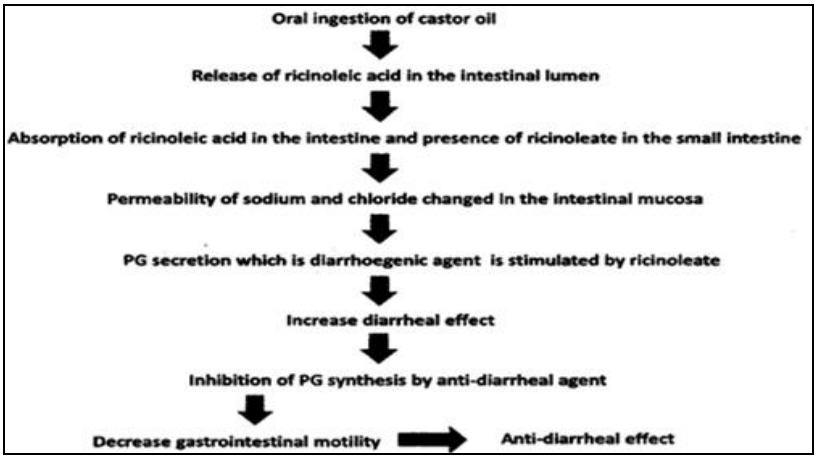

FIG. 5: MECHANISM OF ACTION OF ANTIDIARRHEAL ACTIVITY WITH SERPENTINE [43, 46]

Effect of *Rauwolfia serpentina* in Breast Cancer: In 1960 to 1970 A.D. and a purported association to breast carcinoma was established in medical literature in 3 case-controlled investigations, thus the employment with *Rauwolfia* and the Reserpine products was reduced. However, studies and analysis that remove exclusion bias reveal that *Rauwolfia* has no bearing on the incidence of cancer of the breast in patients. Ratherthan generating cancer, it possesses antitumor activity [47, 48].

Mechanism of Action:

Mitochondrial-mediated Apoptosis: Alkaloids can disrupt mitochondrial membrane potential., This leads to cytochrome-c release → activation of caspase-9 and caspase-3 → apoptosis.

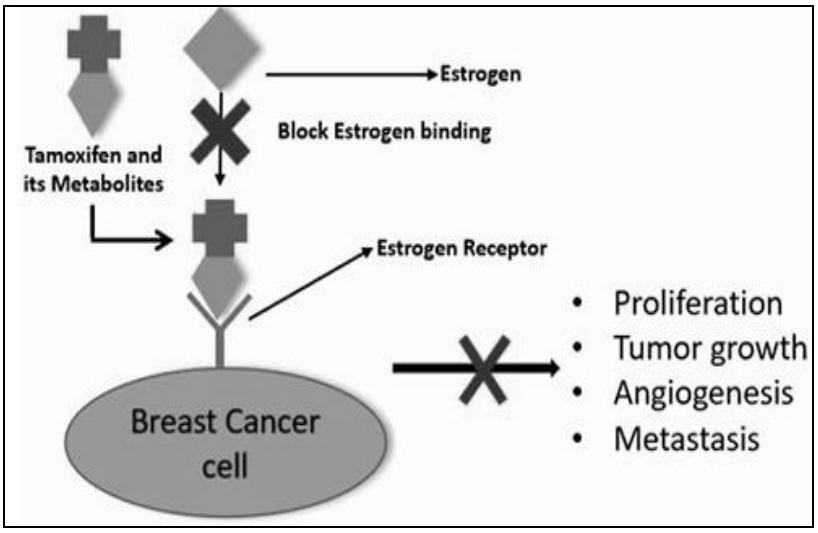

FIG. 6: MECHANISM OF ACTION OF TAMOXIFEN AND ITS METABOLITES ON BREAST CANCER CELLS. TAMOXIFEN AND ITS METABOLITES INHIBIT BINDING OF STROGEN HORMONE TO ESTRAGON RECEPTORS OF THE BREAST CANCER CELLS [49]

Antipsychotic Activity: Reserpine it was additionally employed for the treatment of schizophrenic and tardive dyskinesia. It relieves fever or acts as a febrifuge drug [50, 51].

The study found that a person with schizophrenia, Reserpine and chlorpromazine have comparable incidence of adverse effect show ever that the drug was lesser effective than the drug chlorpromazine for enhancing an individual's worldwide condition.

Mechanism of Action:

Serotonin (5-HT): Reserpine irreversibly blocks VMAT2 (Vesicular Monoamine Transporter-2) in presynaptic neurons. This leads to depletion of: Dopamine (DA), Norepinephrine (NE).

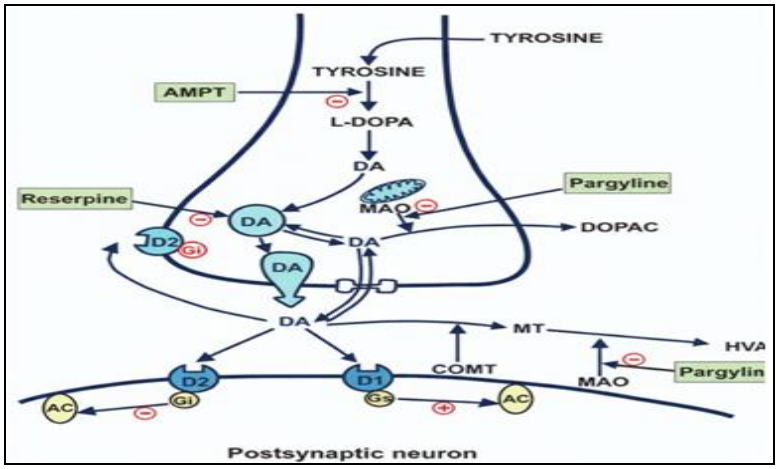

FIG. 7: SCHEMATIC DRAWING OF A DOPAMINERGIC NERVE TERMINAL. AMPT, RESERPINE AND PARGYLINE ARE DRUGS USED IN THE THESIS. Abbreviations: DA= Dopamine, D1= D1-Like Receptor, D2= D2-Like Receptor, Gi= Gi-Protein [52]

Other Pharmacological Activity:

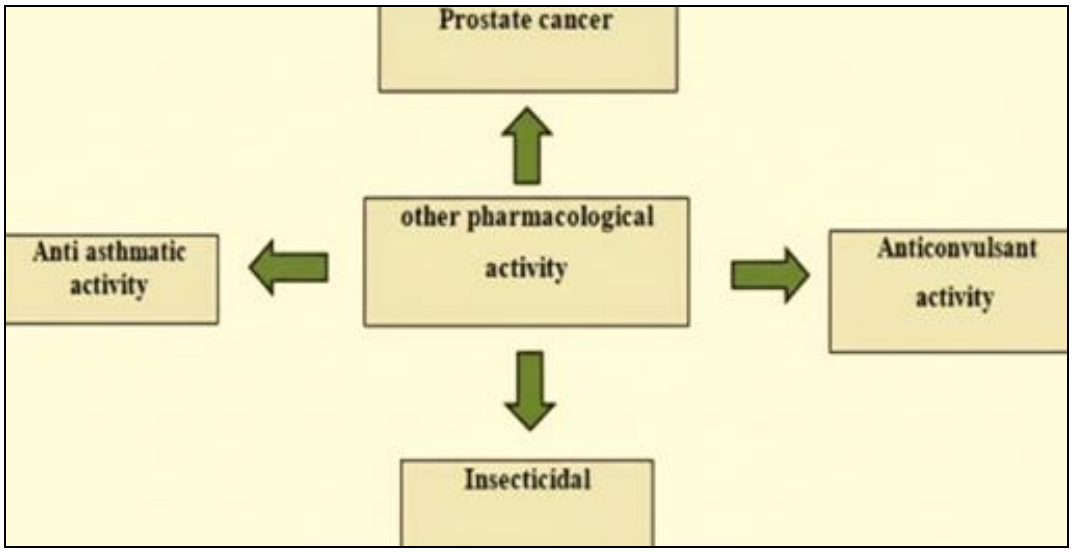

FIG. 8: SHOWING THE OTHER ACTIVITIES *RAUWOLFIA SERPENTINA*

Prostate Cancer: It is believed that prostate cancer, one of the leading causes of cancer-related death in men, is carcinoma of the prostate. There has been no noticeable improvement in the overall survival rate for patients with prostate cancer after they undergo contemporary medical practices, such as radiation and chemotherapy.

Contemporary medical practices, such as radiation and chemotherapy. As an alternative to conventional cancer treatments like chemotherapy and radiation, natural products have emerged as a rich source of potential new medicines. Fever, widespread weakness, intestinal infections, liver problems, and mental abnormalities are just some of the many ailments that have traditionally been treated using various parts of this plant. Alstonine is the primary component of the ß-carboline family of chemicals found in abundance in extracts from this plant's root bark. When administered to animals, this compound inhibited the proliferation of Ehrlich ascites cells and YC8 lymphoma cells, two types of tumour cells. According to analyses of gene expression patterns in prostate cancer cells that have undergone treatment [53-55].

The impacts on DNA damage and cell cycle control signalling pathways may explain why the plant extract is effective against prostate cancer in both in vitro and in vivo model cultures. The mechanism of action involves the following actions: activation of caspase-3 and caspase-9, increase of pro-apoptotic proteins (Bax), decrease of anti-apoptotic proteins (Bcl-2), and the use of alkaloids and extracts, particularly reserpine, ajmaline, and serpentine.

Mental Illness, Schizophrenia, High Blood Pressure and Other Diseases: Use of the plant's root as a sedative has several medical applications, including the treatment of schizophrenia, insomnia, hypertension, and other mental disorders. The medical community in many countries has come to regard the root extract as the best therapy for high blood pressure. The next alkaloids are directly affected by hypertension and are commonly used in medicine manufacture. *R. serpentina* extracts have a wide range of potential medical applications, including the treatment of fever, malaria, eye ailments, pneumonia, asthma, AIDS, headaches, skin diseases, and spleen abnormalities.

Antiasthmatic Activity: Intrinsic asthma is more prone to persist over time due to the increased prevalence of status asthmaticus. The study of the botanical components of herbs has tremendous potential for the treatment of a wide range of diseases, including bronchial asthma. Bronchial breathing issues are more common among respiratory illnesses, people suffer from a chronic respiratory illness [56].

The indole alkaloids found in *Rauwolfia serpentina* depress the central nervous system, which in turn has anticonvulsant effects. This class of alkaloids is useful for the prevention or management of

convulsions because it lowers neuronal excitability and inhibits excessive electrical discharges in the brain. *Reserpine* and *ajmaline* are alkaloids that stabilize neuronal activity and reduce catecholamine levels; they are primarily responsible for this effect [57]. The indole alkaloids in the plant impede synaptic transmission and neurotransmitter release, resulting in a decrease in neural excitability. The alkaloids serve to normalize neuronal activity and decrease aberrant electrical discharges that cause seizures by depleting monoamines such as dopamine, norepinephrine, and serotonin.

Insecticidal: *Rauwolfia serpentine* contains bioactive alkaloids and other phytochemicals that are poisonous to insects, giving it insecticidal qualities. The plant's extracts paralyze and kill insects by interfering with their neurological systems. To ward off or eliminate pests in the home and garden, people have long utilized powdered roots and crude extracts [58]. *Rauwolfia serpentina* is a natural pesticide that kills insects by interfering with their neurotransmission and metabolic activities [58].

Rational: The indole alkaloids found in *Rauwolfia serpentina* are primarily responsible for its insecticidal effects, which target the insects' central nervous systems. These chemicals hinder the normal conduction of nerve impulses and ion channels, which in turn disrupts normal neurotransmission. The insect dies as a result of losing its coordination and being paralyzed. Furthermore, alkaloids might compound their toxicity to insects by interfering with energy consumption and inhibiting essential metabolic enzymes [59].

The effect is an anti-asthma measure that is activated by stress, anxiety, or emotional excitement; it reduces stress-induced bronchospasm with breathing; it depletes serotonin, norepinephrine, and dopamine in the central nervous system; and it produces tranquility and drowsiness. As a plant of considerable medicinal importance (family *Apocynaceae*), *Rauwolfia serpentina* (L.) Benth. ex-Kurz. is known as Indian snakeroot or *Sarpagandha*. It is rich in bioactive secondary metabolites of the volatile indole alkaloid type, including reserpine, ajmaline, serpentine, and yohimbine, among others. The plant is on the IUCN list of threatened species due to illegal harvesting for medicinal purposes, as well as its poor rooting capacity and low seedling viability in 2015 [60].

CONCLUSION: *Rauwolfia serpentina* is not only a practical plant but also a highly effective antihypertensive drug. More study into the medicinal properties of cabbage *serpentina* and its constituents might help alleviate illness and its associated social costs. *Reserpine*, the active component of *Rauwolfia serpentina*, exhibits several biological actions and a strong affinity for the treatment of hypertension, as described in the aforementioned comprehensive literature.

A Low dose of *Rauwolfia serpentina* are both safe and effective in treating hypertension. Although most doctors recommend 250 mg for hypertension patients, the recommended daily dosage is less than 500 mg. The photochemical components of *Rauwolfia serpentine* include alkaloids, flavonoids, phenolic compounds, and many more. Because it does not contain any phenolic chemicals, the plant may possess antibacterial characteristics.

It is possible to use synthetic derivatives of pure alkaloids or use them as a foundational medical therapy due to their medicinal, therapeutic, and bactericidal characteristics. If administered to animals, they can reveal changes in their physiological state.

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