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A review on phytochemical, pharmacological and therapeutic effects of *Rauvolfia serpentina*

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Abstract
Rauvolfia serpentina (Indian snake root) is a medicinal plant with a wide range of pharmacological activities, attributed primarily to its alkaloid content, particularly reserpine. Traditionally used in India and Southeast Asia, it has proven therapeutic effects for treating hypertension, cardiovascular diseases, psychiatric disorders, and diabetes. Extensive research highlights its diverse actions, including antihypertensive, anti-inflammatory, antioxidant, anti-cancer, and anti-diabetic properties. *R. serpentina* is also effective in managing bacterial, fungal, and venous toxicity, with additional benefits such as hepatoprotective and cardioprotective effects. Its alkaloids, especially ajmaline, have been shown to support glucose utilization and lower blood pressure. Despite its therapeutic potential, *R. serpentina* carries a risk of side effects, including gastrointestinal disturbances, depression, and sexual dysfunction, particularly with overdose. Toxicity concerns such as weight gain, increased appetite, and potential psychiatric symptoms are noted. Given its wide range of applications, *R. serpentina* holds promise as a natural remedy, but further pharmacological and toxicological investigations are necessary to optimize its use and ensure safety in clinical settings.

Keywords: *Rauvolfia serpentine*, reserpine, antihypertensive, pharmacological activities, toxicity concerns

Introduction
Herbal medicine has been gaining popularity as a natural, cost-effective alternative to modern medication. It aims to reduce side effects and cure diseases more effectively. Additionally, social media and the internet can supply people with information on herbal medicine and its possible benefits. The use of herbal remedies in evidence-based medicine is still up for discussion [1]. The research of natural sources for bioactive substances has significantly pushed the search for novel treatments for a range of health diseases, despite concerns about the quality control and dependability of herbal medications [2].

The *Rauvolfia* genus is part of the Apocynaceae family and contains 80 tropical species. In North America, *Rauvolfia tetraphylla* and *Rauvolfia ligustrina* are common, while in Africa, *Rauvolfia caffra*, *R. macrophylla*, and *R. vomitoria* are common. Throughout Asia, *R. densiflora*, *R. verticillata, and R. serpentina* are abundant [3]. There are five species of the genus in India: *R. hookeri* Srinivas et Chithra, *R. micrantha* Hook f., *R. serpentina* (L.) Benth. ex Kurz, *R. verticillata* (Lour.) Baill., *R. tetraphylla* L., and the imported species *R. vomitoria* Afzel. Only two of the six species—*R. hookeri* and *R. micrantha* are found in South India's Western Ghats. There are too many *Rauvolfia* species, but as of now, we are only focusing on *Rauvolfia serpentina* because it is easily available, especially in India and Southeast Asia [4].

In traditional medicine, *Rauvolfia serpentina*, which is also known as Sarpagandha, Chandrabagha, Snake root plant, Chotachand, Chandrika, and Harkaya, is highly valued for its medicinal qualities. The medicinal properties of *Rauvolfia serpentina*, commonly referred to as Sarpagandha, Chandrabagha, Snake root plant, Chotachand, Chandrika, and Harkaya, make it a significant component of traditional medicine.

In India, the roots of *R. serpentina*, often known as 'Indian snake root' or 'Sarpagandha' for centuries, were traditionally used in traditional medicine to treat anxiety, psychotic behavior, schizophrenia, insanity, sleeplessness, and epilepsy. It has been used as an anthelmintic and has been used to treat dangerous bites from snakes and insects, and treat intestinal diseases, cholera, and colic. Given the plant's significant traditional use and therapeutic potential, this review will look at the botanical description, chemical ingredients, and different medicinal applications of *Rauvolfia serpentina*. Evaluating *R. serpentina's* pharmacological, phytochemical, and therapeutic qualities can help us comprehend its potential as a natural cure for many diseases [5].

English - *Rauvolfia* or Indian snake roots
Latin - *Rauvolfia serpentina*
Hindi - Sarpagandha, Chandrabagha
Latin - *Rauvolfia serpentina*
Sanskrit - Sarpagandha
Kannada - Keramaddinagaddi
Bengali - Chandra
Tamil - Chevanamalpodi
Chinese - Lu fu mu

Taxonomical classification
Kingdom - Plantae
Phylum- Angiosperms
Subphylum - Eudicots
Order - Gentianales
Family - Apocynaceae
Genus - Rauvolfia
Species - Serpentina [6]

History
India has traditionally used the root of *Rauvolfia serpentina* for hundreds of years. Sarpagandha is a term used in Ayurveda to describe using as a snake bite remedy [7]. India has been using *Rauvolfia* over more than 3000 years [8], and Africa has been using it for hundreds of years. Around 1000 B.C., *Rauvolfia*—also known as Sarpagandha and Chandra—was mentioned in Indian literature (Yarnell and Abascal, 2001). This plant is known to be *Rauvolfia serpentina*, named after the 16th-century German physician Dr. Leonhard Rauwolff [10]. In 1949, A.D. Jal Vakil provided an innovative research study on the antihypertensive characteristics of *Rauvolfia serpentina* in a British medical magazine [11].

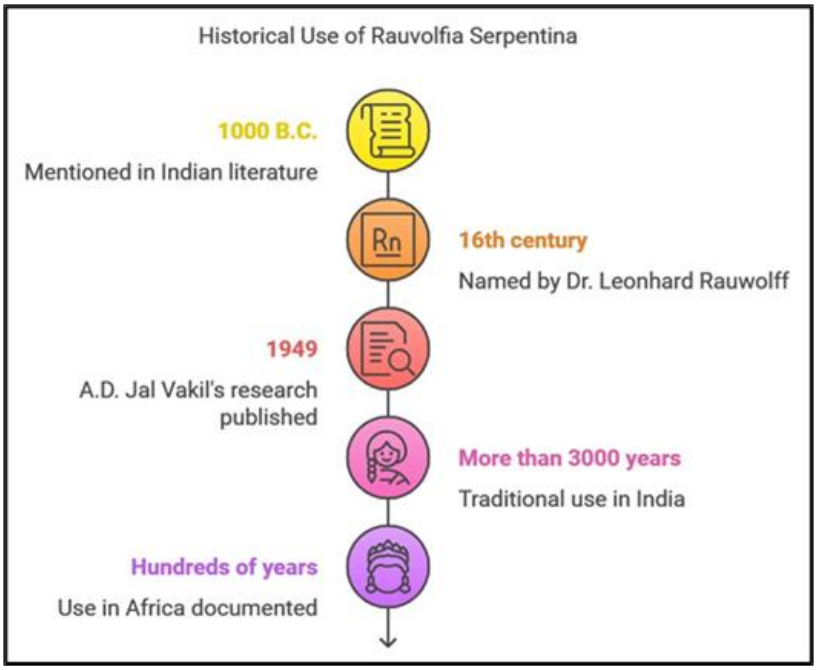


Fig 1: Shows pictorial representation of history of *Rauvolfia serpentina*

Morphology
Sarpagandha, frequently referred to as *Rauvolfia serpentina*, is a climbing shrub or herb with a height of around 60 cm [12]. This tree has a light-colored viscous latex, cylinder-shaped stems, and pale bark. The leaves have an oval or lanceolate shape and are pale green in color. Fruits are bright, either purple or black [13].

Roots - 10-8 cm long
Size - 1-3 cm diameter
Shape - Sub-cylindrical, slightly tapering, and torturous
Fracture - Short and irregular
Color - Greyish yellow to brown

Fig 2: *Rauvolfia serpentina* plant

Cultivation

Rauvolfia grows in a variety of climates. It grows effectively in shade and thrives in hot, humid climates. A lot of humus, good drainage, and clay-loamy soil are ideal for cultivation. It flourishes in temperatures between 10 and 38 °C and has a pH of about 4. There needs to be 250–500 cm of rainfall. Although stem or root propagation is an alternative, seed propagation is a simple plant cultivation method [14].

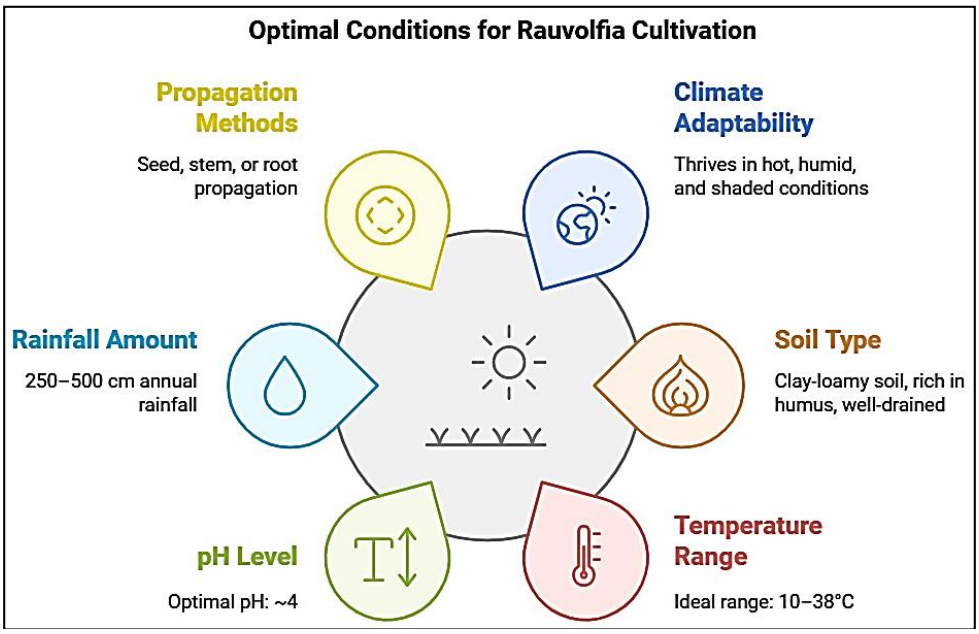


Fig 3; Cultivation conditions for *Rauvolfia serpentina*

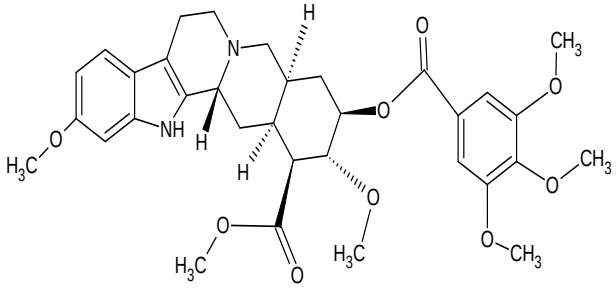
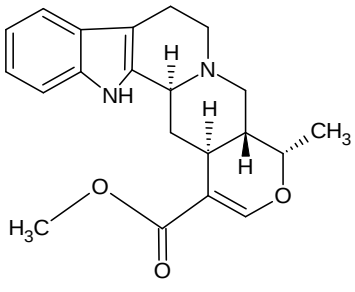
Phytochemical constituent

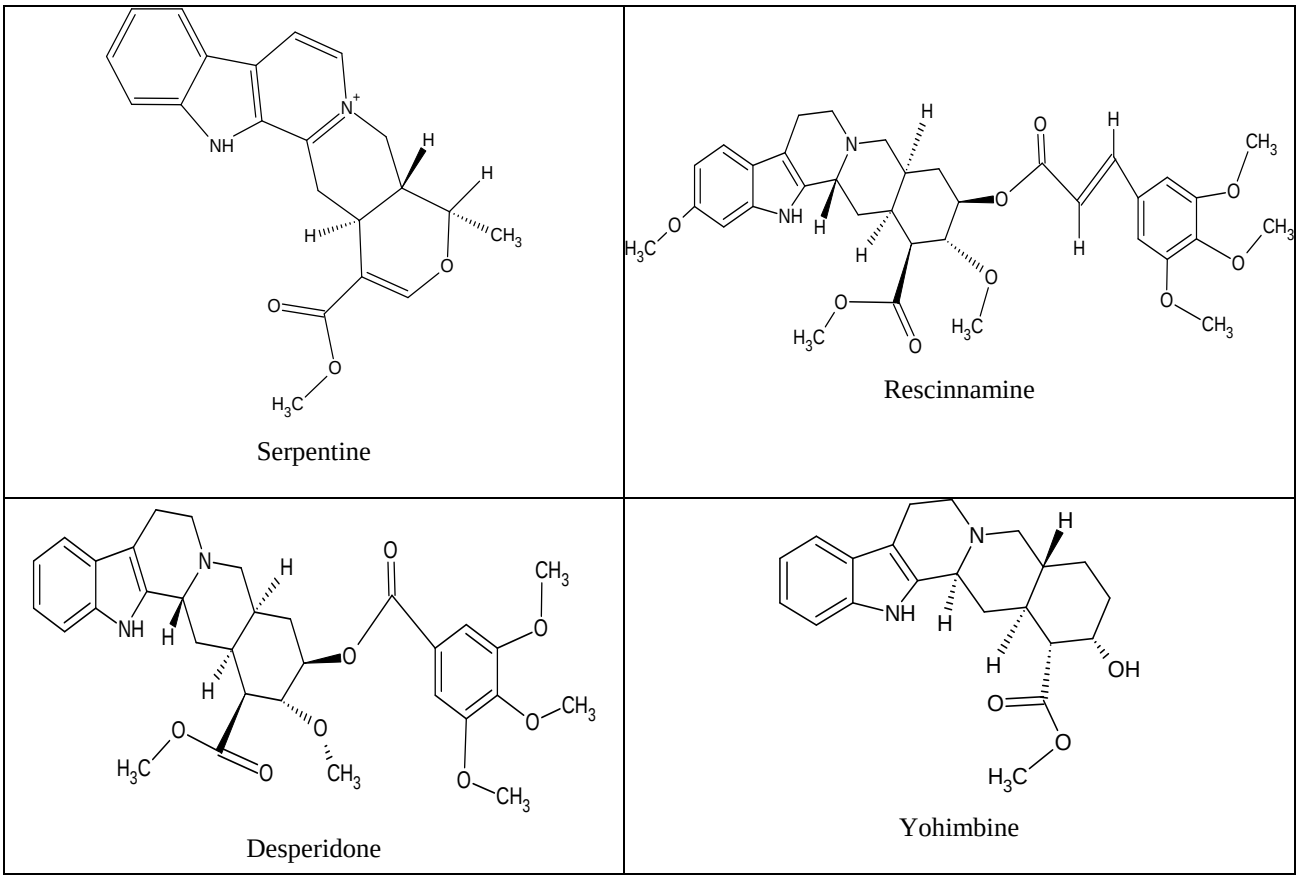
Rauvolfia serpentina has proven an extensively researched area of study for decades, and many researchers have examined its phytochemical characteristics. *R. serpentina* contains several kinds of phytochemical substances or secondary metabolites that consist of alkaloids, phenols, tannins, and flavonoids [15]. Table 1 gives a summary of the properties of the phytochemicals.

Table 1: Phytochemicals present in *Rauvolfia serpentina*

Phytochemica	Description	Key Properties/Uses
Alkaloids	Heterocyclic nitrogen compounds. Found in roots, stem, and leaves.	Analgesic, antispasmodic, antibacterial; reduces blood pressure.
Reserpine	Weak tertiary base in roots.	Treats hypertension, cardiovascular, neurological disorders; reduces catecholamines and serotonin.
Ajmaline	Sodium channel blocker.	Diagnoses Brugada Syndrome; increases gastrointestinal and respiratory motion.
Ajmalicine	Derived from tryptophan via enzymatic steps.	Treats circulatory disorders; restores cerebral blood flow; prevents strokes.
Serpentine	Bisindole alkaloid; inhibits topoisomerase II.	Antipsychotic effects.
Rescinnamine	Ester alkaloid; blocks ACE enzyme.	Treats hypertension; reduces angiotensin II levels and blood pressure.
Deserpidine	Ester alkaloid without methoxy group at C-11.	Antihypertensive, antipsychotic; inhibits angiotensin I conversion.
Yohimbine	Alpha-adrenergic antagonist.	Treats erectile dysfunction; relaxes smooth muscles; potential diabetes treatment.
Phenols	Secondary metabolites with antimicrobial properties.	Antidiabetic, hypolipidemic, antimicrobial, emulsifying agent.
Tannins	Contain gallic and diallic acids.	Enhance wound healing, relieve mucous membrane irritation.
Flavonoids	Water-soluble antioxidants.	Prevent oxidative damage, reduce heart disease risk, anti-inflammatory.
Saponins	Glycosides of sterols and triterpenes.	Promote wound healing, prevent bleeding, bind cholesterol.

Table 2: Structure of most commonly found in *Rauvolfia Serpentina*

 Reserpine	 Ajmalicine



Based on Namita Bhardwaj's estimate of the chemical composition of *Rauvolfia serpentina*, the chemical composition of *Rauvolfia* can be summarized as follows [16]

Table 3: Chemical composition of *Rauvolfia serpentina* (All the quantities are mg/100gm)

Phytochemicals	
Alkaloids	1.50 ± 0.02
Flavonoids	1.65 ± 0.12
Phenols	1.84 ± 0.11
Tannins	0.85 ± 0.20
Mineral composition	
Calcium	0.45 ± 0.10
Magnesium	0.10 ± 0.20
Potassium	0.05 ± 0.11
Phosphorus	0.18 ± 0.22
Sodium	0.03 ± 0.01
Iron	1.90 ± 0.20
Zinc	5.35 ± 0.11
Vitamin composition	
Ascorbic acid	41.04 ± 0.20
Riboflavin	0.52 ± 0.10
Thiamine	0.20 ± 0.02
Niacin	0.05 ± 0.10

Pharmacology

R. serpentina is a significant therapeutic component due to the presence of alkaloids in its roots' oleoresin fraction. A thorough pharmacological examination is required to prove its therapeutic efficacy, determine appropriate dosages, and assure safety when treating illnesses such as cardiovascular disease, hypertension, and psychiatric disorders. It affects glycogen, g-amino butyric acid, nucleic acids, acetylcholine, and anti-diuretic hormone balances. Reserpine inhibits respiration, increases peristalsis and myosis, relaxes nictitating membranes, and influences the temperature-regulating center. It has a long number of pharmacological characteristics, such as sympathomimetic, hypnotic, anticholinergic, hypotensive, anticontractile, hyperthermic, vasodilator, antiemetic, anti-arrhythmic, antifungal, and nematocidal. It is also antidiuretic and anti-fibrillar.

R. serpentina has been proven to have the following pharmacological properties:

1) Acting on the vasomotor center causes systemic vasodilation and lowers blood pressure.
2) By acting as a depressant on the brain centers and soothing the nervous system.
3) It relaxes the stomach mucosa and stimulates the intestinal tract's simple musculature.
4) It also activates the muscles of the bronchi [6].

Fig 4: here

Hypertension activity

Sen and Bose (1931) discovered a novel medication from *R. serpentina* that is used significantly by practitioners in modern medicine to treat hypertension and insanity [17]. Patients being treated with *R. serpentina*-derived alseroxylon, a naturally occurring fat-soluble alkaloid extract, experienced an ongoing blood pressure fall of more than 20 mmHg [18]. In 1953, 51 hypertensive Swiss workers were found to have decreased blood pressure in Switzerland. In 1953, A study in New Zealand found that reserpine drastically decreased blood pressure within 4-6 hours of administration (DOYLE and SMIRK, 1953). *Rauvolfia* was considered the most effective hypertension medication in India throughout the 1950s. It was also estimated that 90% of all physicians, including over 60,000, use it across the country [20].

Ajmaline, an alkaloid derived from *R. serpentina* roots, is widely employed to distinguish between disease subtypes and to diagnose Brugada Syndrome (a genetic heart condition). The Ajmaline test involves giving reserpine to individuals experiencing arrhythmia. It was previously used to promote intestinal motility and breathing. Ajmaline, an alkaloid, has been demonstrated to have the identical effects on systemic and pulmonary blood pressure as serpentine [21]. It was reported that reserpine extracted from *R. serpentina* was used clinically to treat hypertension and reduce diastolic pressure (Shamon and Perez, 2016). Additionally, carried out more research in an outpatient setting to assess the effects of oral reserpine on a sample of hypertensive patients. Reserpine medicine reduced systolic blood pressure to an average of 30.7 mmHg in a few patients, while diastolic blood pressure decreased to 19 mmHg [23].

Ajmaloon, an alkaloidal substance isolated from *R. serpentina*, has been demonstrated to have significant effects on blood pressure due to its impact on vascular baroreceptors [24]. Reserpine's antihypertensive qualities were associated with its calming impact on both the central and peripheral nervous systems, which is done via linking vesicles in nerve cells to catecholamine storage. Reserpine from *R. serpentina* is also known to prevent normal serotonin and catecholamine storage following catecholamine depletion. Reserpine's ability to relax both the central and peripheral nervous systems through linking nerve cell vesicles to catecholamine storage has been related to its antihypertensive effects. Reserpine, derived from *R. serpentina*, has also been demonstrated to inhibit serotonin and catecholamines from being stored normally during the drop of catecholamine levels [25].

Anti-bacterial activity

The effectiveness of *R. serpentina* root extracts against S. typhi, in which the maximum activity was seen at low concentrations. Also, it was discovered that the leaf extract effectively inhibited the roots' ability to proliferate. Therefore, the anti-bacterial and anti-proliferative properties of the root and leaf extracts were caused by the increased concentration of indole alkaloids present in those substances. According to the study, *R. serpentina* has the potential to be utilized as a natural remedy for cervical cancer and bacterial infections [26].

R. serpentina's ethanolic root extract possesses antibacterial properties due to its high diffusion. The study analyzed three gram-negative bacteria (*Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Salmonella typhimurium*) and two gram-positive bacteria (*Bacillus subtilis* and Staphylococcus). Among those, it was found that Bacillus subtilis, *Staphylococcus aureus*, and *Klebsiella pneumoniae* were susceptible [15].

Anti-fungal activity

The antifungal and antibacterial activities of numerous *R. serpentina* fruit extracts. Among the extracts tested, aqueous and chloroform extracts had the strongest inhibitory effect against *E. coli* and *Klebsiella pneumonia*, respectively. Furthermore, pet-ether and ethanolic extracts outperformed other Pet extracts in terms of *S. aureus* and *P. aeruginosa* inhibition. Extracts from ether and ethanol showed good efficacy against *A. flavus* and *A. niger* [27]. *R. serpentina* root extracts are efficient antifungals against three phytopathogenic fungi: *Aspergillus flavus*, Mucor rouxii, and *Alternaria alternata*. *R. serpentina's* aqueous root extract exhibited significant antifungal efficacy against *Alternaria alternata* and *Aspergillus flavus* [28].

Anti-inflammatory activity

Antioxidants and flavonoids have been proved to have anti-inflammatory properties and are used in herbal therapy to treat numerous diseases [29, 30]. Rauvolfian, a pectic polymer derived from *Rauvolfia callus*, demonstrates anti-inflammatory activity. Rauvolfian, a pectic polysaccharide, was isolated from the dried callus of *R. serpentina* via a series of extractions using ammonium oxalate (0.7%) [30]. The extracts of *R. serpentina*, which have a high saponin concentration, are successful at stopping bleeding and healing wounds [31].

Anti-oxidant activity

The antioxidant properties of methanolic leaf extract of *R. serpentina*. The extract was evaluated for antioxidant activity, which comprised DPPH radical scavenging, superoxide anion scavenging, and reducing power. Carotenoids, tocopherols, flavonoids, phenolics, ascorbic acid, and pigment concentration were measured in *R. serpentina*. This species had high total phenolic content, robust DPPH radical scavenging action, and a rich composition of vitamin E pigments [32].

Anti-venomous activity

The harmful effects of Naja naja venom are greatly reduced by the ethanolic extract of the entire *R. serpentina* plant. Approximately 0.14 mg of *R. serpentina* extract totally negated the deadly effects of 2LD50 venomm [33, 34]. *R. serpentina's* procoagulant and hemolytic characteristics enable its aqueous extract to neutralize venom. The harmful effects of the venom of *Daboia russelli* are significantly reduced by *Rauvolfia serpentina* [34].

Insecticidal activity

The larvicidal properties of *R. serpentina* seed solvent extracts against *Culex quinquefasciatus*. The pet-ether extract displayed significantly higher rates of death than the other extracts, as did seed extracts with the five solvents (absolute alcohol, benzene, ethyl acetate, petroleum ether, and acetone). *R. serpentina* seed extract in pet-ether proved to be an effective source of mosquito larvicidal activity (Das and Chandra, 2012). If made from *R. serpentina* leaves that had been shade-dried, mosquito coils displayed smoke toxicity against the filarial vector *Culex quinquefasciatus*. The highest death rate was observed in *Cestrum diurnum* seeds, which followed closely by *Cestrum diurnum* leaves, *Rauvolfia serpentina* leaves, and *Polyalthia longifolia* leaves. According to the study, *R. serpentina* leaf smoke can successfully reduce mosquito populations [36].

Cardioprotective activity
Flavonoids discovered in the intestinal system have been scientifically linked to a lower risk of heart disease [29]. the Reserpine's pharmacological effectiveness in comparison to the *Rauvolfia* roots' natural resin portion. Reserpine is usually employed to treat illnesses of the cardiovascular system, blood vessels, and medical specialties [37].

Anti-rheumatic activity
For rheumatic pain, a one-gram paste made from equal parts leaves and flowers was taken with honey twice a day for four days. In addition, they drink 1 litre of water every morning with 5 grams of leaves blended with sugar. To treat rheumatic issues, a paste containing the equal amount of leaves and flowers was given twice a day for five days [38-39].

Anti-diabetic activity
R. serpentina contains higher quantities of total polyphenolic compounds, which have been shown to have significant hypolipidemic and antidiabetic effects. In medicine, it also functions as an emulsifier and expectorant (O'Connor and Maresh, 2006; Rolf *et al*., 2003). According to reports, *R. serpentina* has a unique plant-derived molecule that inhibits aldose reductase, an effective diabetes treatment. Ajmaline from *Rauvolfia* species has been identified as a potent antidiabetic drug [42]. Serpinine extracted from *Rauvolfia* species has been proven to strongly promote glucose utilisation (Chatterjee and Talapatra, 1955; van de Venter *et al*., 2008). The glucose-lowering potential and acute toxicity of *R. serpentina* extract (HMREt) were evaluated. The studies on the acute toxicity of orally administered HMREt (5-250 mg/kg) revealed that it was a sedative and caused mortality [45].
R. serpentina has been demonstrated to cause atherogenic dyslipidemia, arteriosclerosis, and a glycosylation index in alloxan-induced type 1 diabetic rats after 14 days. The 42 mice were placed into four groups: diabetic control, negative, positive, and normal control, with each getting three test doses. Following 14 days of therapy, non-HDL-C, arteriosclerosis, atherogenicity, and glycosylation all significantly decreased. In mice with alloxan-induced diabetes, the study found that *R. serpentina* has therapeutic potential for lowering glycosylation, atherogenic dyslipidemia, and arteriosclerosis[46]. The percentage inhibitory action against the α-amylase enzyme increases with dosage. The wild variety demonstrated higher inhibition than the cultivated *R. serpentina*, with an IC50 value of 0.83 µg/ml [47].

Anti-cancer activity
A total of 109 case-control pairs with hypertension were used to calculate the incidence of breast cancer. About 109 patients were treated with *Rauvolfia* drugs and other medications. When compared to other agents, Rauvolfia had a relative risk of getting breast cancer ranging from 0.9 to 1.11 [48]. *R. serpentina* root and bark extract contains alstonine-suppressed tumor cell proliferation in mice infected with YC8 lymphoma cells. The anti-cancer effectiveness of an *R. serpentina* extract was tested using both in vivo and in vitro models [49, 50].

Mental disease
The Ajmaline group is effective at depressing the heart, although the serpentine group inhibits respiration, depresses the nerves, and stimulates the heart [51]. *R. serpentina* contains reserpine and alseroxylon, which have been clinically proven to effectively reduce anxiety in ambulatory people. The root extract of *R. serpentina* was used to treat excessive blood pressure, sleeplessness, and sedation. It has been found to treat various conditions, including fever, malaria, eye problems, pneumonia, asthma, AIDS, headaches, skin diseases, and spleen disorders. Reserpine is an antipsychotic medication derived from *R. serpentina* dried root and used to treat schizophrenia. Reserpine, ajmaline, and serpentine are antipsychotic (neuroleptic) chemicals found in *R. serpentina* root powder [52, 53].

Hepatoprotective activity
R. serpentina root aqueous-ethanolic preparations showed hepatoprotective effectiveness against rats' liver damage caused by paracetamol. The extract decreases thiobarbituric acid, glutathione, glutathione-S-transferase, glutathione reductase, superoxide dismutase, catalase, glycogen, serum bilirubin, glutathione reductase, liver glutathione, Na + K + ATPase activity, and serum marker enzymes [54].

Anti-hyperglycemia
The ability *of R. serpentina* extracts to prevent hyperglycemia, hematinic, and antioxidant dysfunction in a mouse model of diabetes produced by alloxan. Blood glucose levels were shown to have dramatically dropped when different amounts of *R. serpentina* extract were increased. The liver's functions were also restored, as evidenced by the return of normal protein concentrations and ALT and other enzyme levels [46].

Hypolipidemic activity
R. serpentina root powder exhibits hypolipidemic action by giving rabbits oral medicine for a duration of 12 days. For proof of the significant hypolipidemic activity, the test determined serum triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), alanine aminotransferase (ALT), and lactate dehydrogenase levels [55].

Anti-diarrheal activity
investigated the potential of *R. serpentina* leaf methanolic extract to prevent diarrhea in mice by evaluating its antidiarrheal castor oil properties. The anti-diarrheal effect was demonstrated to be caused by a dose-dependent decrease in intestinal weight and fluid volume [56].

Toxicology and Side effects
Despite all the pharmaceutical actions, just a few negative effects were noted in the *Rauvolfia* species.
Rauvolfia species have a few drawbacks, including increased intestinal motility, lower energy expenditure, weight gain, and increased hunger. An overdose may cause shaking, anxiety, depression, and nightmares. Women do not have the same libido or desire for sex that males have [57].
Reserpine has been linked to several negative side effects, including breast enlargement, lethargy, sleepiness, gallbladder rhea, gastric ulcers, psychiatric nightmares, depression, hypotension, skin rash, nausea, vomiting, abdominal cramping, and sexual dysfunction (Yarnell and Abascal, 2001).
Reserpine can induce minor edema in some persons [58].
The observed consequences include an ongoing increase in blood pressure and the recurrence of unwanted symptoms [59].

Conclusion
This narrative review highlights the significant therapeutic potential of *Rauvolfia serpentina*, a cornerstone of traditional

medicine, in managing diverse health conditions. The plant's bioactive compounds, particularly alkaloids like reserpine and ajmaline, demonstrate efficacy in treating hypertension, diabetes, psychiatric disorders, and microbial infections. Additionally, its antioxidant, anti-inflammatory, and anti-cancer properties underscore its role in promoting overall health. While *R. serpentina* shows promise as a natural remedy, challenges related to quality control, standardization, and potential side effects necessitate further research. Large-scale clinical trials and improved cultivation practices are essential to validate its integration into modern evidence-based medicine.

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