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Pharmacological Review on *Rauwolfia serpentina*

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Abstract: *The existence of significant therapeutic capabilities makes Rauwolfia serpentina a prominent medicinal plant in the pharmaceutical sector. Sarpgandha is a blooming plant in the Apocynaceae family that has been utilized in Ayurveda for centuries. Rauwolfia Serpentina is a herbal remedy for hypertension that is both safe and efficient. It contains alkaloids, glycosides, resins, phenols, carbohydrates, and other phytoconstituents. The scientific literature on the use of Rauwolfia in the treatment of hypertension, mental disorders and some diseases is reviewed by this author. The morphology, chemical composition, pharmacology, mode of action, medicinal uses, dose, side effect, toxicity & drug interaction of Rauwolfia alkaloids are all covered in this review. The plant offers clinicians a safe and effective treatment option for a variety of ailments.*

Keywords: Reserpine, hypertension, sarpgandha, rauwolfia serpentina, alkaloids

I. INTRODUCTION

India has the diverse, oldest and richest cultural tradition associated with the medicinal. plants for curing numerous diseases. Plant-based treatments are safe, accessible, economic, reliable, and effective. Rauwolfia serpentine is the dried root of rauwolfia serpentine (linne) bentham ex kurz.(family: Apocynaceae). It is an erect shrub that grows 1 meter in the height and has cylindric stems. These stem have pale bark and consist of light colored viscous latex. [1][2]

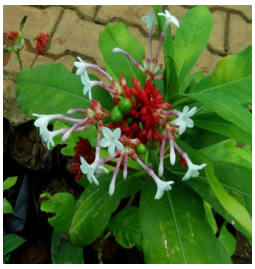

Fig. 1. Plant of Rauwolfia serpentina

Scientist have been working on the phytochemical analysis of the plant due to its medicinal importance. It has been used as anthelmentic and anti-hypertensive drugs. It is used as an antidote against snake bite and bite of other poisonous insects. In diarrhea, dysentery, cholera, fever, opacity of cornea and central epilepsy and ebolic R. serpentine is known to cure various circulatory disorders[3]. the room juices or extract is used to treat liver and abdominal pain, various gastrointestinal disorders and to expel intestinal worms from the children.

Kingdom	plantae
Phylum	Tracheophytes
Subphylum	Angiospermae
Class	Magnoliopsida
Order	Gentianales
Family	Apocynaceae
Genus	Rauwolfia

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Species	R. serpentina
Common name	Sarpagandha

Table 1: Taxonomy of Rauwolfia serpentina

The roots used externally on the affected areas. The other diseases such as pneumonia, malaria, body aches, eczema, burns, menstrual disorders, scabies, skin cancer, asthma, respiratory problems, eye inflammation, spleen diseases and fever can also be cured using R. Serpentina

1.1 Morphology

It is an erect evergreen perennial bush with along irregular, yellowish root stalk to a length of 60 -90 cm the fruits are drupe 0.5 cm in measurement and sparkling dark when completely ready. The plant is found in tropical Himalayas in lower hills himachal Pradesh.

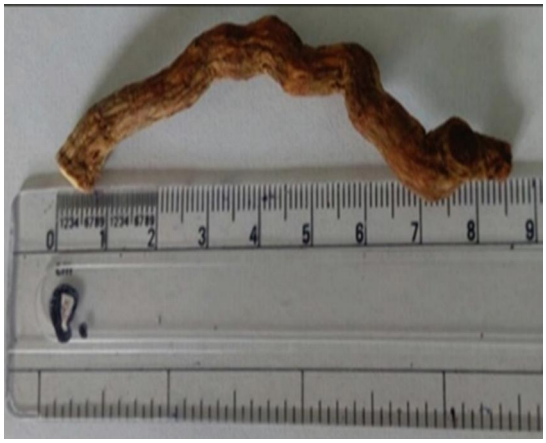

Fig. 2. Root of Rauwolfia serpentina

1.2 Chemical Composition

Alcohols, sugars, and glycosides, fatty acids, flavonoids, phytosterols, oleoresins, steroids, tannins, and alkaloids are some of the phytochemicals found in Rauwolfia. The most important alkaloids identified in the plant are indole alkaloids, which account for more than 50 of the plant's alkaloids.[4]

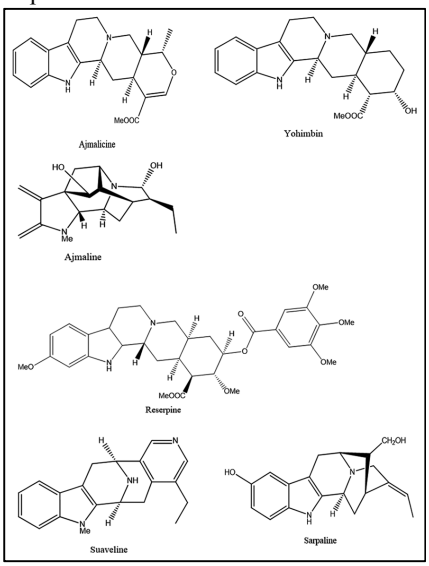

Fig. 3. chemical constituents of rauwolfia.

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Indole alkaloids are a group of nitrogenous compounds that are derived from the amino acid tryptophan. They share a common 5 and 6 carbon heterocyclic ring structure with 1 nitrogen molecule.[5] All part of the plant, including the stem and leaves, contain indole alkaloids, but they are found in highest concentration in the bark of the root.[6] The the identified indole alkaloid include ajmalidine, ajmaline, ajmalinine, ajmalicine, aricine, canescine, coryanthine, deserpidine, isoajmaline, isoserine, isoserpiline, lankanescine, raucaffricine, rauhimbine, rauwolfinine, recanscine, rescinamine, reserpiline, reserpine, reserpinine, thebaine, yohimbine, and yohimbinine.[6][7]

1.3 Pharmacology

The alkaloid reserpine is the most studied in R. Serpentina. Robert Wallace wigging was the first to isolate and use it in 1950. The alkaloid reserpine is classed as an indole alkaloid. It's a white to yellow powder that darkens in the presence of light. It has no odour, is insoluble in water, soluble in alcohol only slightly, and easily soluble in acetic acid. Its chemical formula is C33H40N209, and it has a molecular mass of 609 g. It has a harsh taste. Isolated reserpine was first used in the treatment of hypertension, tachycardia, and thyrotoxicosis in 1952 as the medication serpasil.

Reserpine is distributed in the brain, liver, spleen, kidney, and adipose tissue, among other places.[8] It has been discovered that its initial half life in the blood is 4 to 5 hours. In plasma, its elimination half life has been calculated to range between 45 and 168 hours. Because of its binding to protein and blood cells, it has a relatively long elimination half life. Hepatic metabolism responsible for about 62 % of reserpine degradation, whereas renal elimination is accomplished through faecal excretion. Reserpine alone has been found to include between 30% and 60% of excreted metabolites.

1.4 Mechanism of Action

Reserpine's mechanism of action has been extensively studied and recorded. Reserpinine binds to vesicular protein receptors. VMATs (vesicular monoamine transporters) are transporters of monoamines in the brain. Membranes of specific Secretory Organelles Presynaptic neuron vesicles. Reserpine hinders the release of intracellular neurotransmitters interacting to VMAT proteins and inhibiting secretory function vesicles formed by neurotransmitter uptake Finally, the usage of reserpine ensures that there are no or few side effects. Only a few neurotransmitters are released by the brain. presynaptic neuron is a type of presynaptic neuron. As a result, there is no or only one option. Nerve impulse propagation is modest.

The postsynaptic neuron is where this happens. VMAT1 and VMAT2 are two vesicular transport protein isoforms. VMAT1 is mostly located in the brain's neuroendocrine cells. particularly in the peripheral nerve system In the adrenal medula, there are chromaffin granules. platelets, sympathetic neurons VMAT2 is mostly located in the brain and spinal cord. system of the sympathetic nervous system Mast cells, as well as, In the stomach, histamine-containing cells can be discovered. pancreas. Reserpine is attracted to VMAT2 is three times more powerful than VMAT1. VMAT1 is a protein with which it has a strong affinity and attaches to certain targets nearly irrevocably platelets' receptors. [9][10]

1.5 Pharmacological Activities

A. Hypertension

The pharmacologic aspects of Rauwolfia serpentina are as follows[11]:-

1. It causes vasomotor hyperactivity by acting on the vasomotor centre.Vasodilation of the whole body, leading to a drop in blood pressure
2. It acts as a depressant on the cerebral center. Relaxes the general nervous system [12].
3. It improves the function of the bronchial musculature.
4. Pharmacological Actions of the root of Rauwolfia serpentina, as well as its constituent parts. From time to time, alkaloids have been studied. Hamet [13] reported on the hypotensive effects of numerous Rauwolfia serpentina alkaloids in 1940. In 1944, Bhatia and Kapur [14] reported that isoajmaline and In healthy people, neoajmaline lowers blood pressure. animals with or without spinal cords and decerebrate animals. Hypertension that has been produced in a laboratory setting. On the one hand, Muller and associates 3 in 1952 and Bein [15] in 1953, on the other hand, The novel alkaloid was discovered based on animal tests. Reserpine has a strong and long-lasting hypotensive effect. In 1954, Goto [16] discovered that the alkaloid Reserpine was efficacious in 12 different ways, out of 15 hypertension cases The hypotensive effect was observed. It becomes noticeable three to seven days

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after it has been suspended. Vakil[17] reported a good hypotensive reaction to the drug in 1953. In 72 percent of instances, the alkaloid Reserpine was found, with minor adverse effects.

B. CNS

Reserpine is the principal alkaloid with a diverse pattern of activity, mostly involving changes in amine concentration in the brain. It is capable of altering the concentration of nucleic acid, glycogen, acetyl choline, g-amino butyric acid anti-diuretic hormone and acids Reserpine's side effects include respiratory inhibition, peristalsis stimulation, and miosis, nictating membrane relaxation, and also temperature regulating centre is influenced. It improves the Gastric secretion volume and free acidity. The Pitkriya is a Sanskrit word that contains Arsol (R.)[18] is present in the capsule (Unani formulation). Musakkin-wo-Munawwim ,Mudir (diuretic), Musakkin-eAsab (nervine sedative), and Mukhaddir (sedative and hypnotic) (anesthetic). Its Anticholinergic, anti-sedative, relaxant, hypotensive, anticontractile, antidiuretic, sympathomimetic, hypnotic, hyperthermic tranquillizing vasodialater, antiemetic, anti-fibrillar action Anti-arrhythmic, antifungal, and nematocidal agents are all available.[19][20]

C. Antibacterial Activity

The antibacterial properties of R. serpentina were studied by Rathi et al. Using the well-diffusion method, root ethanol extract was assessed. Bacillus subtilis) two Gram-positive three Gram-negative bacteria (including Staphylococcus) (Pseudomonas aeruginosa, Klebsiella pneumoniae, and Which involved the use of Salmonella typhimurium) only three bacteria: Staphylococcus aureus, Klebsiella pneumonia, and B. subtilis bacteria are discovered to be vulnerable.[22]

D. Antivenom Activity

According to Rajashree et al., the ethanolic extract of the entire R. serpentina plant exhibits antivenom action by counteracting the harmful effects of Naja naja venom. The fatal action of 2LD50 of N. naja venom was entirely neutralised by 0.14 mg of R. serpentina plant extract. [23]

By procoagulant, direct, and indirect hemolytic activities, James et al. investigate the venom-neutralizing potential of the aqueous extract of R. serpentina. The venom of the Daboia russelli was efficiently neutralised in it by the plant extract from R. serpentina. [24]

E. Hypolipidemic activity

Shamim et al. looked into the 12-day oral administration to rabbits of R. serpentina root powder to see if it has any hypolipidemic effects. In order to estimate the serum triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), alanine aminotransferase (ALT), and lactate dehydrogenase, blood samples from each group were taken on the first, fourth, eighth, and twelfth day. Significant hypolipidemic activity was detected by the test. [25]

F. Hepatoprotective Activity

Gupta *et al.* investigated the hepatoprotective activity of aqueous ethanolic extract (AET) of the root of *R. serpentina* against paracetamol-induced hepatic damage in rat. The AET has reversal effect on the level of liver glutathione, Na+ K+-ATPase activity, serum marker enzyme, serum bilirubin and thiobarbituric acid, liver glutathione peroxide, glutathione-S-transferase, glutathione reductase, superoxide dismutase, catalase, and glycogen. Hepatoprotective activity was observed due to oxidant effect and normalization of impaired membrane function activity.

G. Antidiarrheal Activity

Ezeigbo *et al.* introduced the antidiarrheal property of methanolic extract of leaves of *R. serpentina* in castor oil-induced diarrhea in mice.The dose of 100, 200, and 400 mg kg of extract was administered to the mice. The dosedependent reduction in intestinal weight and fluids volume was observed which are responsible for antidiarrheal effect of *R. serpentina.*

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H. Antidiabetic Activity

Azmi *et al.* studied the atherogenic dyslipidemia, arteriosclerosis, and glycosylation index of MREt of *R. serpentina* in alloxan-induced type-1 diabetic mice for 14 days. 42 mice were divided into diabetic control, negative, positive, and normal control with three test dose groups. After 14 days of respective treatments, fasting blood glucose, insulin, hemoglobin (Hb), glycosylated HbA1c, TG, TC, LDL-C, very LDL-C, and HDL-C levels were determined with other parameters. A significant reduction in glycosylation, atherogenic, arteriosclerosis, and non-HDL-C was observed. The obtained results highlighting therapeutic

potential of MREt in lowering the risk of atherogenic dyslipidemia, arteriosclerosis and glycosylation in alloxane induced diabetic mice.

I. Other Diseases

R. serpentina is also helpful in curing other diseases such as fever, malaria, eye diseases, pneumonia, asthma, AIDS, skin disease and spleen disorder.

Side Effect and Toxicology

Lethargy, sedation, psychiatric depression, hypotension, nausea, vomiting, abdominal cramping, gastric ulceration, nightmares, bradycardia, angina-like symptoms, bronchospasm, skin rash, itching, galactorrhea, breast enlargement, sexual dysfunction, and withdrawal psychosis are some of the adverse side effects of reserpine. Nasal congestion was the most prevalent side effect reported by all patients, with % to 15% of them experiencing it.[21] Mental depression can arise and continue after several months of usage. Parkinsonian symptoms, extrapyramidal responses, and convulsions can develop with exceedingly high doses. Rauwolfia causes just a few allergic symptoms, such as asthma. Gastric ulcers can be caused by adequate doses of reserpine that lower blood pressure. In rare people, reserpine has been reported to create a mild edema. Cardiac glycosides, ephedra, alcohol, antipsychotic drugs, barbiturates, diuretics, ephedrine, levodopa, monamine oxidase inhibitors, propranolol, stimulant drugs, and tricyclic antidepressants are all possible drug interactions.Corticosteroids, bilirubin, catecholamines, stomach acidity, norepinephrine, prolactin, thyroxine, and vanillymandelic acid tests, among others, interact with Rauwolfia.

II. CONCLUSION

According to a study of the research, when used in proper low doses, rauwolfia appears to be a safe and effective treatment for hypertension, mental disorders, and various diseases. These results hold true in the case of sarpgandha, as reserpine has been reported to have developed drug resistance, resulting in the discontinuance of reserpine in the treatment of hypertension, although sarpgandha root is still widely used. Pure rauwolfia alkaloids, also known as asteroxylon extract or pure reserpine, can also be used to treat hypertension in an equivalent amount. The LDR can be safely advised to patients who have been examined and shown to benefit from the treatment, according to the author.

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