



Phytochemical & Pharmacological Activity Of Rauwolfia Serpentina – A Review

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The root of the Rauwolfia serpentina Benth (N. O. Apocyanaceae) has been in use in India for hundreds of years for a host of unrelated ailments. Since 1949, after the English publication of a clinical report by the author on Rauwolfia serpentina therapy in fifty cases of essential hypertension, the plant has gained universal acclamation as a useful therapeutic weapon in high blood pressure states. The whole subject of Rauwolfia serpentina therapy in hypertension has been reviewed up to the present time, including discussions on the history of the plant, its various species and types, nomenclature, geographic distribution, chemistry, pharmacologic actions and clinical studies, reported on the subject from all over the world.

Indian medicinal plant (Rauwolfia serpentina) analyzed for its chemical composition, vitamins and minerals. This herb is a good source of minerals such as Ca, P, K, Mg, Na, Fe and Zn. The importance of these chemical constituents is discussed with respect to the role of these herbs in ethnomedicine in India. Alkaloids are very important in medicine and constitute most of the valuable drugs. Despite the use of this plant for such purposes ,importance of these medicinal plants and their importance there is little information on the nutritional and chemical in the pharmaceutical industry.

Key Words:-High blood pressure, Rauwolfia Serpentina, Alkaloids, Ethnomedicine

Introduction-

In India, many indigenous plants are used in herbal medicine to cure diseases and heal injuries. Some important chemical substances found in plants are alkaloids, carbon compounds, hydrogen, nitrogen, glycosides, essential oils, fatty oils, resins, mucilage, tannins, gums and others [1]. Most of these are potent bioactive compounds found in medicinal plant parts that can be used for therapeutic purpose or which are precursors for the synthesis of useful drugs [2]. The active principles differ from plants to plant due to their biodiversity and they produce a definite physiological action on the human body. Calixto [3] reported that most of the cultivated medicinal and aromatic plants exported as crude drugs. Ijeh *et al.* [4] noted the growing interest on the medicinal properties of a number of common plants. Edeoga *et al.* [5, 6] have elucidated the importance of medicinal plants and their importance in the pharmaceutical industry. The root of the *Rauwolfia serpentina* Benth (N. O. Apocynaceae) has been in use in India for hundreds of years for a host of unrelated ailments. Since 1949, after the English publication of a clinical report by the author on *Rauwolfia serpentina* therapy in fifty cases of essential hypertension, the plant has gained universal acclamation as a useful therapeutic weapon in high blood pressure states.[7]

Common Name:-

Hindi	-	Chandrabhaga, Chota-chand, Sarpagandha
English	-	Rauwolfia /Indiansnakeroot
Latin	-	Rauwolfia serpentina
Sanskrit	-	Sarpagandha
Tamil	-	Chevanamalpodu, Sarpagandha
Kannada	-	Keramaddinagaddi
Telgu	-	Patalaguni, Patalagandha, Sarpagandha
Malayalam	-	Churannavilpori, Suvapavalporiyam., Amalpori

Marathi	-	Harkaya, Harki, Hadaki/Adakai
Assamese	-	Arachoritita
Bengali	-	Chandra
Kannada	-	Sutranabhi
Chinese	-	Lu fu mu[8]

Distribution-

Sarpagandha is an important medicinal plant distributed in the foot-hills of Himalayan range, up to the elevation of 1300-1400 m. and almost all over the country. It is used in traditional medicine in India, China, Africa and many other countries. It grows in India, Pakistan, Sri Lanka, Burma and Thailand. In India, it is widely distributed in the sub-Himalayan tract from Punjab to Nepal, Sikkim and Bhutan. It is also found in the lower hills of Gangetic plains, eastern and Western Ghats and Andaman's. It is mostly found in moist deciduous forests at altitudes ranging from sea level to an altitude of 1,200 m high. In the Deccan, it is associated with bamboo forests.[7]

Morphological Features-

Rauwolfia serpentina is an evergreen, perennial, glabrous and erect under shrub. The maximum height of the plant is up to 60 cm. Its roots are tuberous with pale brown cork. The Leaves of the plant are in whorls of three, elliptic to lanceolate or obovate, bright green above and below pale green and thin.



Serpentina Plant with fruits



Serpentina roots

Its flowers are in irregular corymbose cymes, white, often tinged with violet. The flowering time is from March to May in Indian conditions. Its fruits are Drupe, single or didymous, shining black, the inflorescence with red pedicels and calyx and white corolla. [8]

Cultivation-

- **Land preparation:-**

The plant requires slightly acidic to neutral soils for good growth with medium to deep well drained fertile soils. Clay-loam to silt-loam soils, rich in organic content are suitable for its commercial cultivation. It grows well in frost-free tropical to sub-tropical situations under irrigation.

- **Planting:-**

The crop can be propagated by seed, stem cutting and root cuttings. Seed propagation is the best method for raising commercial plantation.

(i) **By root cutting:** Nearly 5 cm long root cutting are planted during spring season closely in nursery beds containing well matured FYM, sand and saw-dust. The beds are kept moist through watering. The cuttings begin to sprout within 3 weeks. These can be planted in field during rainy season after 8 to 10 cm rains are received; the seedlings are transplanted at 45 cm row to row and 30 cm plant to plant distance. In this manner, an estimated 100 kg of root cuttings are found sufficient for planting one hectare area.

(ii) **By stem cuttings:** Hard wooded stem cutting measuring 15 to 22 cm are closely planted during June in the nursery beds where continuous moisture is maintained. After sprouting and giving out

roots, these plants are transplanted in the main field at given spacing.

(iii) By root stumps: About 5 cm of roots, intact with a portion of stem above the collar, are directly transplanted in the field having irrigation facilities.

(iv) By seed: Seed germination in *Rauwolfia* is highly variable. It is reported to vary from 5 to 30 percent even when only heavy seeds are chosen for sowing purpose. Light and heavy seeds can easily be separated by simple water flotation. Germination of heavy seeds during May-June after soaking them in water for 24 hours was 20-40 percent and 62.77 % germination was recorded in freshly collected heavy seed lot. In all, 6 kg of seeds are sufficient to raise one-hectare plantation. The nursery is prepared by raised beds of 10x10 m. dimension under partial shade made up of one-third of well matured FYM and leaf mould, and two-thirds amount medium of silt-loam soil. About 500 sq m. seed bed area is sufficient for raising seedlings enough for planting one hectare land. The seeds sown, 2-3 cm apart in rows in shallow furrows during April end. The furrows are then covered with a fine mixture of soil and FYM. Keep the beds just moist by light watering. Germination starts after 15-20 days and continues up to 30 to 40 days. Seedlings are ready by mid-July for transplanting. The seedlings are transplanted at 30 cm distance within the rows spaced at 45 cm. If rains are not received during or immediately after transplantation irrigation is necessary for better stand. *Rauwolfia* is long duration (18 months) and slow growing. [8]

Chemical Constituents-

The major alkaloid present in root, stem and leaves of the plant is Reserpine varies from 1.7 to 3.0 %. The root barks has more than 90% of the total alkaloids in roots. The minor alkaloids present in the plant are Ajmalicine, ajmaline, isoajmaline, ajmalinine, chandrine, rauwolfinine, renoxidine, rescinnamine, reserpiline, reserpin, reserpinine, sarpagine, serpentine, serpentinine, tetraphyllicine, yohimbine, 3-epi-yohimbine. The root contains ophioxylin, resin, starch and wax.[7]

Chemical Composition *Rauwolfia serpentina* was evaluated by *Harisaranraj R. et al.* which are presented in table no. 1, 2 & 3.[9]

Table 1: Phytochemical composition of *Rauwolfia serpentina* and expressed as mg/100 g dry weight

Phytochemicals	<i>Rauwolfia serpentina</i>
Alkaloids	1.48±0.02
Flavonoids	1.72±0.11
Phenols	1.86±0.11
Tannins	0.51±0.20

Results are mean of triplicate determinations on a dry weight basis ± Standard Deviation

Table 2: Mineral composition of *Rauwolfia serpentina* and on mg/100 g dry weight

Minerals Macroelements	<i>Rauwolfia serpentina</i>
Magnesium	0.10±0.20
Calcium	0.32±0.10
Potassium	0.04 V 0.11
Phosphorus	0.18±0.22
Sodium	0.02±0.10

Mineral Microelements	<i>Rauwolfia serpentina</i>
Iron	1.85±0.20
Zinc	5.38±0.11

Results are mean of triplicate determinations on a dry weight basis± Standard Deviation.

Rauwolfia serpentina showed that the plant are rich in vitamins (Table 3). Ascorbic acid (vitamin C) was found to be 44.03 mg/100 g in *Rauwolfia serpentina* and Riboflavin, thiamine and niacin were also detected. The presence of phenolic compounds in the plant indicates that this plant may be anti-microbial agent.[9]

Pure isolated alkaloids and their synthetic derivatives are used as basic medicinal agents for their analgesic, antispasmodic and bactericidal effects [11, 12]. They exhibit marked physiological activity when administered to animals. Flavonoids, on the other hand are potent water-soluble antioxidants and free radical scavengers, which prevent oxidative cell damage, have strong anticancer activity [13,14,10]. Flavonoids in intestinal tract lower the risk of heart disease. As antioxidants, flavonoids from this plant provide anti-inflammatory activity [10] used for the treatment of diseases in herbal medicine.

Tannins have stringent properties, hasten the healing of wounds and inflamed mucous membranes. The lower sodium content of *Rauwolfia serpentina* might be an added advantage due to the direct relationship of sodium intake with hypertension on human [16]. The presence of zinc in the plant could mean that the plant can play valuable roles in the management of diabetes, which result from insulin malfunction [15]. This plant is a good source of ascorbic acids, riboflavin, thiamin and niacin (Table 3). Natural ascorbic acid is vital for the body performance [10]. Lack of ascorbic acid impairs the normal formation of intercellular substances throughout the body, including collagen, bone matrix and tooth dentine, defect is the weakening of the endothelial wall of the capillaries due to a reduction in the amount of intercellular the mouth and gastro-intestinal tract, anemia, pains in the joints can be related to the association of ascorbic acid and normal connective tissue metabolism. This function of ascorbic acid also accounts for its requirement for normal wound healing. As a result of the availability of ascorbic acid in *Rauwolfia serpentina* this plant is used in herbal medicine for the treatment of many diseases[10]

Pharmacology-

Reserpine has a highly complex pattern of activity. Besides the amine concentration in brain, it is also reported to influence the concentration of glycogen, acetyl choline, γ -amino butyric acid, nucleic acids and anti-diuretic hormone. The effects of reserpine include respiratory inhibition, stimulation of peristalsis, myosis, relaxation of nictating membranes, and influence on the temperature regulating centre. It increases the volume and free acidity of gastric secretion. Reserpine reduces glycaemia in some cases but the effect is short-lived. In some patients it has a stimulating effect on prothrombin activity. Reserpine also favors permeation of blood into areas rendered ischemic by burns. It produces sedation and a lowering of blood pressure. If administered orally, in hypertension, the effects of reserpine are slow, seldom appearing before 3-6 days of administration and continuing for some time after withdrawal of the drug and have a cumulative effect. It is most valuable in young patients with mild labile hypertension associated with tachycardia. In long established hypertension, it is best used in conjunction with more potent hypertensive drugs such as Hexamethonium or Hydralazine. Combined with polythiazide, it is a useful hypotensive in mild to moderate thiazide, it is a useful hypotensive in mild to moderate conditions. The response to reserpine varies in patients and the dosage must be adjusted to individual requirements. In severe hypertension, it may be given by intravenous or intramuscular injection when the effect begins within a few hours. Parenteral therapy of reserpine is indicated in the treatment of hypertension only when oral administration is impracticable.

Deserpidine is almost as active as reserpine in its hypotensive and sedative activity, reduces hypotension and inhibits intestinal movements. Given with an equal amount of reserpine it was more hypotensive than either of the drugs in equivalent doses. It possesses anti-fibrillar activity. *Serpentina* causes marked inhibition of succinate dehydrogenase in brain and liver tissues. It produces a systemic and pulmonary hypotension due to a decrease in cardiac output; there is no change in coronary flow, but coronary vascular resistance is decreased and myocardial oxygen consumption is unaffected. Ajmaline has been reported to stimulate respiration and intestinal movements. The action of ajmaline on systemic and pulmonary blood pressure is similar to that of serpentine. Rauwolfinine has hypertensive properties on the autolysis of rat brain and liver tissue, but to a lesser extent than reserpine. In contrast to reserpine, the total extract of *R. serpentina* inhibited the acetylcholine-induced contraction of the enervated dorsal leech muscle. The whole crude drug is reported to contain some principles which bring about undesirable side effects such as purgation and sexual debility.[7]

Serpentina As A Medicinal Herb-

The roots of *Rauwolfia* is generally used in medicine. *Rauwolfia* is mainly used for the treatment of various central nervous system disorders associated with psychosis, schizophrenia, insanity, insomnia, and epilepsy. Extracts of the roots are valued for the treatment of intestinal disorders, particularly diarrhoea and dysentery and also as anathematic. Mixed with other plant extracts, they have been used in the treatment of cholera, colic and fever. The root was believed to stimulate uterine contraction and recommended for use in child-birth in difficult cases. The juice of the leaves has been used as a remedy for opacity of the cornea. *Rauwolfia's* main uses are:

High blood pressure: The *Rauwolfia* herb is the best remedy for high blood pressure and it has been adapted by medical fraternity in most countries. Those alkaloids which have a direct effect on hypertension have been isolated in it and are widely used by the practitioners of modern medicine. But they have certain unpleasant side effects which the drug taken in its raw form, does not have. Half a teaspoon of its powder taken thrice a day is effective in relieving hypertension.

In insanity: The *Rauwolfia* plant is highly beneficial in treating insanity. One gram of powdered root can be taken twice a day with 250 ml of goat's milk, sweetened with sugar candy. It is unsuitable for those with a low blood pressure, depressed and hypotensive patients.

In insomnia: *Rauwolfia* is a well-known remedy in treating insomnia because of its sedative properties. The very first dose of *Rauwolfia* enables the patient of a phlegmatic and gouty nature to go to sleep. About 0.6 to 1.25 grams of the powder of its root is mixed with some scented vehicle and taken. It is non-stimulating and should be given in doses of 0.25 grams to the patient at bedtime for sound sleep.

In Hysteria: *Rauwolfia* is useful in treating hysteria. One gram of powdered root can be administered thrice with milk. Treatment should be continued till a complete cure is obtained.

In itching skin: It relieves itching in urticaria. One gram of powdered root can be taken with water.

Other uses: It is used as an antidote to the bites of poisonous reptile like snakes. It is also used to treat dysentery and other painful affections of the intestinal canal. The root of *Serpentina* also possess anti bacterial properties. Infusion, decoction and extract of the roots are employed to increase uterine contractions for expulsion of foetus, to treat painful affections of bowels, diarrhoea, dysentery, cholera, colic and fever.

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Recent Research Work-

- The *Rauwolfia* root is an effective blood-pressure lowering agents, acting on the central nervous system.
- Very high doses used for hypertension, *Rauwolfia* alkaloids cause a depletion of norepinephrine, resulting in a tranquilizing effect.
- Many researchers discovered that only *Rauwolfia* alkaloids and clonidin do not have an undesirable influence on balance
- In a Chinese study on 200 patients with moderate hypertension, *Rauwolfia* alkaloids lowered blood pressure was reduced by as much as 30-40% with minimal side effects.
- *Rauwolfia* root has proven highly effective (89%) in cases of chronic hives.
- In epidemiological studies, *Rauwolfia* alkaloids did not increase the risk of breast cancer.
- *Rauwolfia* root has occasionally proven effective in cases of malnutrition that were unresponsive to high protein or high-energy diets.[8]
- Chemically, the root contains a number of alkaloids. Sen and Bose (1931) found two alkaloids, with different melting points.[17] Siddiqui and Siddiqui (1931) have reported five alkaloids to which they

have given names of Ajmaline, Ajmalinine, Ajmalicine, Scrpentine, and Serpentinine[18]. Von Italie and Steenhaur mention the presence of a least three alkaloids, the nature and identity of which is more or less the same, as found by Siddiqui and Siddiqui. An alkaloid isolated by the Chemistry Department of the Tropical School of Medicine, Calcutta, was experimentally studied by Chopra, Gupta and Mukherjee (1933).As a result of their pharmacological studies they found that this alkaloid has a toxic action on lower forms of life like *Paramoecia Caudatum* in dilution of 1 in 20,000. Its toxicity on higher animals was variable. Frogs were quite tolerant, whereas the white mice were very susceptible. The toxicity also varied with the route of administration, the drug being much more toxic, when given intravenously or intraperitoneally, than when given subcutaneously.[19,20]

- **On the circulatory system,** the drug lowered the blood pressure of cats under anesthesia, effect lasting for a considerable time. If spinal cats were used the effect produced was very slight, which showed that probably the fall in blood pressure was due to vasodilatation, resulting from the depression of the vasomotor centre in the medulla oblongata. The fall in blood pressure was also noticed after the terminations of the vagi were paralyzed with atropine, showing that vagal inhibition does not play much part in the fall produced. The fall in blood pressure was also partly due to diminished cardiac output, which they found on myocardiographic studies. On perfusing the drug through isolated vessels, Chopra and his co-workers found, that it definitely decreased the number of drops of the per fusate per minute, which meant that it produces 'vasoconstriction' though they have erroneously called it vasodilatation. Both on the intact, as well as the isolated mammalian heart, the drug seemed to have a slight depressant action. The alkaloid had a stimulant action on the plain muscles of the alimentary canal and the uterus.
- **Central nervous system:-** However, its most interesting action was noticed on the central nervous system, which it seems to depress in the reverse order of development. That is, the highest centres, which are the last to be developed, are usually the first to be affected. It produces drowsiness, diminution in motor activity, diminution in the appreciation of sensory stimuli, depression of the medullary centres.
- In view of the fact, that the chemistry of this drug is not finally settled (Siddiqui and Siddiqui having recently revised their own findings) and because the pharmacological action of the other alkaloids had not yet been worked out, I decided to use the crude drug for this clinical investigation. The preparation which was used in most of the cases was *Serpina* tablets, prepared by The Himalaya Drug House, Dehra-Dun. In some cases liquid extract of *Rauwolfia serpentina* prepared by Smith Stanistreet, Calcutta, was also used.[20]
- Trapold, J H. et al have been studied in the dog. effects of Serpasil, a crystalline alkaloid obtained from *Rauwolfia serpentina* Benth.

The hypotension produced by Serpasil is initially due to vascular relaxation. However, this hypotension ultimately appears to be due to the antagonism by Serpasil of vasomotor reflexes necessary to compensate for a gradual progressive reduction in cardiac output which follows the administration of either Serpasil or its vehicle. The occurrence of an increase in the A-V oxygen difference of venous origin without a concomitant significant increase in oxygen consumption is additional evidence of a vascular relaxation after the administration of Serpasil. Although Serpasil produces a significant depression of the respiratory rate and volume of anesthetized dogs, arterial oxygen is not reduced to hypoxic levels. Evidence indicating a central site of activity for Serpasil has been cited, confirmed and extended. The postulation has been presented and discussed that Serpasil

produces a central inhibition of the sympathetic nervous system, possibly through specific hypothalamic depression. [21]

- Use of *Rauwolfia Serpentina* Benth.in Neuro Sychiatric conditions By Nathan S. Kline reported in March of 1953, the New York Times that Dr. R.A. Hakim of India, has been awarded a gold medal for the presentation of a paper on the cure of schizophrenia with a compound used for hundred of years by ayurvedic practitioners .

In view of the tremendous paucity of pharmacological methods of treating mental disease, our interest increased , the major ingredient in the compound was *Rauwolfia Serpentina* Benth.[22]

Conclusion:-

The use of various drugs in high blood pressure, such as nitrites, iodides, calcium, diuretin, luminal and bromides.I have no hesitation in saying, that in *Rauwolfia serpentina*, we have a drug, which is far superior, in its effect on high blood pressure, to those, which we have so far used. The drug is effective in small doses; it is well tolerated and the effect produced is lasting. The drug is particularly useful in relieving the nervous symptoms of high blood pressure, such as headache, tinnitus, vertigo, giddiness, insomnia, etc. It was not so effective in palpitation or precordial pain. Every patient remarked that he got very good sleep with this drug. In all probability, the beneficial effect of the drug in high blood pressure is produced through its action on the nervous system; that is, by its sedative action on the psychic areas, where by mental calmness is produced and by its depressant action on the vasomotor centre in the medulla oblongata. The drug is not curative but is undoubtedly the best for the relief of symptoms caused by high blood pressure.With small doses blood pressure can be maintained within tolerable limits. It lowers both the systolic as well as diastolic blood pressure. In my opinion, in small doses, which I have used clinically, it does not produce any depression of the heart. On the contrary, by lowering the peripheral resistance, it proved useful in hypertensive heart failure cases. [20]

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