

CHAPTER 16

PHARMACOLOGICAL PROPERTIES OF *RAUVOLFIA SERPENTINA*

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Introduction

Rauvolfia serpentina is an evergreen shrub, perennial, glabrous and the maximum height of the plant is 60 cm, a member of apocynaceae family. There are more than 100 species of *Rauvolfia* found in tropical and subtropical regions of the world, including Asia, Africa, Europe, Australia and the Central and South America. *Rauvolfia serpentina* (Fig.-1) is native to the moist, deciduous forests of Southeast Asia, including India, Burma, Bangladesh, Sri-lanka and Malaysia. The plant's roots are tuberous with a pale brown cork, and the leaves are three whorls, elliptic to lanceolate or obvate, pale green below and bright green above, and thin. It has irregular corymbose cymes with white blooms that are often tinged with violet. According to Indian circumstances, flowering occurs from March to May. The fruits are drupes, single or didymous, glossy black, with red pedicles and calyx, and a white corolla on the inflorescence. The plant produces a large number of lustrous, black or purple spherical fruits with a diameter of around 0.5 cm. It contains little pink or white flowers as well. The tuberose is prominent on the plant. The plant also possesses a tap root with a length of 30 to 50 cm and a diameter of 1.2 to 2.5 cm. The plant is known by various common names in India e.g., as *Sarpaghandha* or *Chandrabhaga*, *Rauvolfia* or *Indian snake root*, *Chandra*, *Chevanamalpod*i in Hindi, English, Bengali and Tamil respectively. *Rauvolfia serpentina*, commonly known as *Sarpaghandha*, is an essential medicinal plant found in India's Himalayan foothills, up to a height of 1300–1400 metres. *Rauvolfia serpentina*, is frequently utilised in modern medicine, as well as Ayurveda, Unani, and folk medicine. For millennia, Hindus have utilised this herb as an antidote to venomous snake bites. In the 1940s, many physicians in India employed the plant, and in the 1950s, it was used all over the world, including in the United States and Canada (Biradar *et. al.*, 2016).⁴



Fig.-1: Indian snakeroot's leaves and fruits (*Rauvolfia serpentina*).

Main phytochemicals found in *Rauvolfia serpentina*

Various phytochemicals, primarily alkaloids, alcohols, sugars, and glycosides, fatty acids, flavonoids, phytosterols, oleoresins, steroids and tannins are among the phytochemicals found in *Rauvolfia*. The most important alkaloids identified in the plant are indole alkaloids, which account for more than 50 of the plant's alkaloids (Verma and Verma, 2010). Indole alkaloids are a class of nitrogenous chemicals produced from tryptophan, an amino acid. They have a 5 and 6 carbon heterocyclic ring structure in common, as well as 1 nitrogen molecule (Leete, 1960). Alkaloid's concentration varies, according to one study, total alkaloids output ranged from 0.8 percent to 1.3 percent of the plant's dry weight (Woodson et. al., 1957).

According to another study, the total production of alkaloids ranges from 0.7 to 3.0% of the root content (Brijesh, 2011). In regenerated roots, the maximum alkaloid level was found to be 3.3 percent (Panwar and Guru, 2011).

Rauvolfia serpentina has been a popular topic of study for decades, and various researchers have looked into it because of its phytochemical qualities. Alkaloids, phenols, tannins, and flavonoids are some of the phytochemical substances or secondary metabolites found in *R. serpentina* (Mittal et. al., 2012; Singh et. al., 2009; Mallick et al., 2012; Poonam et al., 2013; Dey and De, 2010).

2.1 Alkaloids and their medical application

Alkaloids are organic compounds with a heterocyclic nitrogen ring. Alkaloids are produced by a variety of species, including mammals and bacteria, but plants produce a particularly broad range of alkaloids. Alkaloids are secondary metabolites produced by around 10% of plant species, and they are primarily used to protect plants from herbivores and diseases. Analgesic, antispasmodic, and antibacterial properties of pure isolated alkaloids and their synthetic derivatives are used as therapeutic agents (Okwu et. al., 2004). When compared to other blood-pressure reducing medications, the alkaloids derived from the root extract operate directly on the central nervous system, lowering blood pressure.



Fig.-2: *Rauwolfia serpentina* roots, the Indian snakeroot, devil's pepper or serpentine wood (Sarpagandha).

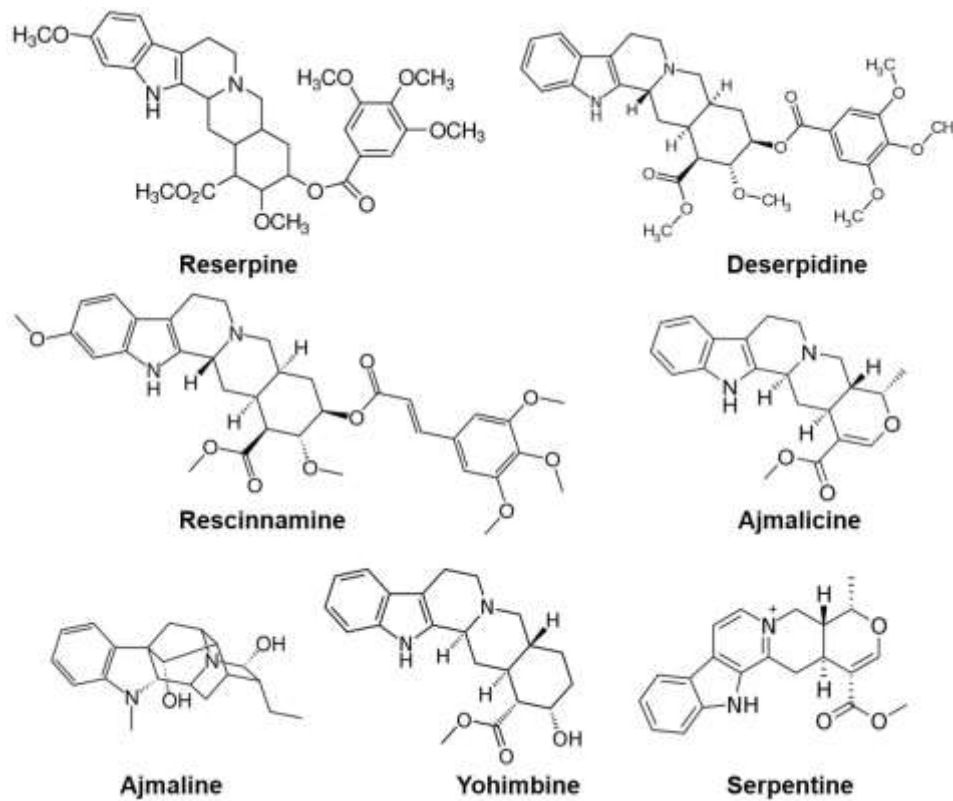


Fig.-3: Chemical structures of different alkaloids present in *Rauwolfia serpentina*

210 PHARMACOLOGICAL PROPERTIES OF RAUVOLFIA SERPENTINA

Reserpine, an indole alkaloid, is claimed to be present in 0.7–3.0% of total alkaloids and roughly 0.1 percent of total alkaloids in *R. serpentina* root (Fig.-2). As a result, this plant's root biomass production could be economically significant. There are three types of alkaloids based on their structure: weak basic indole alkaloids, intermediate basicity alkaloids, and strong anhydronium bases. Ajmaline, ajmalimine, ajmalicine, deserpidine, indobine, indobinine, reserpine, reserpiline, rescinnamine, rescinnamidine, serpentine, serpentinine, and yohimbine are some of the alkaloids found in Rauwolfia (Fig.-3). (Srivastava et. al., 2006; Goel et. al., 2009)

Reserpine is the most important alkaloid, with a wide range of clinical uses (O'Connor and Maresh, 2006; Gawade and Fegade, 2012). Yohimbine, serpentine, deserpidine, ajmalicine, and ajmaline, in addition to reserpine, are used to treat hypertension and breast cancer (Von et. al., 1990; Klushnichenko et. al., 1995)

2.1.1 Reserpine

Sen and Bose published the first modern paper on reserpine in the Indian Medical Journal in 1931 (Sen & Bose, 1931). It's a single crystalline alkaloid obtained from *Rauwolfia* roots that was originally identified in 1952 with a chemical formula of $C_{33}H_{40}N_2O_9$, a molecular mass of 608.68g/mol, and a bitter taste (Schlittler et. al., 1954). Reserpine is the alkaloid discovered in *R. serpentina* that has been investigated the most (McQueen & Doyle, 1954). Reserpine is one of the plant's most important alkaloids (Friedli, 2021). The root has the most reserpine, whereas the stems and leaves have the least (Ruyter et al., 1991). It was once thought to be the most abundant indole alkaloid in the plant; however multiple assays have cast doubt on that claim. The amount of reserpine discovered in the plant ranges from 0.03 percent to 0.14 percent of the dry weight of the plant (Kumar et. al., 2010). The reserpine concentration of the root varied from 0.038 percent to 0.14 percent in different plants, according to the same study. The reserpine concentration of the Rauwolfia root was found 0.955 mg/g in another investigation (Deshmukh et. al., 2012). It's a rather weak tertiary base found in the oleoresin fraction of the roots, and it's used to treat hypertension, cardiovascular illness, and neurological disorders (Howes and Louis, 1990; Weiss and Fintelmann, 2000). Reserpine is thought to be responsible for Rauwolfia roots' antihypertensive effects (3,4,5-trimethyl benzoic acid ester of reserpine acid, an indole derivative of 18- hydroxy yohimbine type). It's the most well-known of all alkaloids, and it's mostly utilised as a natural tranquillizer (Pullaiah, 2002; Banerjee and Modi, 2010).

It also aids sedation and blood pressure reduction, particularly in cases of hypertension brought on by stress and sympathetic nervous system activity. Reserpine causes 5-hydroxytryptamine (5-HT) to be released from all tissues where it is normally held, resulting in an increase in urine metabolites (Prusoff, 1961). Isolated reserpine was also released in 1952 as the medication "Serpasil" to treat hypertension, tachycardia, and thyrotoxicosis (Jerie, 2007). The alkaloid reserpine is classified 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.

The bioavailability of reserpine after oral consumption has been estimated to be between 50 and 70 percent, though most investigations have revealed it to be around 50 percent. Although slower absorption of between 2 and 4 hours has been documented, absorption is very rapid, occurring between 1 and 2 hours after oral administration. Reserpine is found in the brain, liver, spleen, kidney, and adipose tissue, among other places (Inchem, 2021). Reserpine is also broadly dispersed in red blood cells and peripheral neurons, according to other investigations. It has been discovered in breast milk and has the ability to

pass the placenta and the blood-brain barrier. It has been discovered that its first half-life in the blood is 4 to 5 hours. In plasma, elimination half-life of reserpine has been calculated to range between 45 and 168 hours. Because of its attachment to proteins and red blood cells, it has a comparatively lengthy elimination half-life. The liver is responsible for roughly 62 percent of reserpine breakdown, whereas renal elimination accounts for less than 8%. Fecal excretion accounts for the majority of its removal. Reserpine alone has been discovered to include between 30% and 60% of removed metabolites (Inchem, 2021; Stitzel, 1976).

Reserpine is increasingly being used in pharmacological investigations as well as physiologic studies of bodily processes. Reserpine's antihypertensive effects are attributable to its depressive effects on the central nervous system (CNS) and peripheral nervous system (PNS) through binding to catecholamine storage vesicles in nerve cells. This prevents catecholamines and serotonin from being stored normally as catecholamine levels drop. It disrupts the autonomic nervous system's function by diminishing the transmitter material in adrenergic neurons and perhaps triggering the central parasympathetic system (Ellenhorn and Barceloux, 1988; Gilman et. al., 1990; Nammi et. al., 2005). Heart rate, cardiac contraction, and peripheral resistance are all controlled by these chemicals.

Reserpine is the principal alkaloid with a complicated pattern of activity, mostly involving changes in amine concentration in the brain. Glycogen, acetyl choline, g-amino butyric acid, nucleic acids, and anti-diuretic hormone concentrations are all influenced by it. Reserpine inhibits respiration, stimulates peristalsis, myosis, and relaxes nictating membranes, as well as influencing the temperature regulating centre. It enhances gastric secretion volume and free acidity (Mittal et. al., 2012).

Reserpine's mechanism of action has been extensively studied and recorded. Reserpine interacts to vesicular monoamine transporters (VMATs), which are protein receptors found in the organelle membranes of specialised secretory vesicles in presynaptic neurons (Schuldiner, et. al., 1993; Qu et. al., 2009). Reserpine inhibits the binding of intracellular neurotransmitters to VMAT proteins and the uptake of neurotransmitters by secretory vesicles (Gopalkrishnan et. al., 2007). To conclude, reserpine causes the release of no or few neurotransmitters from the presynaptic cell. As a result, no or only minor nerve impulse propagation occurs in the postsynaptic neuron. VMAT1 and VMAT2 are two isoforms of vesicular transport proteins. VMAT1 is mostly found in peripheral nervous system neuroendocrine cells, including chromaffin granules in the adrenal medulla, sympathetic neurons, and platelets. VMAT2 is mostly located in the brain, sympathetic nervous system, mast cells, and cells in the stomach and pancreas that contain histamine. Reserpine has a three-fold higher affinity for VMAT2 than it does for VMAT1 (Wimalasena, 2011; Eiden et. al., 2004). Reserpine has a high affinity for specific VMAT receptors, particularly VMAT2, and binds to them almost irreversibly (Gopalkrishnan et. al., 2007).

2.1.2 Ajmaline

Salimuzzaman Siddiqui isolated the chemical from the roots of *R. serpentina* for the first time in 1931. He named it ajmaline after Hakim Ajmal Khan, one of South Asia's most prominent Unani practitioners (Siddiqui et. al., 1985; Siddiqui, 2013). It is highly useful in diagnosing Brugada Syndrome (hereditary cardiac disorder) and differentiating between subtypes of patients with this disease. Derived from *R. serpentina* roots as a class I antiarrhythmic agent, it is highly useful in diagnosing Brugada Syndrome (hereditary cardiac disorder) and differentiating between subtypes of patients with this disease (Rolf et. al., 2003). On the basis of their mechanism of action, these drugs are divided into four categories: sodium channel blockade, beta-adrenergic blockade, repolarization prolongation, and calcium

212 PHARMACOLOGICAL PROPERTIES OF RAUVOLFIA SERPENTINA

channel blockade. Ajmaline is a sodium channel blocker that takes effect immediately when administered intravenously, making it excellent for diagnostic use. The "Ajmaline Test" is the delivery of Rauwolfia alkaloid to patients with this form of arrhythmia (Kostin et. al., 1986; Brugada et. al., 2000). It has been claimed that it stimulates breathing and bowel motions. Ajmaline has a comparable effect on systemic and pulmonary blood pressure as serpentine (Gawade and Fegade, 2012).

2.1.3 Ajmalicine

The alkaloid ajmalicine has a wide range of uses in the treatment of circulatory disorders, particularly in restoring normal cerebral blood flow. It has an effect on smooth muscle action, helps to avoid strokes, and lowers blood pressure (Srivastava et. al., 2006). Pharmaceutical companies extract an estimated 3500 kg of ajmalicine from Rauwolfia or Catharanthus spp. each year for the treatment of circulatory illnesses. The synthetic route begins with geraniol and proceeds through iridodial and iridotrial reactions to produce loganin, which is then oxidised to produce secologanin. This aids the production of ajmalicine by assisting the tryptamine in forming a corynanthe type nucleus (Oconnor and Maresh, 2006; Li et. al., 2004). Tryptophan is metabolised to tryptamine via secologanin, strictosidine, and cathenamine, resulting in ajmalicine. NADPH and tryptophan decarboxylase aid in the conversion of cathenamine to ajmalicine (TDC). In Rauwolfia, decarboxylase may be the primary enzyme involved in the manufacture of ajmalicine (Liu et. al., 2012).

2.1.4 Serpentine

Serpentine is an antipsychotic drug that inhibits type II topoisomerase (Dassonneville et. al., 1999; Costa-Campos et. al., 2004). Peroxidase (PER) catalyses the conversion of ajmalicine to serpentine by catalysing the bisindole alkaloid found in the vacuole (Oconnor, 2006)

2.1.5 Rescinnamine

Rescinnamine is a pure ester alkaloid of the alseroxylyon fraction found in Rauwolfia species; it is chemically and pharmacologically linked to reserpine and has similar use. In the 1950s, it was discovered and used as an antihypertensive medication to treat hypertension. It's a less strong alkaloid than reserpine in terms of clinical efficacy and it's not as good at lowering blood pressure (Klohs et. al., 1954). Rescinnamine inhibits the peptidyl dipeptidase angiotensin converting enzyme, which catalyses the conversion of angiotensin I to the vasoconstrictor substance angiotensin II, which promotes aldosterone secretion by the adrenal cortex. It works by blocking the conversion of angiotensin I to angiotensin II by inhibiting the Angiotensin Converting Enzyme (ACE). Angiotensin II levels in the blood are reduced when ACE is inhibited. Because angiotensin II is a vasoconstrictor and a negative-feedback mediator for renin activity, lowering its concentration lowers blood pressure and stimulates baroreceptor reflex mechanisms, resulting in decreased vasopressor activity and aldosterone release (Drugbank, 2021)

2.1.6 Deserpidine

Deserpidine is an ester alkaloid, it only varies from reserpine in that it lacks a methoxy group at C-11, which is present in reserpine. Its antipsychotic and antihypertensive effects are the main reasons for its usage. It works by regulating nerve impulses throughout several neural pathways to lower blood pressure. As a result, they have an effect on the heart and blood vessels, lowering blood pressure and alleviating psychotic symptoms. Deserpidine also binds to the angiotensin-converting enzyme and inhibits it, as well as competing with

angiotensin I for binding. It also prevents angiotensin I from converting to angiotensin II (Varchi et. al., 2005)

2.1.7 Yohimbine

Yohimbine is a pharmacologically well-characterized alkaloid that is used to treat erectile dysfunction as a selective alpha-adrenergic antagonist or alpha-blocker in the blood vessels. It helps to improve erectile function by dilating blood vessels and increasing blood flow in the penis (Morales, 2000; Andersson, 2001; Andersson, 2001; Goldberg and Robertson, 1983). In animal and human models with polymorphisms in the 2A-adrenergic receptor gene, yohimbine was also tested as a diabetic treatment. Smooth muscle relaxes and blood pressure drops when these receptors are blocked. It dilates the pupils of the eye by boosting specific substances in the body (Rosenren, 2009).

2.2 Phenols

Phenols are secondary plant metabolites found in a wide range of plants, primarily herbs, shrubs, vegetables, and trees (Naira et. al., 2013; Bonilla et. al., 2003). The presence of phenols is thought to be hazardous to certain pests and diseases' growth and development (Singh and Sawhney, 1988). *R. serpentina* has substantial antidiabetic and hypolipidemic characteristics due to its high content of total polyphenolic components (Azmi and Qureshi, 2013; Qureshi and Udani, 2009). It's utilised as an expectorant and emulsifier in medicine. Because phenolic chemicals are present, this substance can be employed as an antimicrobial agent.

2.3 Tannins

The presence of gallic acid and diagallic acid in tannin makes it an oxidation inhibitor (Ihekoronye and Ngoddy, 1974). Tannins contain astringent qualities that help wounds and irritated mucous membranes heal faster. As a result, explain why traditional medicine practitioners in South Eastern India utilise *R. serpentina* to cure a variety of ailments (Harisaranraj et. al., 2009; Agoha, 1974).

2.4 Flavonoids

Flavonoids are potent antioxidants and free radical scavengers that protect cells from oxidative damage and have anti-cancer activities (Salah et. al., 1995; Del-Rio et. al., 1997). Flavonoids present in the colon aid to lower heart disease risk. Flavonoids are antioxidants with anti-inflammatory qualities that are used in herbal medicine to treat a variety of diseases (Mittal et. al., 2012; Okwu, 2004).

2.5 Saponins

Saponins are triterpene and sterol glycosides that have been found in over 70 plant groups. Saponins have a number of qualities, including the ability to create foam in aqueous solutions, hemolytic activity, cholesterol binding capabilities, and bitterness (Sodipo et. al., 2000). Saponin has the ability to cause red blood cells to coagulate. *Rauwolfia serpentina* extracts are used to halt bleeding and cure wounds because of their high saponin content (Harisaranraj et. al., 2009; Basu and Rastogi, 1967).

2.6 Minerals and Vitamins

Rauwolfia is also known to contain a wide range of macro and micronutrients, with calcium being the most abundant macronutrient (Agoha, 1974). *R. serpentina*'s ability to halt bleeding and usage in wound treatment may be attributed to its high calcium concentration,

which aids in blood coagulation. Because of the direct association between salt intake and hypertension in humans, *R. serpentina* has a low sodium content, which can be an added benefit (Dahl, 1972). The presence of zinc suggests that plants can help treat diabetes, which is caused by a failure of insulin (Agoha, 1974). *R. serpentina* also contains high levels of ascorbic acids, riboflavin, thiamin, and niacin (Okwu, 2003). Ascorbic acid is essential for bodily performance because it aids regular wound healing and prevents the production of intercellular chemicals throughout the body (including collagen, bone matrix and tooth dentine) (Okwu, 2004). Because it is a rich source of phytochemicals, minerals, and vitamins, *R. serpentina* is employed in herbal medicine as a potential source of beneficial medications for the treatment of various ailments (Mittal et. al., 2012; Harisaranraj et. al., 2009).

3. *R. serpentina* as a medicinal herb and therapeutic agent

Rauvolfia serpentina has been discovered to have pharmacologic effects, causing widespread vasodilation and blood pressure reduction through its action on the vasomotor centre. The bronchial musculature is stimulated. It calms the nervous system by acting as a depressant on the cerebral centers (Vakil, 1949; Werner, 1953). The presence of different alkaloids in the oleoresin fraction of *R. serpentina's* roots has earned it a prominent position in the pharmaceutical industry. Alkaloids of *R. serpentina* have a great medicinal importance to treat the disease like cardiovascular diseases, high blood pressure (Vakil, 1955), hypertension (vonPoser et al., 1990), arrhythmia (Kirillova et al., 2001), psychiatric diseases (Bhatara et al., 1997), mental disorders (Noce et al., 1954), breast cancer (Stanford et al., 1986), human promyelocytic leukaemia (Stanford et al (Dey and De, 2010).

R. serpentina has a wide range of beneficial therapeutic effects, including the treatment of hypertension and psychotic illnesses such as schizophrenia, anxiety, epilepsy, sleeplessness, and insanity, as well as being used as a sedative and hypnotic (Poonam et. al., 2013; Kirtikar and Basu, 1993). Anticholinergic, hypotensive, anticontractile, sedative, relaxant, hyperthermic, antidiuretic, sympathomimetic, hypnotic, vasodilator, antiemetic, anti-fibrillar activity tranquilizing agent, anti-arrhythmic, antifungal, and nematocidal are some of the pharmacological properties of *R. serpentina* (Dey and De, 2010; Macphillamy, 1963). *R. serpentina* is thought to have a variety of pharmacological properties, including action on the vasomotor centre, which leads to generalised vasodilation by lowering blood pressure, depressant action on the cerebral centres, which soothes the general nervous system, sedative action on the gastric mucosa, and stimulating action on the intestinal tract's plain musculature, as well as stimulating the bronchial musculature (Poonam et. al., 2013).

The *Arsol* (*R. serpentina*) in the Pitkriya capsule (Unani formulation) functions as *Musakkin-wo-Munawwim* (sedative and hypnotic), *Mudir* (diuretic), *Musakkin-e-Asab* (nervine sedative), and *Mukhaddir* (anesthetic) (Shamsi et al., 2006).

The plant is said to have a large number of medically beneficial indole alkaloids, which are primarily found in the roots. Fabricant and Fransworth (2001) emphasised the use of ethnobotanical remedies to treat a variety of circulatory problems. The roots' extracts are used to treat digestive ailments, particularly diarrhoea and dysentery, as well as as anathematics. They've been used to treat cholera, colic, and fever when combined with other plant extracts. The root was thought to help in labour because it stimulated uterine contractions.

Azmi and Qureshi (2012) found that *Rauvolfia* has therapeutic effects in diabetic hypertensive patients with partial hypoglycemic activity. The juice of the leaves has been used as a treatment for corneal opacity (Sukumaran and Raj, 2008) The juice and extract from the root of *Rauvolfia* can be used to treat gastrointestinal and circulatory problems. Tender

leaf juice and root extract are used to treat liver discomfort, stomach pain, diarrhoea, and worms in the intestine (Anisuzzaman et. al., 2007). The *R. serpentina* has been studied by various researchers at various times in various diseases as mentioned below.

3.1 Rauvolfia in cancer treatment

In a recent study the crude *R. serpentina* aqueous leaf extract and R-AuNPs were found to successfully treat bacterial infections and act as an anti-cancer agent (Alshahrani et al., 2021). Various investigations have revealed anticancer activity at different times. Prostate cancer is thought to be one of the leading causes of cancer-related death in males. Patients with prostate cancer have not seen significant survival advantages from modern methods like chemotherapy and radiotherapy (ACS, 2008). In comparison to chemotherapy and radiotherapy, natural products have proven to be a valuable resource for identifying bioactive substances used in the treatment of a number of maladies and disorders, including cancer. For generations, different portions of this plant have been utilised as traditional medicine to cure a variety of maladies such as fever, general weakness, digestive infections, liver difficulties, and mental abnormalities (PDR, 2021). This plant's root bark extracts are high in chemicals from the β -carboline alkaloid family, with alstonine as the predominant ingredient. In mice implanted with YC8 lymphoma cells or Ehrlich ascitic cells, this chemical has been shown to inhibit tumour cell proliferation (Beljanski and Beljanski, 1986).

The plant extract possesses anti-prostate cancer action in both in vitro and in vivo model systems, which may be controlled by its effects on DNA damage and cell cycle control signalling pathways, according to gene expression patterns of treated prostate cancer cells (Bemis et. al., 2006).

3.2 *R. serpentina* in Hypertension

Rauvolfia has been adopted by the medical communities in most of the countries. Alkaloids that have a direct influence on hypertension have been discovered in it and are routinely employed by modern medicine practitioners. It relieves urticaria itching. (Sen & Bose, 1931). In 1949, Vakil published the results of a trial involving 50 patients with essential hypertension who were given Rauvolfia. In that study, 85 percent of patients had a decrease in systolic blood pressure and 81 percent saw a decrease in diastolic blood pressure (Vakil, 1955). *R. serpentina* has been found to have a therapeutic impact in the management of hypertension and hypercholesterolemia, most likely by protecting the liver and renal structures, according to a recent study (Shah et. al., 2020).

3.3 Mental illness, schizophrenia and other diseases

The roots of *R. serpentina* is used to treat high blood pressure, anxiety, sleeplessness, and sedation (Meena et. al., 2009; Singh et. al., 2010). The root extract obtained is thought to be the most effective treatment for high blood pressure, and it has been used by medical professionals in most nations. Extracts of *R. serpentina* is also helpful in curing other diseases such as fever (Nayak et. al., 2004), malaria, eye diseases (Anisuzzaman et. al., 2007), pneumonia (Rai, 2004), asthma (Britto and Mahesh, 2007), AIDS, headache (Rahmatullah et. al., 2010), skin disease (Behera et. al., 2006) and spleen disorder (Mia et. al., 2009).

Conclusion

India is a hub, a great source of various medicinal plants. *Rauvolfia serpentina* is one the important medicinal plant as being used for various kinds of ailments traditionally in India over the generations and later proved by various studies carried out by different scientist, medical practitioners at different times.

References

1. Agoha RC, Medicinal plants of Nigeria, offset Drakkerij, Faculteit der Wiskunde in Naturwetenschappen, the Netherlands, 1974, pp 41-33.
2. Alshahrani, M.Y.; Rafi, Z.; Alabdallah, N.M.; Shoaib, A.; Ahmad, I.; Asiri, M.; Zaman, G.S.; Wahab, S.; Saeed, M.; Khan, S. A Comparative Antibacterial, Antioxidant, and Antineoplastic Potential of *Rauwolfia serpentina* (L.) Leaf Extract with Its Biologically Synthesized Gold Nanoparticles (R-AuNPs). *Plants* 2021, 10, 2278. <https://doi.org/10.3390/plants10112278>
3. American Cancer Society, *Cancer Facts and Figures 2006*, Atlanta: American Cancer Society, 2006.
4. Andersson KE, Pharmacology of lower urinary tract smooth muscles and penile erectile tissues, *Pharmacological Reviews*, 45(1993), 254-308.
5. Andersson KE. Pharmacology of penile erection, *Pharmacological Reviews*, 53(3), 2001, 417-450.
6. Anisuzzaman M, Rahman AHMM, Harunor-Rashid M, *et al.* An ethnobotanical study of Madhupur, Tangail, *J Appl Sci Res.* 2007; 3(7): 519–530p.
7. Anisuzzaman M, Rahman AHMM, Harunor-Rashid M, Naderuzzaman ATM, Islam AKMR, An ethnobotanical study of Madhupur, Tangail, *Journal of Applied Sciences Research*, 3(7) 2007, 519-530.
8. Anitha S, Kumari BDR, Stimulation of reserpine biosynthesis in the callus of *Rauwolfia tetraphyla* L. by precursor feeding, *African Journal of Biotechnology*, 5, 2006, 659-661.
9. Azmi MB, Qureshi SA, Methanolic root extract of *Rauwolfia serpentina* Benth. improves the glycemic, antiatherogenic, and cardioprotective indices in alloxan-induced diabetic mice, *Journal of Applied Pharmaceutical Science*, 3(7), 2013, 136-141.
10. Banerjee M, Modi P, A novel protocol for micropropagation of *Rauwolfia serpentina*: In low concentration of growth regulators with sucrose and phenolic acid. *International Journal of Plant Sciences*, 5(1), 2010, 93-97.
11. Basu N, Rastogi RP, Triterpenoid, Saponins and Sapogenins, *Photochemistry*, 6, 1967, 1249-1270.
12. Behera SK, Panda A, Behera SK, *et al.* Medicinal plants used by the Kandhas of Kandhamal district of Orissa, *Indian J Tradition Know.* 2006; 5(4): 519–528p.
13. Behera SK, Panda A, Behera SK, Misra MK, Medicinal plants used by the Kandhas of Kandhamal district of Orissa, *Indian Journal of Traditional Knowledge*, 5(4), 2006, 519-528.
14. Beljanski M, Beljanski MS, Three alkaloids as selective destroyers of cancer cells in mice, synergy with classic anticancer drugs, *Oncology*. 1986; 43: 198–203p.
15. Beljanski M, Beljanski MS, Three alkaloids as selective destroyers of cancer cells in mice, synergy with classic anticancer drugs, *Oncology*, 43, 1986, 198-203.
16. Bemis DL, Capodice JL, Gorroochurn P, Katz AE, Buttyan R, Antiprostata cancer activity of a beta-carboline alkaloid enriched extract from *Rauwolfia vomitoria*, *International Journal of Science*, 2009, 217-220.
17. Bhatara VS, Sharma JN, Gupta S, Gupta YK, Images in psychiatry *Rauwolfia serpentina*: The first antipsychotic, *American Journal of Psychiatry*, 154, 1997, 894-894.

18. Biradar, N., Hazarika, I., Chandy, V (2016) Current Insight to the Uses of Rauwolfia: A Review. *Research & Reviews: A Journal of Pharmacognosy* 3(3): 1–4p.
19. Bonilla EP, Akoh CC, Sellappan S, Krewer G, Phenolic content and antioxidant capacity of muscadine grapes, *Journal of Agriculture & Food Chemistry*, 51, 2003, 5497-5503.
20. Brijesh KS. Rauwolfia: cultivation and collection. Biotech Articles Web site. <http://www.biotecharticles.com/Agriculture-Article/Rauwolfia-Cultivationand-Collection-892.html>. Published May 23, 2011. Accessed December 30, 2021.
21. Britto JD, Mahesh R, Exploration of kani tribal botanical knowledge in agasthiyamalai biosphere reserve-south India, *Ethnobotan Leaflets*. 2007; 11: 258–265p.
22. Britto JD, Mahesh R, Exploration of kani tribal botanical knowledge in agasthiyamalai biosphere reserve-south India, *Ethnobotanical Leaflets*, 11, 2007, 258-265.
23. Brugada R, Brugada J, Antzelevitch C, Kirsch GE, Potenza D, Towbin JA, Brugada P, Sodium channel blockers identify risk for sudden death in patients with ST-segment elevation and right bundle branch block but structurally normal hearts, *Circulation*, 101(5), 2000, 510-515.
24. COMSATS newsletter: Biographies of eminent scientists: Dr Salimuzzamman Siddiqui, COMSATS Secretariat, Islamabad– Pakistan 5(3), 2013.
25. Costa-Campos L, Dassoler SC, Rigo AP, Iwu M, Elisabetsky E, Anxiolytic properties of the antipsychotic alkaloid alstonine, *Pharmacology Biochemistry & Behaviour*, 77, 2004, 481-489.
26. Dahl LK, Salt and Hypertension, *American Journal of Clinical Nutrition*, 25, 1972, 231-238.
27. Dassonneville L, Bonjean K, Pauw-Gillet MCD, Colson P, Houssier C, Quetin-Leclercq J, Angenot L, Bailly C, Stimulation of topoisomerase II-mediated DNA cleavage by three DNAintercalating plant alkaloids: Cryptolepine, matadine, and serpentine. *Biochemistry*, 1999, 38, 7719-7726.
28. Del-Rio A, Obdulio BG, Casfillo J, Marin FG, Ortuno A, Uses and properties of citrus flavonoids, *Journal of Agriculture and Food Chemistry*, 45, 1997, 4505-4515.
29. Deshmukh SR, Ashrit DS, Patil BA. Extraction and evaluation of indole alkaloids from Rauwolfia serpentina for their antimicrobial and antiproliferative activities. *Int J Pharm Pharm Sci*. 2012;4(suppl 5):329-334.
30. Dey A, De JN, *Rauwolfia serpentina* (L). Benth. Ex Kurz. - A Review, *Asian Journal of Plant Sciences*, 9(6), 2010, 285-298.
31. Eiden LE, Schafer MK, Weihe E, Schutz B. The vesicular amine transporter family (SLC18): amine/proton antiporters required for vesicular accumulation and regulated exocytotic secretion of monoamines and acetylcholine. *Pflugers Arch*. 2004;447(5):636-640.
32. Ellenhorn MJ, Barceloux DG, *Medical Toxicology*, New York, NY, Elsevier Science Publishing Company, Inc, 1988, 644-659.
33. Fabricant DS, Farnsworth NR, 2001, The value of plants used in traditional medicine for drug recovery, *Environmental Health Perspectives* 2001, 109 (1), 69-75. PMID: 11250806

34. Friedli GL. Indole alkaloids. Friedli Enterprises Web site. <http://www.friedli.com/herbs/phytochem/alkaloids/alkaloid5.html>. Accessed December 25, 2021.
35. Gawade BV, Fegade SA, *Rouwolfia* (reserpine) as a potential antihypertensive agent – a review, International Journal of Pharmaceutical and Phytopharmacological Research, 2(1), 2012, 46-49.
36. Gilman AF, Rall WT, Nies AD, Taylor P, Goodman and Gilman's: The Pharmacologic Basis of Therapeutics, 8th ed, Pergamon Press, New York, New York, 1990, 795.
37. Goel MK, Mehrotra S, Kukreja AK, Shanker K, Khanuja SP, *In vitro* propagation of *Rauwolfia serpentina* using liquid medium, assessment of genetic fidelity of micropropagated plants and
38. Goldberg MR, Robertson D, Yohimbine: a pharmacological probe for study of the α 2-adrenoceptor, Pharmacological Reviews, 35, 1983, 143-180.
39. Gopalakrishnan A, Sievert M, Ruoho AE. Identification of the substrate binding region of vesicular monoamine transporter-2 (VMAT-2) using iodoaminoflisopolol as a novel photoprobe. *Mol Pharmacol.* 2007;72(6):1567-1575.
40. Hareesh Kumar V, Nirmala, Shashidhara S, Rajendra CE. Reserpine content of *Rauwolfia serpentina* in response to geographical variation. *Int J Pharm Biosci.* 2010;1(4):429-434.
41. Harisaranraj R, Suresh K, Babu SS, Achudhan VV, Phytochemical based strategies for pathogen control and antioxidant capacities of *Rauwolfia serpentina* Extracts, Recent Research in Science and Technology, 1, 2009, 67-73.
42. Howes LG, Louis WJ, *Rauwolfia* alkaloids (Reserpine), pharmacology of antihypertensive therapeutics, Handbook of Experimental Pharmacology, 93 (1), 1990, 263-285.
43. <http://www.drugbank.ca/drugs/DB01180>.
44. Ihekoronye, AI, Ngoddy PO, Integrated Food Science and Technology for the Tropics, Macmillam Education Ltd, 1985.
45. Jerie P. Milestones of cardiovascular therapy, IV: reserpine [in Czech]. *Cas Lek Cesk.* 2007;146(7):573-577.
46. Journal of Physiology and Pharmacology , 83(6), 2005, 509-15.
47. Kirillova NV, Smirnova MG, Komov VP, Sequential isolation of superoxide dismutase and ajmaline from tissue culture of *Rauwolfia serpentina* Benth, Applied Biochemistry and Microbiology, 37, 2001, 181-185.
48. Kirtikar KR, Basu BD, *Indian Medicinal Plants*, 2 Ed, Dehra Dun Publishers, Calcutta, India, 1993, 289p.
49. Kirtikar KR, Basu BD, *Indian Medicinal Plants*, 2 Ed, Dehra Dun Publishers, Calcutta, India, 1993, pp 289.
50. Klohs MW, Draper MD, Keller F, Alkaloids of *Rauwolfia serpentina* Benth III. Rescinnamine, A new hypotensive and sedative principle, Journal of American Chemical Society, 76(10), 1954, 2843.
51. Klushnichenko VE, Yakimov SY, Tuzova TP, Syagailo YV, Kuzovkina IN, Vulf'son AN, Miroshnikov AI, Determination of indole alkaloids from *R. serpentina* and *R. vomitoria* by HPLC and TLC methods, Journal of Chromatography, 704, 1995, 357-362.
52. Kostin YV, Melokhova EI, Gendenshtein EI, Volkova ND, Astakhova TV, Savel'eva EK, Antiarrhythmic activity of the total alkaloids from a *Rauwolfia serpentina* tissue culture, Pharmaceutical Chemistry Journal, 20(3), 1986, 214-217.

53. Leete E. The biogenesis of the Rauwolfia alkaloids, I: the incorporation of tryptophan into ajmaline. *J Am Chem Soc.* 1960;82(24):6338-6342.
54. Li S, Long J, Ma Z, Xu Z, Li J, Zhang Z, Assessment of the therapeutic activity of a combination of almitrine and raubasine on functional rehabilitation following ischaemic stroke, *Current Medical Research and Opinion*, 20, 2004, 409-415.
55. Liu W, Chen R, Chen M, Zhang H, Peng M, Yang C, Ming X, Lan X, Liao Z, Tryptophan decarboxylase plays an important role in ajmalicine biosynthesis in *Rauwolfia verticillata*, *Planta*, 236(1), 2012, 239-250.
56. Macphillamy HB, *Drugs from plants*, *Plant Science Bulletin*, 9(2), 1963.
57. Mallick SR, Jena RC, Samal KC, Rapid *in vitro* multiplication of an endangered medicinal plant sarpgandha (*Rauwolfia serpentina*), *American Journal of Plant Sciences*, 3, 2012, 437-442.
58. Mc Queen EG, Doyle AE, *et al.* Mechanism of Hypotensive Action of Reserpine, an alkaloid of *Rauwolfia serpentina*, *Nature*. 1954; 174: 1015p.
59. Meena AK, Bansal P, Kumar S, Plants-herbal wealth as a potential source of ayurvedic drugs, *Asian Journal of Traditional Medicines*, 4(4), 2009, 152-170.
60. Mia MMK, Kadir MF, Hossan MS, *et al.* Medicinal plants of the Garo tribe inhabiting the Madhupur forest region of Bangladesh, *Am-Eurasian J Sustain Agr.* 2009; 3(2): 165–171p.
61. Mia MMK, Kadir MF, Hossan MS, Rahmatullah M, Medicinal plants of the Garo tribe inhabiting the Madhupur forest region of Bangladesh, *American-Eurasian Journal of Sustainable Agriculture*, 3(2), 2009, 165-171.
62. Mittal B, Meenakshi, Sharma A, Gothecha VK, Phytochemical and pharmacological activity of *Rauwolfia Serpentina* - a review, *International Journal of Ayurvedic & Herbal Medicine* 2(3), 2012, 427-434.
63. Morales A, Yohimbine in erectile dysfunction: the facts, *International Journal of Impotence Research*, 12(1), 2000b, S70-74.
64. Naira VD, Panneerselvama R, Gopia R, Hong-bob S, Elicitation of pharmacologically active phenolic compounds from *Rauwolfia serpentina* Benth. Ex. Kurtz, *Industrial Crops and Products*, 45,2013, 406-415.
65. Nammi S, Boini KM, Koppula S, Sreemantula S, Reserpine-induced central effects: pharmacological evidence for the lack of central effects of reserpine methiodide, *Canadian*
66. Nayak S, Behera SK, Misra MK, Ethno-medico-botanical survey of Kalahandi district of Orissa, *Indian Journal of Traditional Knowledge*, 3(1), 2004, 72-79.
67. Nayak S, Behera SK, Misra MK. Ethno-medico-botanical survey of Kalahandi district of Orissa, *Indian J Tradition Know.* 2004; 3(1): 72–79p.
68. Noce RH, Williams DB, Rapaport W, Reserpine (Serpasil) in the management of mentally ill and mentally retarded, *Journal of American Medical Association*, 156, 1954, 821-824.
69. O'Connor SE, Maresh J, Chemistry and biology of monoterpene indole alkaloid biosynthesis, *Natural Product Reports*, 23, 2006, 532-547.
70. Okwu DE, Okwu ME, Chemical composition of *Spondias mombin* linn plant parts, *Journal of Sustainable Agriculture and Environment*, 6(2), 2004, 140-147.
71. Okwu DE, Phytochemicals and vitamin content of indigenous spices of Southeastern, Nigeria, *Journal of Sustainable Agriculture and Environment*, 6(1), 2004, 30-37.

72. Okwu DE, The potentials *Ocimum gratissimum*, *Pongoluria extensa* and *Tetrapleura tetraptera* as spice and flavouring agents, Nigeria Agricultural Journal, 34, 2003, 143-148.
73. Oncology, 29(5), 2006, 1065-1073.
74. Panwar GS, Guru SK. Alkaloid profiling and estimation of reserpine in Rauwolfia serpentina plant by TLC, HP-TLC and HPLC. *Asian J Plant Sci.* 2011;10(8):393-400.
75. PDRHealth.com. *Rauwolfia*. Available at: www.pdrhealth.com. Accessed on December 12th 2021
76. Poonam, Agrawal S, Mishra S, Physiological, biochemical and modern biotechnological approach to improvement of *Rauwolfiaserpentina*, *J Pharm Biol Sci.* 2013; 6(2): 73–78p.
77. Poonam, Agrawal S, Mishra S, Physiological, biochemical and modern biotechnological approach to improvement of *Rauwolfia serpentina*, *Journal of Pharmacy and Biological Science*, 6(2), 2013, 73-78.
78. Prusoff WH, Effect of reserpine on the 5-hydroxytryptamine and adenosinetriphosphate of the dog intestinal mucosa, *British Journal of Pharmacology* 17, 1961, 87-91.
79. Pullaiah J, Medicinal plants in India, New Delhi, Regency Publ, 2, 2002, pp 441-443.
80. Qu L, Akbergenova Y, Hu Y, Schikorski T. Synapse-to-synapse variation in mean synaptic vesicle size and its relationship with synaptic morphology and function. *J Comp Neurol.* 2009;514(4):343-352.
81. Qureshi SA, Udani SK, Hypolipidaemic activity of *Rauwolfia serpentina* Benth, *Pakistan Journal of Nutrition*, 8(7), 2009, 1103-1106.
82. Rahmatullah M, Jahan R, Azad AK, *et al.* Medicinal plants used by folk medicinal practitioners in three villages of Natore and Rajshahi districts, Bangladesh, *Am-Eurasian J Sustain Agr.* 2010b; 4(2): 211–218p.
83. Rahmatullah M, Jahan R, Azad AK, Seraj S, Rahman MM, Chowdhury AR, Begum R, Nasrin D, Khatun Z, Hossain MS, Khatun MA, Miajee Z, Medicinal plants used by folk medicinal practitioners in three villages of Natore and Rajshahi districts, Bangladesh, *American-Eurasian Journal of Sustainable Agriculture*, 4(2), 2010b, 211-218.
84. Rai SK, Medicinal plants used by meche people of Jhapa District, Eastern Nepal, *Our Nature.* 2004; 2: 27–32p.
85. Rai SK, Medicinal plants used by meche people of Jhapa District, Eastern Nepal, *Our Nature*, 2, 2004, 27-32.
86. Reserpine. International Programme of Chemical Safety Web site. www.inchem.org/documents/pims/pharm/reserpn.htm. Accessed December 25, 2021.
87. Rolf S, Bruns HJ, Wichter T, Kirchhof P, Ribbing M, Wasmer K, Paul M, Breithardt G, Haverkamp W, Eckardt L, The ajmaline challenge in Brugada syndrome: diagnostic impact, safety, and recommended protocol, *European Heart Journal*, 24(12), 2003, 1104-1112.
88. Rosenren AH, Jokubka R, Tojjar D, Granhall C, Hansson O, Li DQ, Nagaraj V, Reinbothe TM, Overexpression of alpha2A-adrenergic receptors contributes to type 2 diabetes, 327 (5962),

89. Ruyter CM, Akram M, Illahi I, Stockigt J. Investigation of the alkaloid content of *Rauwolfia serpentina* roots from regenerated plants. *Planta Med.* 1991;57(4):328-330.
90. Salah N, Miller NJ, Pagange G, Tijburg L, Bolwell P, Rice E, Evans C, Polyphenolic flavonoids as scavenger of aqueous phase radicals as chain breaking antioxidant, *Archives of Biochemistry & Biophysics*, 2, 1995, 339-346.
91. Schlittler E, Saner H, Muller JM, Reserpine, ein neues Alkaloid aus *Rauwolfia serpentina*. *Experientia*, 10: 1954, 109-133.
92. Schuldiner S, Liu Y, Edwards RH. Reserpine binding to a vesicular amine transporter expressed in Chinese hamster ovary fibroblasts. *J Biol Chem.* 1993;268(1):29-34.
93. Sen G, Bose K. *Rauwolfia Serpentina*, a new Indian drug for insanity and Hypertension, *Indian M. World.* 1931; 21: 194p.
94. Shamsi Y, Kumar H, Tamanna SA, Khan EA, Effect of a polyherbal Unani formulation on chronic urticaria, *Indian Journal of Traditional Knowledge*, 5, 2006, 279-283.
95. Siddiqui S, Ahmad SS, Haider SI, Siddiqui BS, Isolation and structure of a new alkaloid from the roots of *Rauwolfia Serpentina* Benth, *Heterocycles*, (3), 1985, 617-622.
96. simultaneous quantitation of reserpine, ajmaline and ajmalicine, *Methods in Molecular Biology*, 547, 2009, 17-33.
97. Singh P, Singh A, Shukla AK, *et al.* Somatic embryogenesis and in vitro regeneration of an endangered medicinal plant sarpgandha (*Rauwolfia serpentina* L), *Life Sci J.* 2009; 6(3): 74-79p.
98. Singh P, Singh A, Shukla AK, Singh L, Pande V, Nailwal TK, Somatic embryogenesis and in vitro regeneration of an endangered medicinal plant sarpgandha (*Rauwolfia serpentina* L), *Life Science Journal*, 6(3), 2009, 74-79.
99. Singh PK, Kumar V, Tiwari RK, Sharma A, Rao CV, Singh RH, Medicobotany of 'Chatara' Block of District Sonbhadra, Uttar Pradesh, India, *Advances in Biological Research*, 4(1), 2010, 65-80.
100. Singh R, Sawhney SK, *Advances in frontier areas of Plant Biochemistry*, Prentice Hall in India Private Ltd, New Delhi, 1988, 487.
101. Sodipo OA, Akinyi JA, Ogunbamusu JU, Studies on certain characteristics of extracts of bark of *Pansinystalia macruceras* (K. schemp) pierre Exbelle, *Global Journal of Pure Applied Science*, 6, 2000, 83-87.
102. Srivastava A, Tripathi AK, Pandey R, Verma RK, Gupta MM, Quantitative determination of reserpine, ajmaline and ajmalicine in *Rauwolfia serpentina* by reversed-phase high-performance liquid chromatography. *Journal of Chromatographic Science*, 44, 2006, 557-560.
103. Stitzel RE. The biological fate of reserpine. *Pharmacol Rev.* 1976 Sep;28(3):179-208. PMID:16280.
104. Sukumaran S, Raj ADS, Rare and endemic plants in the sacred groves of Kanyakumari District in Tamilnadu, *Indian Journal of Forestry*, 31(4), 2008, 611-616.
105. Vakil R.J., A clinical trial of *Rauwolfia serpentina* in essential Hypertension, *Brit Heart J.* 1949; 11(4): 350-355p.
106. Vakil RJ. *Rauwolfia serpentina* in the treatment of high blood pressure: a review of the literature. *Circulation.* 1955;12(2):220-229.

222 PHARMACOLOGICAL PROPERTIES OF RAUVOLFIA SERPENTINA

107. Varchi G, Battaglia A, Samori C, Baldelli E, Danieli B, Fontana G, Guerrini A, Bombardelli E, Synthesis of deserpidine from reserpine, *Journal of Natural Products*, 68, 2005, 1629-1631.
108. Verma KC, Verma SK. Alkaloids analysis in root and leaf fractions of sarpaghandha (*Rauwolfia serpentina*). *Agric Sci Dig*. 2010;30(2):133-135.
109. von-Poser G, Andrade HH, Da-Silva KV, Henriques AT, Henriques JA, Genotoxic, mutagenic and recombinogenic effects of *Rauwolfia* alkaloids, *Mutation Research Journal*, 232, 1990, 37-43.
110. Weiss RF, Fintelmann V, *Herbal medicine*, 2nd ed. Thieme, Stuttgart, 2000, 229-230, 387-416.
111. Werner G. The central control of the blood pressure, *Indian M. Gaz*. 1953; 88: 111p.
112. Wimalasena K. Vesicular monoamine transporters: structure-function, pharmacology, and medicinal chemistry. *Med Res Rev*. 2011;31(4):483-519.
113. Woodson RE, Youngken HW, Schlittler E, Schneider JE. *Rauwolfia: Botany, Pharmacognosy, Chemistry and Pharmacology*. Boston, MA: Little, Brown and Company; 1957:32-33.

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