Review Article

www.ijrap.net (ISSN:2229–3566)

A REVIEW ON POTENTIAL BIOACTIVE CHEMICAL FROM *RAUWOLFIA SERPENTINA*: RESERPINE

Mukul Srivastava [1], Shikha Kesharwani [1], Roohi Kesharwani [1], Dilip K Patel [1]*, S.N. Singh [2]
[1] Chandra Shekhar Singh College of Pharmacy, Koilaha, Kaushambi, Uttar Pradesh, India
[2] Director, Ayurvedic Services, Uttar Pradesh, India

Received on: 23/11/20 Accepted on: 09/01/21

***Corresponding author**
E-mail: dilippatel87mp@gmail.com

DOI: 10.7897/2277-4343.120123

ABSTRACT

The drug *Rauwolfia serpentina* is known to Indian system of medicine since last many centuries. Because of snake like shape of drug, it has been known as sarpgandha. Although *Rauwolfia serpentina* contain more than 50 alkaloids but Reserpine is the principal alkaloid of *Rauwolfia serpentina*. Reserpine has a success application in antihypertensive even at a smaller dose. Rhizomes of *Rauwolfia serpentine* also have hepatoprotective activity including antihypertensive, hepatoprotective, *Rauwolfia serpentina* have many other medicinal uses like: Antidiahoerreal, antipsychotic, sedative, anticancer (in breast) etc. Although *Rauwolfia serpentina* contains major four Indole alkaloids but main object of this context is to provide knowledge about the main active alkaloid Reserpine, having more concentration in the root of plant, play a major role in antihypertensive activity of *Rauwolfia serpentina*. A much lesser dose of Reserpine is required to provide an antihypertensive effect otherwise it can cause some serious adverse effect like- lethargy, sedation, psychiatric depression, hypotension, nausea, bradycardia, bronchospasm and withdrawal psychosis. Because of its potent activity Reserpine is still used as antihypertensive and sedative agent.

Keyword: *Rauwolfia serpentina*, Reserpine, Antihypertensive, sedative, Antipsychotic, Hepatoprotective, Hypotension.

INTRODUCTION

Rauwolfia consist of dried roots of the plant known as *Rauwolfia serpentina* Benth belonging to family *Apocynaceae*, more than 100 species are included in the *Rauwolfia* genus and they are native to tropical and subtropical Region of world including Europe, Africa, Australia, Asia and central and south Americas.[1] In India it is cultivated in Utter Pradesh, Bihar, Orissa, Tamilnadu, West Bengal, Karnataka, Maharashtra and Gujarat. The plant is large climbing or twinning herb or shrub, has pale green leaves that are elliptical or lanceolate shaped and occur in whorls of 3-5 leaves. The fruits of this plant are shiny, black or purple, round and are approximately 0.5 cm in diameter. Roots of plant reaches a length 30-50 and diameter between 1.2-2.5 cm. Hindus used this plant for centuries as an antidote to the bite of poisons snake.[2] Reserpine was first isolated by muller, schlittler and bein in 1952 A.D. with formula $C_{33}H_{40}O_9N_2$.[1,4] In different places the plant is known as different names like-

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

Taxonomical classification [2]
Kingdome- *Plantae*
Phylum- *Angiosperms*
Subphylum- *Eudicots*
Order- *Gentianales*
Family- *Apocynaceae*
Genus- *Rauwolfia*
Species- *Serpentina.*

Sarpagandha or *Rauwolfia serpentina* L. Benth Kurz is a small, woody, perennial shrub and is believed as one of the best-known medicinal plants in the world.[4] Traditional medical practitioners recognizes the root of Sarpagandha for reducing high blood pressure and for treating various neurological symptomatic disorders including anxiety, psychosis, schizophrenia, epilepsy and insomnia.[5-9]

Reserpine

Reserpine is a white to light yellow, crystalline alkaloid, practically insoluble in water, obtained from various species of *Rauwolfia*. In common with other compounds with an Indole nucleus, it is susceptible to decomposition by light and oxidation, especially when in solution. In the dry state discoloration occurs rapidly when Reserpine is exposed to light, but the loss in potency is usually small.

History

The root of *Rauwolfia serpentina* benth has been used in India from century. In Ayurveda sarpgandha refers to use as an antidote for snake bite.[10] *Rauwolfia* has been used in Africa for hundreds of years, in India for at least 3000 years.[11] *Rauwolfia* was mentioned in Indian manuscripts as long as 1000 B.C. and also known as Sarpagandha and Chandra.[12] On the name of German physician Dr. Leonhard Rauwolf (16th century) the name of this plantae said to be *Rauwolfia* sarpentina.[13] In 1949 A.D. Jal Vakil published a watershed paper on the antihypertensive properties of *Rauwolfia serpentina* in the British medical journal.[14]

Morphology

Serpentina rauwolfia or Sarpagandha is a climbing herb or shrub having height near about 60 cm.[15] this tree has cylindrical stems, have pale bark and latex is viscous and light in colour. Leaves are

pale green that are elliptical or lanceolate shaped. Fruits are shiny, black or purple.[16]

Figure 1: *Rauwolfia serpentina* (pale green leaves)

Roots- 10-18 cm long
Size- 1-3 cm diameter
Shape- Sub-cylindrical, slightly tapering, and torturous. Fracture short and irregular
Colour- Greyish yellow to brown.

Cultivation

Rauwolfia grows under various climatic conditions. It flourishes in hot humidity conditions and grows satisfactory in shade. For cultivation, the clay loamy soil with much amount of humus and good drainage are favourable. It grows best at 10-38'C temperature and PH around to 4. Rainfall should be from 250-500 cm.[17] the plant can be cultivated easily by seed propagation but can also be propagated by stem or root.[15,18]

Chemical constituents

Rauwolfia contains many different photochemical including oleo-resins, phytosterol, fatty acids, alcohol, sugar and alkaloids. About 50 alkaloids are isolated from this plant.[19] all alkaloids are broadly classified into the following types-

1) Indole alkaloids
2) Indolenine alkaloids
3) Oxindole alkaloids
4) Pseudo indoxyl alkaloids
5) Indole alkaloids

In above all, the Indole alkaloids are important.[17] the major alkaloid of the plant is Reserpine. Sarpagandha yield Reserpine from 1.7 - 3.0%. About 90% of alkaloid is present in roots and bark.[20]

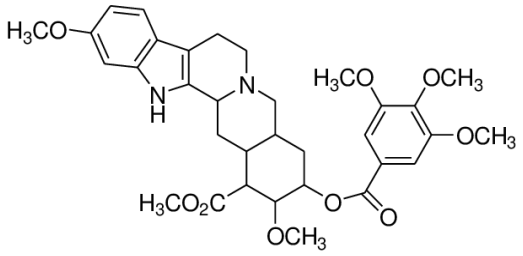

Figure 2: Structure of Reserpine

On the basis of evaluation of the chemical composition of *Rauwolfia serpentina* by Namita Bhardwaj [21] chemical composition of *Rauwolfia* may be summarised as follow-

Table 1: Photochemical

Alkaloids	1.50 ± 0.02
Flavonoids	1.65 ± 0.12
Phenols	1.84 ± 0.11
Tannins	0.85 ± 0.20

Table 2: 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

Table 3: Vitamin composition

Ascorbic acid	41.04 ± 0.20
Riboflavin	0.52 ± 0.10
Thiamine	0.20 ± 0.02
Niacin	0.05 ± 0.10

All the quantities are mg/100gm.

Pharmacological Effect of *Rauwolfia* Alkaloids

1. Antihypertensive activity

Rauwolfia serpentina is the most likely known to be as an antihypertensive drug due to presence of alkaloid called Reserpine. Reserpine is a major alkaloids present highest in root and leaves and also in lowest part of stem.[22] The first man, SEN And BOSE published modern paper on Reserpine in 1931 A.D. in Indian medical journal.[13] The Reserpine content of per gram root is 33 mg of 496 mg of total alkaloids.[23] In the study of vakil's 50 patients, 85% patient found to be a drop in systolic blood pressure and 81% of patient found to be a drop in diastolic blood pressure.[24] Reserpine is effective orally and parentally for the treatment of hypertension. After a single intravenous dose, the onset of antihypertensive action usually begins in about 1 hour. After intramuscular injection, the maximum effect occurs within approximately 4 hours and lasts about 10 hours. When it given orally, the maximum effect occurs within about 2 weeks and may persist up to 4 weeks after the final dose. When used in conjugation with other hypotensive drugs in the treatment of severe hypertension, the daily dose varies from 100 to 250 micrograms.

Mechanism of action of Reserpine

Reserpine lowers the blood pressure by depleting the stores of catecholamine at nerves ending. It prevents reuptake of nor epinephrine at storage sites, allowing enzymatic destruction of neuronal transmitter.[17] Reserpine binds to *vesicular monoamine transporter* (VMATs) in organelle membrane of presynaptic neurons.[25,26] Reserpine irreversibly blocks the H^+ coupled vesicular monoamine transporters, VMAT1 and VMAT2. VMAT1 is rich in Neuro-endocrine cells. VMAT2 is rich in neurons. Thus, Reserpine block neuronal system that inhibits uptake and reduces stores of the monoamine neurotransmitters, nor epinephrine, dopamine, serotonin and Histamine in the synaptic vesicles of neurones.[18]

2. Anti-diarrhoeal activity

Dr. EZEIGBO II in its research to evaluate the Anti-diarrhoeal activity of methanolic extract of leaves of *Rauwolfia serpentina* in experimental diarrhoeal induced by castor oil in mice found

that the extract of *Rauwolfia serpentina* leaves has significant Anti-diarrhoeal activity.[27]

3. Effect of *Rauwolfia serpentina* in breast cancer

In 1960-1970 A.D. and an alleged relationship to breast cancer was arises in medical literature, in 3 case-controlled studies, so the use of *Rauwolfia* and Reserpine product was reduced.[28] But research and analysis eliminating exclusion bias shows that there is no role of *Rauwolfia* in rate of breast cancer occurred in patient.[29] Rather than causing cancer it possesses anticancer activity.[30,31]

4. Antipsychotic activity

Reserpine has also used for treatment of schizophrenia and tardive dyskinesia. It is used as febrifuge or fever relieving drug.[32,33] A review found that in person with schizophrenia, Reserpine and chlorpromazine had similar rates of adverse effects but that Reserpine was less effective than chlorpromazine for improving a person's global state.[34]

5. Treatment of hysteria

Rauwolfia is useful in treating hysteria. 1 gm of powdered root can be administered thrice with milk. Treatment should be continued till a complete cure is obtained.

6. Other uses

The products of *Rauwolfia serpentina* are also useful in treatment of disease like: Fever, malaria, eye disease, pneumonia, asthma, AIDS, headache, skin disease and spleen disorder.[35-40]

CONCLUSION

Rauwolfia serpentina is a relevant plant as well as having a great medicinal use in antihypertensive drug. The use of *Rauwolfia serpentina* and its alkaloids can be further investigated to provide a benefit of humanity to cure the disease. The major alkaloid of *Rauwolfia serpentina,* Reserpine has a great affinity for treatment of hypertension along with other pharmacological action as well defined in above whole literature. Although *Rauwolfia serpentina* is affective in hypertension but it appears safe and well effective when taken at lower dose. A patient has hyper tension should take less than 500 mg of drug per day, even in most of the cases physician prefer 250 mg per day. *Rauwolfia serpentina* consist of many photochemical like alkaloids, flavonoids, phenolic compounds etc. The presence of phenolic compound in the plant indicates that this plant may be anti-microbial agent. Pure isolated alkaloids and their synthetic derivatives may used as basic medicinal agent for their analgesic, antispasmodic and bactericidal effects. They can mark physiological activity when administered to animals.

REFERENCES

1. Vakil R.J. *Rauwolfia serpentina* in the treatment of high blood pressure: Review of the Literature, circulation 1995; 12: 220-229.
2. Medical plant *Rauwolfia serpentina* gits 4u .Com.
3. Muller J.M., Schlittler E. *et al*, Serpentina (Benth) Experiential 1952; 8: 338.
4. Kirtikar KR, Basu BD. Indian Medicinal Plants. 2nd edition, Calcutta: Dehra Dun Publishers; 1993.
5. Mia MMK, Kadir MF, Hossan MS, *et al*. Medicinal plant of the Garo tribe inhabiting the Madhupur forest region of Bangladesh, AM – Eurasian J Sustain Agr 2009; 3(2): 165-171.
6. Lowinger P. *Rauwolfia serpentina* in the control of anxiety. Psychiatry Q 1957; 31(3): 445-453.
7. Rastogi RP, Dhawan BN. Research on medicinal plants at the Central Drug Research Institute, Lucknow (India). Indian J Med Res 1982; 27-45.
8. Baumeister AA, Hawkins MF, Uzelac SM. The myth of Reserpine-induced depression: role in the historical development of the monoamine hypothesis. J Hist Neurosci 2003; 12(2): 207-220.
9. Dey A, De JN. Ethnobotanical aspects of *Rauwolfia serpentina* (L). Benth. Ex Kurz. in India, Nepal and Bangladesh. J Med Plant Res 2011; 5(2): 144-150.
10. Joseph Monachino, *Rauwolfia serpentina* – Its history, Botany and Medical use, Economic Botany 1954; 8(4): 349-365.
11. Gupta K. Ajay, Chitme Havagiray, Dass K. Sujata and Misra Neelam, Hepatoprotective Activity of *Rauwolfia serpentina* Rhizome in Paracetamol Intoxicated Rats, Journal of Pharmacology and Toxicology 2006; 1(1): 82-88.
12. Yarnell E., Abascal K. Treating hypertension botanically. Altern Complement Ther 2001; 7(5): 284-290.
13. Jerie P. Milestones of Cardiovascular Therapy, IV: reserpine (in Czech), Cas Lek Cesk 2007; 146(7): 573-577.
14. Isharwal S., Gupta s. Rustom Jal Vakil: his contributions to cardiology. Tex Heart Inst J 2006; 33(2): 161-170.
15. Biradar Nitin, Hazarika Iswar, Chandy Vineet, Current Insight to the use of *Rauwolfia*: A Review, Research and Reviews: A Journal of Pharmacognosy 3: 2394-7276.
16. B.V. Gawade and S.A. Fegade, *Rauwolfia* (serpentina) As a potential Antihypertensive Agent: A Review, International Journal of Pharmaceutical and Phytopharmacology Research 2012; 2(1): 46-49.
17. Kokate C.K, Purohit A.P., Gokhale S.B., Pharmacognosy, Nirali Prakashan, 15.23.
18. Yaffe D, Forrest LR, Schuldiner S. The ins and outs of vesicular monoamine transporters. J. Gen. Physiol. 2018; 150 (5): 671–682.
19. Verma KC, Verma SK. Alkaloids analysis in root and leaf fraction of Sarpagandha (*Rauwolfia serpentina*), Agric Sci Dig. 2010; 30(2): 133-135.
20. Herbal Monograph, the Himalaya Drug Company, http//www. Himalayahealthcare.Com /herbfinder/h _ berber.html 2016.
21. Bhardwaj Namita, Yadav Manish, Evaluation of the chemical composition of *Rauwolfia serpentina* and *Leucas aspera* – A comparative study 5(10): 914-920.
22. 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.
23. Leete E. The biogenesis of the *Rauwolfia* alkaloids, I: the incorporation of tryptophan into Ajmaline. J Am Chem Soc 1960; 82(24): 6338-6342.
24. Vakil RJ, A clinical trial of *Rauwolfia serpentina* in essential hypertension. Br Heart J 1949; 11(4): 350-355.
25. Schuldiner S, Liu Y, Hu Y, Edwards RH, Reserpine binding to a vesicular amine transporter expressed in Chinese hamster ovary fibroblasts. J Biol chem 1993; 268(1): 29-34.
26. 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.
27. II Ezeigbo, MI Ezeja, KG Madubuike, DC Ifenkwe, IA Ukweni, NE Udeh, SC Akomas. Antidiarrheal activity of leaf methanolic extract of *Rauwolfia serpentina*. Asian Pacific Journal of Tropical Biomedicine 2012; 430-432.
28. Weiss RF. Weiss's Herbal Medicine. New York, NY, Theime; 2001. p. 153-158.

29. Horwitz RI, Feinstein AR. Exclusion bias and false relationship and breast cancer, Arch Intern med 1985; 145(10): 1873-1875.
30. Bhatara VS, Sharma JN, Gupta S, Gupta YK, Images in psychiatry, *Rauwolfia serpentina*: the first herbal antipsychotic. Am J. Psychiatry 1997; 154(7): 894.
31. Stanfort JL, Martin EJ, Brinton LA, Hoover RN, *Rauwolfia* use and Breast Cancer: a case – Control study, J Natl Cancer Inst 1986; 76(5): 817–822.
32. Singh P, Singh A, Shukla Ak, *et al*. Somatic embryogenesis and *in vitro* regeneration of an endangered medicinal plant Sarpagandha (*Rauwolfia serpentina* L), Life Sci J 2009; 6(3): 74–79.
33. Hoenders HJ, Bartels – Velthuis AA, Vollbehr NK, Bruggeman R, Knegtering H, de Jong JY. Natural medicine for Psychotic disorders: A systematic Review. J. Nerv. Ment. Dis 2018; 206(2): 81-101.
34. Nur S., Adams CE. Chlorpromazine versus reserpine for schizophrenia, Cochrane Database syst Rev. 4: CD 012122; 2016.
35. Nayak S, Behera SK, Misra MK, Ethnomedico – botanical survey of Kalahandi district of Orissa, Indian J. Tradition know 2004; 3(1): 72-79.
36. Anisuzzaman M. Rahman AHMM, Harunor – Rashid M., *et al*. An ethnobotanical study of Madhupur, Tangali, J Appl Sci Res 2007; 3(7): 519-530.
37. Rai SK, Medicinal plant used by meche people of Jhapa District, Eastern Nepal, Our Nature 2004; (2): 27-32.
38. Britto JD, Mahesh R. Exploration of kanitribal botanical knowledge in agasthiayamalai biosphere reserve – South India, Ethnobotany Leaflets 2007; 11: 258-265.
39. Rahmatullah M, Jahan R, Azad AK, *et al*. Medicinal plant used by folk medicinal practitioner in villages of Natore and Rajshahi districts, Bangladesh, Am – Eurasian J Sustain Agr 2010; 4(2): 211-218.
40. Behera SK, Panda A, Behera SK, *et al*. Medicinal plant used by the Kandhas of Kandhamal district of Orissa, Indian J Tradition know 2006; 5(4): 519-528.

Cite this article as:

Mukul Srivastava *et al*. A Review on Potential Bioactive Chemical from *Rauwolfia serpentina*: Reserpine. Int. J. Res. Ayurveda Pharm. 2021;12(1):106-109 http://dx.doi.org/10.7897/2277-4343.120123

Source of support: Nil, Conflict of interest: None Declared