Available on line at : www.eijppr.com

International Journal of Pharmaceutical and Phytopharmacological Research

ISSN (Online) 2249 – 6084

ISSN (Print) 2250 – 1029

Int.J.Pharm.Phytopharmacol.Res. 2012, 2(1): 46-49

(Review Article)

Rauwolfia (Reserpine) As a Potential Antihypertensive Agent: A Review

Gawade B.V.* and Fegade S.A.

Shri Fattechand Jain College of Pharmacy, Chinchwad, Pune-411019, Maharashtra, India.

Received on: 17/08/2012 ***Accepted on:*** 22/08/2012

ABSTRACT

The root of Rauwolfia serpentina Benth has been used in India from century. The genus name was selected in honor of Dr. Leonhard Rauwolf, a 16th century German botanist, Physician & explorer. Rauwolfia serpentina is a large climbing/twining herb or shrub, belonging to family Apocynaceae and found in the Assam, Pegu, Himalayas, Java, Tennasserim, Deccan, Peninsula, Bihar and the Malay Peninsula. Reserpine is the principle alkaloid of Rauwolfia serpentina and has its clinical application with success to the treatment of high blood pressure. Much smaller dose of Reserpine is required to obtain the antihypertensive action. 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.The present review focuses mainly on chemistry and antihypertensive effect of Rauwolfia alkaloids.

Key Words: *Rauwolfia serpentina*, Reserpine, Indole Alkaloids, Potent, Antihypertensive.

INTRODUCTION

Rauwolfia serpentina is the dried root of *Rauwolfia serpentina* (Linne) Bentham ex Kurz. (Family: Apocynaceae). It is an erect shrub that grows 1 meter in height and has cylindric stems. These stems have pale bark and consist of light colored viscous latex. Leaves of *Rauwolfia serpentina* may be simple and opposite, or more commonly arranged in whorls of 3 to 5. The white or pale rose flowers are arranged in terminal and axillary cymes. The fruit is a single, 2-lobed drupe that turns purplish black when mature. Reserpine was first isolated by Muller Schiltter and Bein in 1952 with formula $C_{33}H_{40}O_9N_2$ [2, 3].

HISTORY

Rauwolfia serpentina is said to be appear in Sanskrit as an Ayurvedic medicine named Sarpgandha and Chandra. Sarpgandha, snakes smell or repellant, refers to the use as an antidote for Snake-bite [4]. Sen and Bose in 1931 reported the Rauwolfia serpentina valuable and safe in the treatment of High blood pressure "almost to a precision not found possible with any other drug, Eastern or western".

In 1949 Vakil concluded that, after extensive trials of various hypotensive remedies in several thousand cases of hypertension, in both private and hospital practice during the previous ten years, He found *Rauwolfia serpentina* to be the most successful drug and maintaining a definite place in medicine, because *Rauwolfia serpentina* lowered both systolic and diastolic blood pressure and It was non-toxic, with only mild toxic effects. In reply to a questionarrie that Vakil issued to 50 Physicians all over India, 46 voted for *Rauwolfia serpentina* as the best antihypertensive agent in their experience.

CHEMICAL COMPOSITION

Three types of alkaloids are present in *Rauwolfia serpentina.*

1. Weakly basic Indole Alkaloids:
   The principal alkaloids are Reserpine, Rescinnamine, despiridine and these are tertiary Indole Alkaloids.
2. Indoline Alkaloids of intermediate basicity:
   Reserpiline, Ajmaline, Iso- Ajmaline, rauwolfinine are tertiary Indoline alkaloids.
3. Strong Anhydronium Bases:
   Serpentine, serpentinine and alsotonine are strongly basic anhydronium alkaloids [1].

While Ajmalinine, Ajmalicine, Chandrine, renoxidine, reserpinine, Sarpagine, Tetraphyllicine, Yohimbine, 3-epi-a-yohimbine are the other alkaloids present in *Rauwolfia serpentina* [5].

Reserpine is the most important alkaloid present in root, stem and leaves of the plant. It contains not less than 0.15% of Reserpine-rescinnamine group alkaloids, calculated as Reserpine [1].

The percentage of alkaloid depends on geographical place from where the plant is collected and also the season of collection. Generally samples from Assam have a higher percentage of alkaloid (2.57%) and December is the best month for the collection for getting more percentage of alkaloid [5].

Structure of Reserpine

The enzyme strictosidine synthase (STR1) from the Indian medical plant *Rauwolfia serpentina* is involved in the biosynthesis of most of the indole alkaloids [6, 7, 8].The biosynthesis of Reserpine is shown in Fig.1.

Tryptamine and the monoterpenoid Secologanine produce glucoalkaloid Strictosidine in the first step of biosynthesis. Then Strictosidine enzyme helps in the biosynthesis of Reserpine.

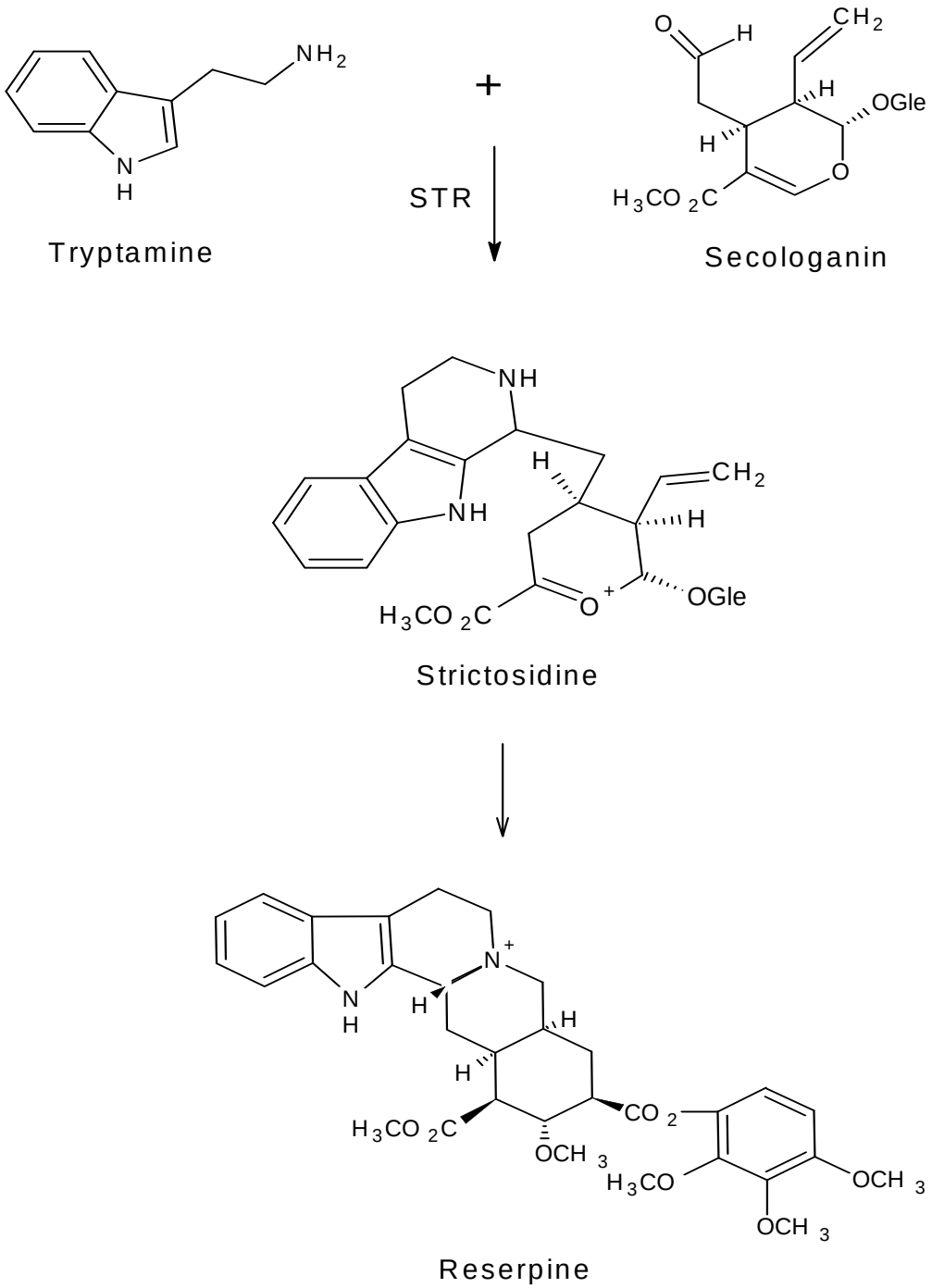

Fig.1: Biosynthesis of Reserpine

MECHANISM OF ACTION OF RESERPINE

Chopra, Gupta and Mukherjee reported that the alkaloids had a marked hypotensive effect which was due to depression of central nervous system mechanisms [9, 10, 11]. It also had inhibitory effect on the musculature of the blood vessels. They demonstrated also a fall in the output of the isolated heart.

Reserpine diminishes reflex vasomotor responses, but also has a direct effect on the peripheral vessels independent of its nervous activity. They also saw this activity clearly in the rabbit. They employed the preparation devised by Gallagher [12] according to this method the isolated hind-limb is perfused with blood-Dextran medium at constant rate. Changes in vasomotor tone in the limb are indicated by alterations in

perfusion pressure. They found that, injections of Reserpine in to the systemic circulation of the rabbit produce an immediate fall in systemic blood pressure which is accompanied by immediate rise in limb perfusion pressure instead of a fall and which was been expected were fall of blood pressure mediated through the nervous system. Furthermore, injection of Reserpine directly in to the artery of the perfused hind-limb causes immediate diminution in vasomotor tone.

So according to this Chopra, Gupta and Mukherjee reported that, a feature of all this reactions is their remarkably prolonged duration, suggesting binding of the drug by the musculature.

They had also obtained evidence that such a direct peripheral effect may play some part in hypotensive action of Reserpine in man.

Mc Queen, Doyle and Smirke have been reported that, direct peripheral effect may play some part in the hypotensive action of Reserpine in Man.

PHARMACOLOGICAL EFFECTS OF RAUWOLFIA ALKALOIDS

Rauwolfia serpentina is said to have the following pharmacologic attributes [13]:

1. By action on the vasomotor centre, it leads to generalized vasodilatation, with a lowering of blood pressure.
2. By depressant action on the cerebral canters, it soothes the general nervous system [14].
3. It stimulates the bronchial musculature.
4. The comparative Pharmacological actions of *Rauwolfia serpentina* root and its individual alkaloids have been investigated from time to time [2].

Siddiqui and Siddiqui on the basis of experiments on frogs in 1931 showed that Ajmaline group acts as a general depressant to the heart while serpentine group causes paralysis of respiration, depression of the nerves and stimulation of the heart [15].

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 hypotensive properties on the autolysis of rat brain and liver tissue, but to a lesser extent than Reserpine [5].

In 1940, Hamet [16] remarked on the hypotensive action of several alkaloids of *Rauwolfia serpentina*.

Bhatia and Kapur [17] in 1944 reported, isoajmaline and neoajmaline causes lowering of blood pressure in intact, spinal and decerebrate animals with or without experimentally induced hypertension.

Muller and associates [3] in 1952 and Bein [18] in 1953, on the basis of animal experiments, found the new alkaloid Reserpine possess marked and long lasting hypotensive activity.

In 1954 Goto[19], found the alkaloid Reserpine effective in 12 out of 15 cases of hypertension. The hypotensive action was apparent three to seven days after its suspension.

In 1953 Vakil [20] reported a good hypotensive response to the alkaloid Reserpine in 72% of cases, and few side effects.

In 1956 Guy Lemieux, Andre Davignon and Jacques [21] reported that orally administered Rescinnamine was clinically a less potent alkaloid than Reserpine and lowering of blood pressure was not significant.

PREPARATIONS AND DOSAGE

In severe hypertension, Reserpine may be given by intravenous or intramuscular injection when the effect begins with a few hours. Parenteral therapy of Reserpine is indicated in the treatment of hypertension only when oral administration is not possible.

Powdered Rauwolfia is *Rauwolfia serpentina* root reduced to a fine powder to confirm to the official requirements for Reserpine-rescinnamine group alkaloids.It contains not less than 0.15% and not more than 0.20% of Reserpine-rescinnamine group alkaloid calculated as Reserpine.

Dosage: The usual dose of Reserpine is initially 500 mg once a day for 1-2 weeks, maintenance 100 to 250 mg once a day. The patient should be advised to notify his physician if a change in mood occurs.

CONCLUSION

Reserpine is a pure crystalline single alkaloid; it cannot produce undesirable effects from unknown alkaloid in the whole root. Much smaller doses of Reserpine are required to obtain the hypotensive action. It has prolonged duration of action. Rauwolfinine has hypotensive properties but to a lesser extent than Reserpine. Rescinnamine is also a less potent alkaloid than Reserpine. So it is interesting to know that in smaller doses it gives more potent hypotensive action and for prolonged duration.

REFERENCES

1) Tyler V.E.,Brady L.R., Robbers J.E.,Pharmacognosy, 9th edition, Lea and Febiger,Philiadelphia,1988,222-224.
2) Vakil R.J., "*Rauwolfia serpentina* in the treatment of High Blood Pressure: Review of the Literature", Circulation, 1955, 12:220-229.
3) Muller J.M., Schittler E., et al, "Reserpine, Der Sedative Wrikstoff aus *Rauwolfia serpentina* (Benth) Experientia"1952, 8: 338.
4) Joseph Monachino, "*Rauwolfia serpentina*- Its History, Botany and Medical use", Economic Botany, 1954,8(4): 349-365.
5) Herbal Monograph, The Himalaya Drug Company, http://www.himalayahealthcare.com/herbfinder/h_berber.htm.
6) Santosh Panjikar, Juergen Koepke etal, "The structure of *Rauwolfia serpentina* Strictosidine synthase is a Novel Six-Bladed β-propeller fold in plant proteins", The Plant Cell ,2006 , 8(4) ,907-920.
7) Kutchan, T.M., "Strictosidine: From alkaloid to enzyme to gene. Phytochemistry"1993, 32, 493-506.
8) Stockigt, J. and Ruppert, M., "Strictosidine: The biosynthetic key to monoterpenoid Indole Alkaloid. In Comprehensive Natural Products Chemistry: Amino acids, Peptides, Porphyrins and Alkaloids", Vol-4, D.H.R. Barton, K. Nakanishi, O. Meth-Cohn and J.W. Kelly, eds (Amsterdam: Elsevier) p. 109-138.
9) Chopra, R.N.Gupta, J.C., and Mukherjee, B. The pharmacological action of an alkaloid obtained from Rauvolfia serpentina. A preliminary note, Ind., J. Med. Res.,1933, 21,261-71.
10) Ray, G.K.Roy, P.K., Dasgupta S.R., et al, Action of Rauwolfia serpentina on vasomotor reflexes, Arch. Exp. Path. U. Pharmakol., 1953, 219,310-14.

11) E.G. Mc Queen, A.E. Doyle, et al, "Mechanism of Hypotensive Action of Reserpine, an alkaloid of *Rauwolfia serpentina*", Nature, 1954,174, 1015.
12) Gallagher, D.J. A., A medium for perfusion of innervated blood vessels, Brit. J. Pharmacol., 1954, 9,129.
13) Rustom Jal Vakil, "A clinical trial of *Rauwolfia serpentina* in essential Hypertension", British Heart Journal, 1949, 11(4):350-355.
14) Werner,G., "The central control of the blood pressure", Indian M. Gaz.,1953, 88:111.
15) Siddiqui, S.S. and Siddiqui, R.H., "The alkaloid of *Rauwolfia serpentina*, Benth", J. Indian Chem. Soc, 1931, 8:667.
16) Hamet R, "Effect inte. Stinaux d' Ajmaline Pure", Compt.rend. Soc.de boil,1940, 134:369.
17) Kapur, R.D., "Pharmacological actions of alkaloids of *Rauwolfia serpentina* Benth. Part I, neo-ajmaline and isoajmaline", Indian J. Med. Res., 1944 32:177.
18) Bein, H.J. "Zur Pharmakologie des Reserpine, eines neuen Alk.aus *Rauwolfia serpentina* (Benth)", Experientia, 1953, 9: 1073.
19) Goto, Y., Personal Communication from Tokyo, Japan.
20) Vakil R.,"Hypotensive action of other *Rauwolfia serpentina* alkaloids: a clinical report", J. Indian M.A., 1953, 23: 97-102.
21) Guy Lemieux, M.D., Andre Davignon, M.D., et al, "Treatment of arterial hypertension with Rescinnamine, A new alkaloid isolated from *Rauwolfia serpentina*",956, 74, 145.

Corresponding Author:
Gawade B.V,
Lecturer, Shri Fattechand Jain College of Pharmacy, Chinchwad, Pune-411019, Maharashtra (India).
Email ID : bhagyashri195@gmail.com