International Journal of Innovation in Agriculture Sciences and Rural Development
Vol.1, NO.1 , P : 13 - 27
Received: 19 Nov 2018
Accepted: 15 Feb 2019

# A review of the therapeutic properties of the medical herb ( Rauvolfia serpentine)

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## Abstract

R. serpentina is an evergreen plant as a member of Apocynaceae family and is used in the treatment of some of the diseases including hypertension. More than 100 species are included in the Rauwolfia genus, and they are native to tropical and subtropical regions around the world, including Europe, Africa, Asia, Australia, and the Central America and South America. The plant usually grows to a height 60 - 90 cm with the leaves as elliptical or lanceolate shaped. It also has small pink or white flowers, with shiny purple or black and round fruits. The root of this plant has been used for a long time in India and the Malay peninsula as an antidote to the sting of insects and poisonous reptiles. It has also been used to reduce fever, as a stimulant to uterine contractions, diarrhea, for insomnia, and particularly for the treatment of insanity. The present study introduces botanical aspects, effective materials and scientific evaluation of using R. serpentine. The author emphasizes on the importance of observing the suitable dose of using R. serpentine plant and screening the patients to minimize its side-effects and introduces this plant a good recommendation to control and treat some diseases such as high systolic hypertension and mental diseases such as anxiety and schizophrenia.

**Keywords**: Rauvolfia serpentina, Asrole, Medicinal herbs, Natural treatment, Blood pressure

## Introduction

Rauwolfia was named in honor of German physician Dr Leonhard Rauwolf, who published a report of his travelling in India. The root of this plant has been used for a long time in India and the Malay peninsula as an antidote to the stings of insects and poisonous reptiles. The name of this plant is recognized as Sarpgandha in Sanskrit in the old Indian books (1000 years before BC) and also in the great works of Charaka (second century, A.D.). This plant also has been used

to reduce fever, as a stimulant to uterine contractions, diarrhea, dysentery, insomnia, and insanity. More than two decades, its clinical applications were successful in the treatment of hypertension. Rauvolfia serpentina or Serpentina is a climbing or twin shrub belongs to Apocynaceae family and is found in Himalaya, Assam, Pego, Java, Tenaserim, Bahar, Deccan and Malay Peninsula. Its variety is recognized as Sarpgandha (ancient times), Chandria (Sanskrite), Chota-Chand (Indian), Chand (Bengal), Danbarova or Pagla-Kadava (Bihar), Chandra, Chota Chanid, Karavi or Harkaya (Bombay), patalagarud or Atalaganidi (Telegu), Kumanmeliour (Tamil), Chovana Vilpouri (Malay) and Danbarova or DIHAN Barea (Oria). It is said that 130 special species of Rauwolfia grow in tropical areas as local. Yang can described five species of this plant as follows: Rauwolfia serpinta, Rauwolfia cansine, Rauwolfia micranta, Rauwolfia densiflora and Rauwolfia praknis. Based on the origin or source of presenting eight species of Rauwolfia growing in India and Rauwolfia species in Indian market, Bengal, Bihar, Osma, Dehar and Seylan are completely recognized. These species show considerable difference in the quality and volume of therapeutical alkaloids. The most useful Rauwolfia species from therapeutical aspects is Rauwolfia serpentina growing to the height of 1.5 to 3 foot and it has pink white flowers (Mia et al., 2009:168).

The history of the application of Rauwolfia in treating diseases

R. serpentine has been used for centuries in fold medicine in India to treat different diseases such as the sting of snake and insects, fever, malaria, abdomen pain and dysentery. It was also used as a uterine stimulant, febrifuge, and cure for insanity. The plant was mentioned in Indian manuscripts since 1000 bc and is also known as sarpagandha and chandriko. Serpentina is selected for study due to its long, tapering, snake-like roots. The Indian political leader, Mahatma Gandhi was known to use the root of Rauwolfia to make a tea that he consumed to help relax .

The Indian physician Rustom Jal Vakil introduced Rauwolfia to western medicine. He collected data on patients undergoing treatment with Rauwolfia for 10 years, from 1939 to 1949. In 1949, he published a paper on watershed in a British Medical journal and presented the antihypertensive properties of R serpentina. He presented his exact results from treating 50 patients who had high blood pressure with the root of Rauwolfia.

The results were considerable and significant. By 1949, more than 90% of Indian physicians were using Rauwolfia in the treatment of high blood pressure. After Vakil's original paper, more than 100 scientific articles were published around the world. After the main article of Vakil, more than 100 scientific papers were published all around the world. In recent years, this drug is used for sedative properties and it is also used for curing insanity and is advertised mostly in non-allowed press. Its application in the treatment of hypertension is a new source of pharmacological researches about this drug. It is said that the consumption cases of this drug is under experiment and any registration of the exact clinical observations is valuable in real evaluation of this drug in the treatment of hyperpicsia. Chemically, the root contains some alkaloids. Sen and Bose (1931) found two alkaloids with different melting points. Siddiqui and Siddiqui (1931) introduced five alkaloids including ajmaline, ajmalimine, ajmalicine, serpentine, serpentinine . Von Italie and Steenhaur mentioned at least three alkaloids that their nature and identity were similar to the findings of Siddiqui and Siddiqui.

An alkaloid isolated by the Chemistry Department of the tropical school of Medicine, Calcutta, was investigated by Chopra, Gupta and Mukherjee (1933). As a result of their pharmacological studies they showed that this alkaloid has a toxic effect on lower forms of life such as Paramoecia Caudatum in dilution of 1 in 20,000. Its toxicity on animals was variable. Frogs tolerated completely, whereas the white mouse was very sensitive. The drug was much more toxic, when injected intravenously or intraperitoneally, than when injected subcutaneously. In the circulatory system, the drug decreased the blood pressure of cats under anaesthesia as it has long-lasting effect. If spine of cats are used, the effect produced is very low, which shows that the fall in blood pressure was due to vasodilatation as a result of the the depression of the vasomotor center in the medulla oblongata. The fall in blood pressure was also noticed after the terminations of the vagi were paralysed with atropine, showing that vagal inhibition is not important in the fall created. The fall in blood pressure was also partly due to decreased cardic output, which was found on myocardiographic studies. During the injection of the drug through isolated vessels, Chopra and his coworkers found that it definitely decreased the number

of drops of the injection per minute, which means that it causes ‘vasoconstriction’ though they have erroneously called it vasodilatation. Both, the subjects were intact. The drug seemed to have a slight depressant action. The alkaloid has a stimulant action on the simple muscles of the alimentary canal and the uterus. However, its most interesting action was observed on the central nervous system, which it seems to act in the reverse order of development of heart congestive system. As by affecting the neural centers can lead to drowsiness, diminution in motor activity, diminution in the sensory stimuli, low performance of the medullary centers (Bhatia, 1942:2).

The introduction of Rouvolfia serpentine or Indian snake root

Family : Apocynaceae

Species : serpentina

Genus : Rouvolfia

R. serpentina is an evergreen plant as a member of Apocynaceae family and is used in the treatment of some of the diseases including hypertension. More than 100 species are included in the Rauwolfia genus, and they are native to tropical and subtropical regions around the world, including Europe, Africa, Asia, Australia, and the Central America and South America. Rauwolfia serpentina is native to the humid forests of Southeast Asia, including India, Burma, Bangladesh, Sri Lanka, and Malaysia. The plant normally grows to a height between 60 and 90 cm and has green leaves as 7 to 10 cm long and 3.5 to 5.0 cm wide. The leaves are elliptical or lanceolate shaped with 3 to 5 leaves. The plant has small pink or white flowers. It has many shiny, black or purple and round fruits that are about 0.5 cm in diameter. The plant has a prominent, soft taproot with a length between 30 and 50 cm and a diameter between 1.2 and 2.5 cm (Kiran, Jothi Priya & Gayatri Devi, 2018:25

Figure 1- Rouvolfia

Figure 2-Another view of Rouvolfia

2. Chemical constituents of Rouvolfia

Rauvolfia serpentina has been an extensive field of research for decades and several individuals have explored this field due to its phytochemical properties. The various phytochemical compounds or secondary metabolites present in R. serpentina include alkaloids, phenols, tannins and flavonoids (Rahman, 2018:45).

Alkaloids

Alkaloids are large group of organic molecules which contain a heterocyclic nitrogen ring. These are obtained by different organisms such as animals and microbes, but different array of alkaloids is produced by plants. It seems that approximately, 10% of plant species produce alkaloids as secondary metabolites. Pure alkaloids and synthetic derivatives are used in treatment-medicine as analgesic, antispasmodic and anti-bacterial effects. The alkaloids obtained from the root extract acts directly on central nervous system and thereby decreases blood pressure as compared to other blood-pressure decreasing agents. It is reported that R. serpentina root contains 0.7-3.0% of total alkaloids and about 0.1% of the active principle reserpine which is an indole alkaloid, existing in the root. Thus, root biomass production of this plant may be of economic importance. On the basis of the structure, there are three types of alkaloids:

Weak basic indole alkaloids, intermediate base alkaloids and strong anhydronium bases. The various alkaloids identified in Rauvolfia include ajmaline, ajmalimine, ajmalicine, deserpidine, indobine, indobinine, reserpine, reserpiline, rescinnamine, rescinnamidine, serpentine, serpentinine and yohimbine etc. (Hernandez-Leon, et al. 2018:36).

Reserpine

It is a pure crystalline alkaloid, derived from the roots of Rauvolfia and was first isolated

in 1952. This alkaloid is a relatively weak tertiary base in the oleoresin section of the roots and is useful in the treatment of hypertension, cardiovascular diseases and neurological diseases. The antihypertensive properties of Rauvolfia roots are dedicated to reserpine (3, 4, 5-trimethyl benzoic acid ester of reserpic acid, derivative of 18-hydroxy yohimbine type). This matter is the most prominent of all alkaloids and used mainly as a natural tranquillizer. Now, Reserpine is being used as a tool in physiologic studies of body functions and in pharmacological studies. The antihypertensive use of reserpine are due to its depressant action on central nervous system (CNS) and peripheral nervous system by binding to catecholamine (fight or flight hormones) storage vesicles in the nerve cell. This prevents the natural storage of catecholamines and serotonin in decline of catecholamine. It interferes with the function of automatic nervous system by depleting the transmitter substance from the adrenergic neurons and possibly by activating the central parasympathetic system. These substances are mostly involved in controlling heart rate, cardiac contraction and peripheral resistance. It also helps in sedation and reduction of blood pressure, especially in cases of hypertension increased by stress and sympathetic nervous system activity. Reserpine causes the release of 5-hydroxytryptamine (5-HT) from all tissues in which it is normally stored and increases urinary metabolites (Bhatia, 1942:5).

Ajmaline

Ajmaline is an alkaloid obtained from the root of R. serpentine which first isolated by Salimuzzaman Siddiqui in 1931 from the roots of R. serpentine. He called it ajmaline, after Hakim Ajmal Khan, one of the most was famous doctors of Unani medicine in South Asia. This plant is useful in the treatment of antiarrhythmic diseases and it is also used in diagnosing Brugada Syndrome (hereditary cardiac disorder), and for differentiating diagnosis of patients with this disease. These agents are primarily classified into four major groups on the basis of their action mechanism such as sodium channel blockade, beta-adrenergic blockade, repolarization prolongation and calcium channel blockade. Ajmaline is a sodium channel blocker that shows instant action when injected intravenously, which makes it suitable for diagnostic issues. The administration of Rauvolfia alkaloid to patients with arrhythmia type is known as the Ajmaline test . It 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 (Rahman, 2018:45).

Serpentine

Serpentine, a type II topoisomerase inhibitor, has antipsychotic properties. The enzyme peroxidase (PER) is responsible for oxidation of ajmalicine to serpentine by catalyzing bisindole alkaloid localized in the vacuole (Jamalpur I, Mogili HR, Koratala, 2017:40).

Phenols

Phenols are the secondary plant metabolites widely distributed in the plant domain as herbs, shrubs, vegetables and trees. The presence of phenols is of great importance for the growth and development of various pest and pathogens. High quantity of total polyphenolic compounds in R. serpentina shows significant antidiabetic and hypolipidemic properties. In medicine, it is used as an expectorant and emulsifying agent. The presence of phenolic compounds indicates this can be used as anti-microbial agent (Jamalpur I, Mogili HR, Koratala, 2017:40).

Tannins

The oxidation inhibiting activity of tannin is due to the presence of gallic acid and diagallic acid. Hard properties of Tannins increase the speed of healing of wounds and inflamed mucous membranes. Thus, R. serpentina is used in treating many disorders in South eastern India (Valki, 2014:31).

Flavonoids

These are effective water-soluble antioxidants and free radical scavengers, which prevent oxidative cell damage and have strong anticancerous activity. Flavonoids in intestinal tract also reduce the risk of heart disease. Asantioxidants, flavonoids provide anti-inflammatory activity for the treatment of diseases in herbal medicine.

Saponins

Saponins are glycoside of triterpenes and sterols and have been identified in over 70 plant families. Some of the characteristics of saponins include formation of foams in aqueous solutions, hemolytic activity, cholesterol binding properties and bitterness. Saponin has the property of coagulating red blood cells. The high saponin content of Rauvolfia serpentina proves the use of these extracts to prevent bleeding and in treating wounds (Valki, 2014:3).

Extensive use of R. serpentina in Pharmacology

R. serpentina has an important position in the pharmaceutical world due to the presence of different alkaloids in the oleoresin section of the roots. Alkaloids of this plant have a great importance to treat cardiovascular diseases, high blood pressure, arrhythmia, various psychiatric diseases, mental disorders and acute leukemia. Reserpine is its main alkaloid that shows highly complex pattern of activity mainly variation of amine concentration in brain. This substance is responsible for influencing the concentration of glycogen, acetyl choline, amino butyric acid, nucleic acids and anti-diuretic hormone. The effects of reserpine include respiratory inhibition, stimulation of peristalsis, myosis, and relaxation of nictating membranes and also influence temperature regulating center. It increases the volume and free acidity of gastric secretion. The Pitkriya capsule (Unani formulation) contains R. serpentina which acts as sedative and hypnotic matter ( Musakkin-wo-Munawwim), control (Diuretic), nerve sedative and (anesthetic) drug. Its various pharmacological activities include anticholinergic, hypotensive, anticontractile, sedative, relaxant, hyperthermic, antidiuretic, sympathomimetic, hypnotic, vaginose, antiemetic, anti-fibrillar activity tranquilizing agent, anti-arrhythmic, antifungal and nematocidal. R. serpentine has following pharmacological attributes: (1) By the action on vasomotor center, it leads to vasodilatation by reducing blood pressure. (2) By depressant action on the cerebral centers as it relaxes the nervous system. (3) It exerts a sedative action on the gastric mucosa and shows stimulating action on the plain musculature of the intestinal tract. (4) It also stimulates the bronchial musculature (Soni et al., 2016:30).

Therapeutic properties of R. Serpentina

Prostate cancer

Prostate cancer is considered to be major causes of cancer-associated deaths among men. Modern techniques such as chemotherapy and radiotherapy have not provided considerable survival benefits to patients with prostate cancer. Natural products have proven to be a major resource for identification of bioactive compounds applied in the treatment of a variety of diseases, including cancer as compared to chemotherapy and radiotherapy. Various parts of this plant have been used as a traditional medicine for centuries to treat a variety of illnesses including fever, general weakness, intestinal diseases, liver problems and mental disorders. Extracts from the root bark of this plant are enriched with

compounds of ß-carboline alkaloid family which is the main constituent of alstonine. This compound has previously reported the reduction tumour cell growth in mice inoculated with YC8 lymphoma cells or Ehrlich ascetic cells. The plant extract has anti-prostate cancer activity in both in laboratory and real model systems which, based upon analyses of gene expression patterns of treated prostate cancer cells, can be modulated by its effects on DNA damage and cell cycle control signaling pathways (Mia et al., 2009:168).

Treatment of high blood pressure

n 1949, Vakil reported on a study of 50 patients with hypertension who were treated with Rauwolfia. In the study, 85% of patients experienced a drop in systolic blood pressure, and 81% of patients experienced a drop in diastolic blood pressure.

In 1952, Vida in Germany and Austria reported a blood pressure fall in 25 patients with hypertension. Arnold and Bach showed a good result in 37 of 50 patients in whom systolic pressure dropped an average of 30 mm Hg and diastolic pressure dropped 15 mm Hg (Harisaranraj, 2009:62). In 1953, Meissner reported Rauwolfiato be effective in 90% of participants of study , with a reduction of systolic blood pressure between 15 and 40 mm Hg. In 1953, Loffler in Switzerland reported a drop of blood pressure among 51 Swiss workers with hypertension. In 1954, Goto in Japan reported low blood pressure in 12 of 15 patients with hypertension. In 1954, Doyle and Smirk in Zealand reported that reserpine showed a considerable drop in blood pressure within 4 to 6 hours of administration. More reports showed that Rauwolfia was the best hypertension cure used in India throughout the 1950s. It was reported that 90% of all physicians or more than 60 000 doctors throughout the country claimed that they sold 94 million tablets of the dried root in 1954, and it was exported to more than 17 countries around the world. In 1952, a pure standardized, isolated alkaloid extract called alseroxylon was introduced in the United States. The active ingredients of the pure extract were a mixture of reserpine and rescinnamine. In the study, 346 patients with hypertension were treated on an outpatient basis in public and private hospitals. Participants' main blood pressures were greater than 150/100 mm /g. During the control period, patients received a placebo. A consistent decrease in blood pressure readings of greater than 20 mm Hg was observed in patients treated with the alseroxylon extract.

A Rauwolfia Serpina product was given to more than 100 patients for periods of 1 month to 1 year. In the study, a daily dose of 1 to 3 Serpina tablets was considered. Its action mechanism was slow to appear, ranging from 3 to 6 days, and it disappeared 7 to 21 days after stopping the drug. It did not create any serious side effects. The product caused sedation and usually improved sleep, although it could sometimes cause nightmares in some individuals, and it could cause bradycardia and nasal congestion in some patients as it apparently was not habit, and its administration could be stopped easily for several days to relieve any unwanted side effects. It promoted a moderate hypotension, particularly in fat patients with hypertension and tachycardia, and it appeared to have a sympatholytic effect but did not produce hypotension. It appeared to be more effective in the youth, neurotic hypertensive patients with tachycardia that in those with fixed hypertension with organic, vascular disease was more effective. Thirty-nine patients with an average blood pressure of 192/122 mm Hg and a pulse of 82 were treated with Serpina alone. The average blood pressure decreased to 165/85 mm and the pulse was 70. In 13 of 39 patients, high blood pressure was controlled and the mean blood pressure was 150/90 mm Hg.

In a clinical trial of R serpentina in hypertension, Vakil treated 50 patients with initial blood pressures greater than 160/95 mm Hg. The study included 30 males and 20 females ranging in age from 39 to 76 years. Thirty-nine of 48 patients who completed the study showed a drop of both systolic and diastolic blood pressure at 1 week after starting the drug. After 4 weeks of taking the medicine, systolic blood pressure dropped between 2 and 54 mm Hg for those patients. 22 of 47 patients (1 was excluded of the study) showed a moderate drop in systolic blood pressure, from 10 to 24 mm Hg. Thirteen of the 47 patients showed a severe drop in systolic blood pressure of greater than 25 mm Hg, and 38 of the 47 patients showed a drop in diastolic blood pressure of between 4 and 34 mm Hg, with an average drop of 11 mm Hg. Twenty-seven patients showed a moderate drop of diastolic blood pressure of between 5 and 14 mm Hg, and 7 patients showed a drop greater than 15 mm Hg (Vakil, 2015:221). The hypotension (low blood pressure) mechanism of action of the drug was detected at 2 weeks after stopping the drug in 91% of patients and at 4 weeks after discontinuing the drug in 75% of patients. No serious side effects were noted. Another study was designed to evaluate various effects of oral reserpine on a group of

hypertensive individuals in an outpatient clinic. Reserpine from CIBA Pharmaceuticals was given in a dosage of 20 mg twice per day to 15 individuals who had initial blood pressures between 160/98 and 240/150 mm Hg. For those patients, systolic blood pressure decreased an average of 30.7 mm Hg and diastolic blood pressure reduced an average of 19 mm Hg. Some patients reported nausea, fatigue, and sore throat. The researchers concluded that the drug was a useful and strong agent in some patients with severe as well as mild hypertension.

A Cochrane database was considered to investigate the dose-related effects of reserpine on blood pressure, heart rate, and side-effects. Medical databases including Central, EMBASE, and MEDLINE were reviewed. The study selected only randomized, controlled trials (RCTs) for review that compared reserpine monotherapy to placebo or no treatment in patients with primary hypertension. Four RCTs were found to meet their criteria. None of the trials reported any adverse effects. The authors concluded that reserpine was effective in reducing systolic blood pressure to the same degree as other antihypertensive drugs; however, they could not make definite conclusions regarding the dose response pattern because of the small number of trials. They suggested that more RCTs were needed to assess the effects of reserpine on blood pressure and to determine the dose-related safety profile before the drug could be widely recommended as a primary antihypertensive drug. Reserpine is also one of the few antihypertensive drugs that have been shown to produce a drop in mortality in RCTs (Vakil, 2015:221).

Other medical use

Rauwolfia has been studied for the treatment of mental diseases, including schizophrenia and bipolar disorder, epilepsy and seizures, and insomnia and sleep problems. A study found Rauwolfia to be effective in the treatment of anxiety. All forms of Rauwolfia were used in that study, including reserpine, alseroxylon, and the whole root, and all gave the same results in the control of overt in patients. Rauwolfia has been studied as a treatment for autistic children between the ages of 3.5 and 9 years. Another study found it to be effective in treatment of delirium tremens in alcohol - addicted patients. The researchers in that study observed a significant decrease in agitation, excitement, and accidental hallucination.

Another study showed that Rauwolfia treated migraine headaches effectively, with an

improvement in quality of life and a decrease in headache. Rauwolfia is also used to treat angina pectoris in patients with coronary artery disease, decrease in angina symptoms and a prolonged therapeutic effect. Half of the patients in that study undergone tests to develop normal electrocardiograms. In another study, Rauwolfia was studied to examine its benefits in improving pruritic and psychogenic dermatosis. It has also been reported to improve psoriatic outbreaks (Lobay, 2015:43).

Side-effects and toxicity

Side effects of reserpine include lethargy, psychiatric depression, hypotension, nausea, vomiting, abdominal cramping, gastric ulceration, nightmares, bradycardia, sore throat, bronchospasm, skin rash, itching, galactorrhea, breast enlargement, sexual dysfunction in 1 case (Yarnell, 2001:43). The most common side effect in all patients was nasal congestion, occurring in 5% to 15% of all patients. After several months of use, mental depression can occur and may continue. In extremely large doses, Parkinson symptoms, extrapyramidal reactions playing a role in motor control and also seizure can occur. Allergic reactions including asthma are rare. Adequate doses of reserpine that produce decreased blood pressure will not cause reserpine-induced gastric ulcerations. Reserpine causes a slight edema in some patients. Possible interactions with other drugs include cardiac glycosides, ephedra, alcohol, antipsychotic drugs, barbiturates, digoxin, diuretics, ephedrine, levodopa, monamine oxidase inhibitors, propranolol, stimulant drugs, and tricyclic antidepressants. Rauwolfia may react to the following laboratory tests, including tests for corticosteroids, bilirubin, catecholamines, gastric acidity, norepinephrine, prolactin, thyroxine, and vanillylmandelic acid.

From 1959 to 1960, 151 cases of toxicity were reported in the United States from consuming Rauwolfia, and only 4% of these cases were in adults. Nausea, vomiting, hypotension, and coma have been described by patients. Also symptoms of bradycardia and facial itching were reported. Depression is most common with doses of reserpine of greater than 0.5 mg per day and was significantly decreased in a daily dose of less than 0.25 mg of reserpine. Between 1962 and 1965, 225 reports of accidental consumption were reported in the United States. Three cases were reported of children between the ages of 30 months and 4 years who were exposed to reserpine in doses above 25 mg. All cases were resolved. It seems that there is no association between reserpine and

cancer. No increased risk of birth defects has been shown in female humans who consumed reserpine at any time during their pregnancy. No mutagenic, genotoxic, or recombinogenic effects of reserpine have been demonstrated (Lobay, 2015:42).

**Rauwolfia and breast cancer**

The use of Rauwolfia and reserpine products was sharply declined in the late 1960s and early 1970s as its relationship to breast cancer was observed in 3 case studies (Weiss,2001:36). A re-evaluation of the main studies showed that those conclusions were wrong. Because patients with cardiovascular disease were excluded as possible controls in the comparison. The next researches showed that no increase in the rate of breast cancer occurred in those patients using Rauwolfia . The study compared 257 women with breast cancer with 257 women that had no breast cancer. They were matched for age, date of admission, and race. The probability ratio of developing breast cancer was 1:1 when comparing those who used Rauwolfia products with those who did not. When 101 women with cardiovascular disease were excluded from the control group, the probability ratio increased to 1:2.5. The researchers concluded that the results suggested that exclusion bias played an important role in creating the false association between reserpine and breast cancer. Another study on the incidence of breast cancer in 109 case cases with hypertension before 1973 was conducted. In that study, 109 patients were treated with Rauwolfia products, and 109 patients were treated with other pharmacologic drugs. The relative risk of developing breast cancer was 0.9 to 1.11 when comparing Rauwolfia to the other factors. The researchers concluded that it is unlikely that the use of Rauwolfia increases the risk of breast cancer.

Reserpine has been observed to increase prolactin levels. Prolactin levels were evaluated in 15 females who used reserpine for at least 5 years to 15 females who used a nonreserpine antihypertensive. Mean prolactin levels were 50% higher in the females who consumed reserpine compared to those who did not. The researchers concluded that such an increase in postmenopausal women would likely cause only a small increase in breast cancer, as it was said in epidemiological studies. They also referred that prolactin does not have a role in breast carcinogenesis in humans (Lobay, 2015:43)

Rauwolfia belongs to Apocynaceae family with numerous pharmacological properties and has been used from ancient times in the treatment of some diseases and physical disorders such as hypertension, uterine dysfunction, prostate, Parkinson, epilepsy and mental disorders such as depression, schizophrenia, etc. This plant is useful and effective for the treatment of hypertension in lower doses (less than 500mg of plant root as dried per day). The purified products of alkaloids of this plant are recognized as the extracts of alseroxylon or respine to be used in the treatment of hypertension and its daily use is less than its dried root. We can use this plant with other medicinal herbs reducing blood pressure such as cranberry and Hibiscus tea by increasing the acidity and dilution of blood and valerian and fennel flower by affecting the vasodilation and Echium, Melissa Officinalis and lavender and German chamomile with neural sedative effects and releasing the excess moist via urine. Extracts from the root bark of this plant are enriched with compounds of ß-carboline alkaloid family which is the main constituent of alstonine and is effective on reduction of prostate cancer cells. In some cases, the use of products of the effective matter of this plant showed some side-effects as depression, hypotension, nausea, vomiting, nasal congestion, gastric ulceration, etc. Also, it has interference with some chemical drugs and their performance dysfunction should also be taken into consideration.

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