REVIEW ARTICLE

Pharmacobotanical and pharmacological evaluation of ayurvedic crude drug: *Rauwolfia serpentina* (Apocynaceae)

Saveena Chauhan[1], Amrinder Kaur[1], R. K. Pareek[2]

[1]Department of Ayurveda, School of Pharmaceutical Sciences, Lovely Professional University, Punjab, India,
[2]Department of Basic Principle, Ayujyoti Ayurvedic Medical College, Sirsa, Haryana, India

Abstract

Rauwolfia serpentina has been used since pre-vedic period for the treatment of snake bite (*sarpadansh*), insect stings, hypertension (Rakta Capa Vriddhi), insomnia (*anidra*), psychological disorders (*manovikar*), gastrointestinal disorders (*Amashay gata roga*), epilepsy (*apasmar*), wounds (*vrana*), fever (*jwara*), and schizophrenia (*unmada*). It is a large glabrous herb or shrub, belonging to family Apocynaceae, and found in the Assam, Pegu, Himalayas, Java, Tennasserim, Deccan, Peninsula, Bihar, and the Malay Peninsula. It is a source of many phytoconstituents including alkaloids, carbohydrates, flavonoids, glycosides, phlobatannins, phenols, resins, saponins sterols, tannins, and terpenes. The main alkaloid of *R. serpentina* is reserpine. It exerts antihypertensive property by depleting the catecholamine which is the main action of the plant. Besides, many studies have been describing multidimensional pharmacological activities of the *R. serpentina*. Hence, the present review describes ancient to modern approach based on pharmacobotanical and pharmacological studies of *R. serpentina*.

Key words: Apocynaceae, hypertension, *Rauwolfia serpentina*, reserpine

INTRODUCTION

Rauwolfia serpentina (Linn.) Benth. Ex Kurz is a glabrous herb or shrub, belonging to family Apocynaceae. The genus name was selected in honor of Dr. Leonhard Rauwolf, a 16th century German botanist, physician, and explorer. The root of *R. serpentina* has been used in India from centuries, especially in hypertension.[1] The drug is also reported for sedative and hypnotic properties.[2] The plant is found in the tropical Himalayas in lowers Hills of Himachal Pradesh, Uttaranchal, Jammu and Kashmir, and at moderate altitude in Sikkim, North Bihar, Patna, Uttar Pradesh, Bhagalpur, Bengal, Konkan, Assam, Burma, Sri Lanka, Andaman, Pegu, Tenasserim, and Deccan Peninsula along with the Ghats of Travancore and Ceylon, Java, and Malay Penisula.[3] Mostly, it is found at 4000 ft height of the sea level in moist jungle and shaded areas. Cultivation of Rauwolfia is started in different areas of India as Dehradun, Lucknow, Jammu, and Indore.[3]

R. serpentina has been used since pre-Vedic period for the treatment of snake bite (*sarpadansh*), insect stings, hypertension (*Rakta Capa Vriddhi*),[4] insomnia (*anidra*), psychological disorders (*manovikar*), gastrointestinal disorders (*amashaygata roga*), epilepsy (*apasmar*), wounds (*vrana*), fever (*jwara*), and schizophrenia (*unmada*).[5] It has been very well described and used by the ancestors of Ayurveda. Acharya Charaka[6] described it as Nakuli, ingredient of vachadi yoga which is used for the treatment of poisoning. Whereas, Sushruta[7] (600 BC) has been included it in Aparajita Gana and Eksara Gana known to treat the mental disorders and rat poisoning, respectively. Vrindamadhav[8] described its use in the treatment of gastroenteritis (V*isuchika*). In Dhanvantari Nighantu,[9] it is described as *Nakuli* with other synonyms such as sugandha and katushna and also reported in the treatment of rat poisoning. Bhavprakasha[10] described it as a type of rasna, synonyms, and description of *R. serpentina*.

Address for correspondence:
Amrinder Kaur,Department of Ayurveda, School of Pharmaceutical Sciences, Lovely Professional University, Phagwara - 144 411, Punjab, India.
Phone: +91-7307552903.
E mail: Amrinder.kaur@lpu.co.in

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In Siddha system of medicine, *R. serpentina* roots are also used to treat hypertension associated cerebral pain, wooziness, amenorrhea, and oligomenorrhea. In Unani system, *R. serpentina* is used as a nervine tonic (Musakkin-e-Asab), sedative and hypnotic (Musakkin-wo-Munawwim), diuretic (Mudir), and anesthetic (Mukhaddir).[11]

VARIOUS VERNACULAR NAME AND SYNONYMS OF *R. SERPENTINA*

Every plant has been identified by their vernacular name throughout the world. These names are mandatory for the ethnobotanical study of a specific tribe. These names are generally based on the appearance, shape, size, habit, habitat, smell, taste, color, utility, therapeutic uses, and other distinguish characteristics of the plants. The vernacular names and synonyms of the *R. serpentina* are mentioned in Table 1.

AYURVEDIC PROPERTIES

Rasa (taste) - Tikta (bitter)[9] and Katu (pungent)[12]

Guna (property) - Ruksha (dry)[12] and Laghu (light)[12]

Virya (potency) - Ushna (hot)[9]

Vipaka (metabolism) - Katu (pungent)[13]

Prabhava (specific action) - Nidrajanan (sedative)[13] and Kaphavatahar[14]

DESCRIPTION OF *R. SERPENTINA*

Morphology of Plant

The drug consists of dried roots of *R. serpentina*[12] (syn. *Ophioxylon serpentinum* Linn.),[15] family Apocynaceae. It is a glabrous herb or shrub of about 1–2 ft in height. Leaves are in whorls 3–4, rarely opposite, ecliptic-lanceolate, or obovate acute or acuminate. They are light green to dark green in color and soft to touch. Flowers are in many flowered cymes.[15] Corolla is salver-shaped, tube cylindrical, white, or finged with red. Fruits are drupes, pea-sized, purple-black when ripe, seeds ovoid.[Figure 1][16] Roots pieces are about 8–15 cm long and 0.5–2 cm in thickness subcylindrical, curved, stout, and thick and rarely branched, externally grayish - yellow to brown with irregular longitudinal

Table 1: Synonyms and vernacular names of *R. serpentina*

Language	Names
Sanskrit	Nakuli,[6] Sarpagandha,[7] Sugandha,[9] Bhogigandhika,[9] Sarpasugandha,[9] Cheeritpatrika,[9] Vishmardini,[9] Mahasugandha,[9] Chhtraki,[9] Suvaha,[9] Sarpakshi,[9] Nakuleshtah,[9] Sursa,[10] Nagasugandha,[10] Bhujangi,[10] Sarpaangi,[10] Vishnashini,[10] Ishwari,[35] Raktapatrika,[35] Ahibhuka,[35] Swarasa,[35] Sarpadini,[35] Naganadha,[35] Vyalgandha,[35] Chandrika,[36] Dhavalavitapa,[36] Gandhanakuli,[37] Chandramarah,[12] Mukta[16] Dhavalvipata,[13]
Hindi	Nakulikanda,[3] Naii,[3] Harkaii Chandra,[3] Chandmarvaa,[9] Chota chand,[10] Nakulkanda,[10] Rasnabheda,[10] Dhavalabaruaa,[12] Chhotaa chaand,[15] Chandrabhaga[15]
English	Serpentina root,[35] Rauvolfia root,[15] Serpentine root[15]
Bengali	Chandra,[10] Gandharasna,[10] Nakuli,[10] Chandara,[35] Chaandar,[12] Chhota chand,[13] Chandar[17]
Bihar and Orissa	Dhan-marna or Dhan-barua,[3] Dhanbarua,[10] Dhavalbarua,[10] Sanochado,[10] Sanochada,[17] Dhanmarva,[38] Chandamarva,[38] Isargaj[38]
Marathi	Amelpodi,[10] Aakayi,[10] Mungusabel,[37] Naaee,[37] Saapand,[37] Adkai,[12] Sayasan,[37] Chandra,[15] Adkaee[38]
Banaras	Dhavalbarua[38]
Bombay	Harkai,[3] Chandra[3]
Telugu	Patalagani,[10] Patala garuda,[35] Paatalagaani,[13] Sarpagandhi,[15] Patalagandhi[17]
Tamil	Chivan melpodi,[3] Covannamilpori,[3] Civan amalpodi,[35] Sarppaganti,[12] Sivan amelpodi,[15] Chivan amelpodi[17]
Malyalam	Chivan avelpori,[3] Civan amalpodi,[35] Amalpori,[12] Chuvannavilpori,[17] Chivana avalapori[17]
Marvadi	Harkaya,[17] Harki[17]
Tulu	Patala-garudada-beru[3]
Gujrati	Amelpodi[13]
Gwalior	Naya[3]
Kannada	Sutranabhi,[10] Sutranaabhu,[12] Sutranavi,[13] Patalagaruda,[15] Sarpagandhi[17]
Farasi	Chhotachanda[10]

R. serpentine: Rauwolfia serpentina

fissures.[12] On breaking, it is circular with centripetal lines [Figure 2].[14]

Microscopy of Root

The transverse section of Rauwolfia root having outermost multilayered stratified cork composed of alternate bands of 5–10 rows of a small suberized cells and 2–5 rows of big-sized lignified cells, phelloderm is parenchymatous embedded with starch grains and small-sized twin prismatic crystals of calcium oxalate,[17] phloem is narrow, parenchymatous, traversed with medullary rays, latex cells, calcium oxalate crystals, and starch grains,[12] cambium ring is distinct, xylem is lignified, composed of few small-sized isolated or radially arranged xylem vessels, tracheids, and fibers alternating with uni- or multi-serate medullary rays, and parenchymatous cells are pitted and embedded with starch grains.[17]

Powder Characteristics of Root

Powder is coarse to fine, yellowish-brown, free-flowing, odor slight, and bitter in taste and characterized by stratified cork cells 8–10 layers, phalloderm cells 10–12 layers in which spherical, simple to compound starch grains, calcium oxalate prisms, and clusters are present.[17] Vessels with simple perforation, occasionally tailed, lignified tracheids, and xylem fibers are present which are irregular in shape, occur singly or in small groups, walls are lignified, tips occasionally forked or truncated, wood parenchyma cells are filled with calcium oxalate crystals and starch grains, whereas, stone cells and phloem fibers are absent.[12]

Figure 1: Sarpagandha whole plant

Figure 2: Sarpagandha root

Chemical Constituents

R. serpentina is a rich source of different varieties of chemical constituents. Alkaloids identified in Rauwolfia include ajmalicine, reserpine, serpentinine,[12] ajmaline, ajmalimine, deserpidine, indobidine, reserpiline, rescinnamine, rescinnamidine, serpentine, and yohimbine. The main alkaloid of *R. serpentina* is reserpine. It exerts antihypertensive property by depleting the catecholamine. Rescinnamine has the same activity like reserpine; however, it inhibits angiotensin-converting enzyme (ACE) that catalysis conversion of angiotensin I, resulting in a decrease of plasma angiotensin II. Ajmaline possesses antiarrhythmic effect by blocking the sodium channel. Serpentine has antipsychotic property because it inhibits type II topoisomerase. Yohimbine is selective alpha-adrenergic antagonist in blood vessels for the treatment of erectile dysfunction. High concentration of phenols *R. serpentina* reveals significant anti-diabetic and hypolipidemic properties, and it can also

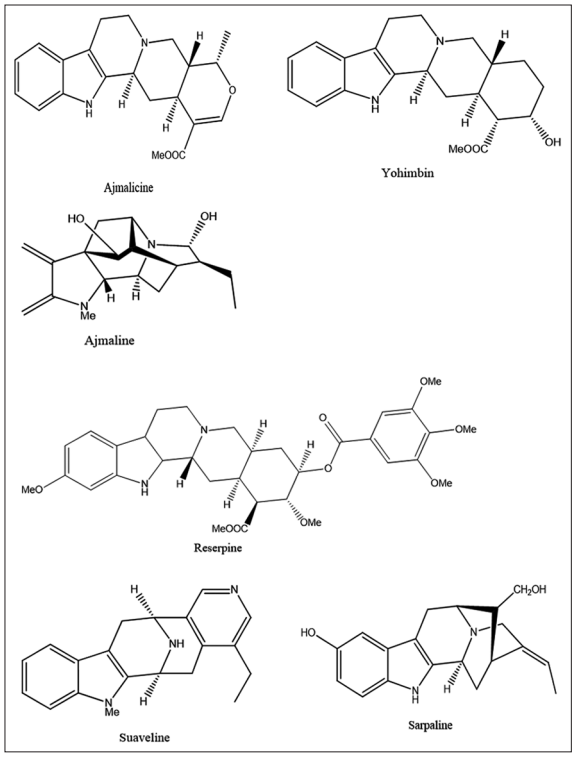

Figure 3: Chemical structures of main constituents of *Rauwolfia serpentina*

be used as antimicrobial agent. Flavonoids of *R. serpentina* help preventing the oxidative cell damage and having anticancer, anti-inflammatory, and antioxidant property.[18] The presence of saponins is responsible for the hemolytic activity and cholesterol binding property.[19] *R. serpentina* is also rich in macro- and micro-nutrients which supports its therapeutic properties, i.e., calcium (Ca), phosphorus (P), potassium (K), magnesium (Mg), sodium (Na), iron (Fe), and zinc (Zn) [Figure 3].[14]

VARIETIES OF *R. SERPENTINA*

Rauwolfia tetraphylla is also widely supplied as Sarpagandha.[16] Its actions are quite similar to *R. serpentina.* It is reported that *Rauwolfia* has about 26 different species such as *Rauwolfia densiflora* (contains sclerenchyma), *Rauwolfia tetraphylla* (has uniform cork, abundant sclereids of fibats but devoid of resinnumine), *Rauwolfia vomitoria* (having very larry vessels), *Rauwolfia conescence, Rauwolfia beddomei, Rauvolfia caffra, Rauwolfia cumminsfi, Rauwolfia obscura, Rauwolfia rosea, Rauwolfia mambasiana, Rauwolfia volkensii, Rauwolfia nitida,* and *Rauwolfia oreogition*. All varieties of *Rauwolfia serpentine* contain reserpine.[19]

In Vitro Studies

In vitro studies based on *R. serpentina* summarized in Table 2 and compiled are as follows:

Antioxidant Activity

Nair *et al.* investigated the antioxidant effect of *R. serpentina*. Methanolic extract of leaves of five species of *Rauwolfia* (*R. beddomei, R. micrantha, R. serpentina, R. tetraphylla,* and *R. densiflora*) was used for evaluating total antioxidant capacity, 1,1-diphenyl-2-picryl hydrazyl (DPPH) radical scavenging activity, reducing power and superoxide anion scavenging activity, and determination of tocopherols, phenolics, flavonoids, carotenoids, ascorbic acid, and pigment composition. *R. serpentina* exhibits the highest total phenolic content, DPPH radical scavenging activity, and also highest pigment composition of Vitamin E content among the five species. Whereas, *R. tetraphylla* had highest flavonoidal content, concentration of β carotene, lycopene, and other nutrient composition, and least amount was found in *R. beddomei*.[20]

Rathi *et al.* used ethanolic root extract of *R. serpentine* for combating the oxidation stress, free radicals using ferric

Table 2: *In vitro* pharmacological activity of *R. serpentina*

***R. serpentina* part used**	**Extract**	**Method**	**Dose**	**References**
Antioxidant activity				
Leaves	Methanolic	DPPH assay	100 µg/ml	Nair *et al.*
Roots	Ethanolic	FRAP method	50–5000 µg	Rathi *et al.*
Antihypertension activity				
Leaves	Aqueous	HHL method	25 µl	Ranjini *et al.*
Antivenom activity				
Whole plant	Ethanolic	-	0.14 mg	Rajashree *et al.*
Whole plant	Aqueous	-	10.99 mg	James *et al.*

R. serpentine: Rauwolfia serpentine, DPPH: 1,1-diphenyl-2-picryl hydrazyl, FRAP: Ferric reducing ability of plasma or plants, HHL: Hippuryl-histidyl-leucine

Table 3: *In vitro* antibacterial activity of *R. serpentina*

***R. serpentina* part used**	**Extract**	**Microorganism**	**Method**	**Dose**	**References**
Roots	Ethanolic	*Klebsiella pneumoniae, Pseudomonas aeruginosa, Salmonella typhimurium, Bacillus subtilis*, and *Staphylococcus*	Agar well diffusion	100 µl	Rathi *et al.*
Roots	Methanolic	*Staphylococcus aureus, Escherichia coli*, and *Proteus vulgaris*	Agar well-diffusion	100 µl	Negi *et al.*
Roots and leaves	Methanolic	*Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Bacillus subtilis*, and *Klebsiella pneumonia*	Disk diffusion	50 µl/ml	Murthy *et al.*
Roots and leaves	Chloroform			100 µl/ml	

R. serpentine: Rauwolfia serpentine

reducing ability of plasma or plants method. A significant effect of extract was found for the activity.[21]

Antibacterial Activity

Following antibacterial activity has been given in Table 3.

Rathi *et al.* explored the antibacterial activity of *R. serpentina*. Ethanolic extract of root was evaluated using well-diffusion method. Two Gram-positive (*Bacillus subtilis* and *Staphylococcus*) and three Gram-negative bacteria (*Klebsiella pneumoniae, Pseudomonas aeruginosa,* and *Salmonella typhimurium)* were used for the activity of which only three bacteria *Klebsiella pneumonia, Staphylococcus,* and *B. subtilis* bacteria are found susceptible.[21]

Negi *et al.* studied the antibacterial activity of methanolic extract of roots (MREt) of *R. serpentina.* Antibacterial activity was evaluated using agar well-diffusion method against Gram-positive and Gram-negative bacteria for the determination of minimum inhibitory concentration (MIC) and the diameter of zone of inhibition (ZOI). The study revealed that *Staphylococcus aureus* shows a highest ZOI (13 mm) with lowest MIC (625 µg) and *Escherichia coli* possess the highest MIC (10 mg), whereas *Proteus vulgaris* was observed resistant to tested extracts up to 10 mg. Hence, *R. serpentina* exhibited strong antibacterial activity.[22]

Murthy *et al.* used methanolic and chloroform extracts of leaf and root of *R. serpentina* for antibacterial activity. The activity was assessed against *S. aureus, E. coli, P. aeruginosa, B. subtilis,* and *K. pneumonia* by disk diffusion method. 50 µl/ml concentrations of leaf and root chloroform extracts showed no ZOI against *S. aureus* and *B. subtilis*. Maximum zone inhibition was observed 15.0 mm and 15.5 mm against *E. coli* for leaf and root extract, respectively. 100 µl/ml concentration showed maximum zone inhibition against all test organisms for both leaf and root extract. All the bacteria were more susceptible to methanolic extract than chloroform.[23]

Antihypertension Activity

Ranjini *et al*. have studied the effect of aqueous extract of *R. serpentina* leaves along with the *Allium sativum* cloves on sheep kidney and lung ACE. Hippuryl-Hiatdyl-Leucine method was used to measure the activity, and hippuric acid release was measured by spectrophotometric analysis at

Table 4: *In vivo* pharmacological activity of *R. serpentina*

R. serpentina **part used**	**Extract**	**Animal**	**Method**	**Dose**	**References**
Hypolipidemic activity					
Roots	Powder	Rabbits	-	30 mg/kg	Shamim *et al.*
Hepatoprotective activity					
Rhizome	Aqueous ethanolic	Albino rats	Paracetamol-induced hepatic damage	425 mg/kg	Gupta *et al.*
Rhizome	Methanolic	Albino rats	CCl4-induced hepatotoxicity model	400 mg/kg	Gupta *et al.*
Hyperglycemic activity					
Roots	Methanolic	Mice	Alloxan-induced diabetic mice	60 mg/kg	Azmi *et al.*
Antidiabetic activity					
Roots	Methanolic	Mice	Alloxan-induced type-1 diabetic mice	10, 30, 60 mg/kg	Azmi *et al.*
Anti-diarrheal activity					
Leaves	Methanolic	Mice	Castor oil-induced diarrhea in mice	100, 200 and 400 mg/kg	Ezeigbo *et al.*
Antivenom activity					
Whole plant	Ethanolic	Patients	-	0.14 mg	Rajashree *et al.*
Whole plant	Aqueous		-	10.99 mg	James *et al.*

R. serpentine: Rauwolfia serpentine

228 nm. The significant anti-hypertensive effect was found in the study.[24]

Antivenom Activity

Rajashree *et al*. reported antivenom activity of the ethanolic extract of the whole plant of *R. serpentina* by neutralizing the toxic effect of *Naja naja* venom. About 0.14 mg of *R. serpentina* plant extract was able to completely neutralize the lethal activity of 2LD50 of *N. naja* venom.[25]

James *et al.* explore the venom neutralizing potential of the aqueous extract of *R. serpentina* by procoagulant, direct, and indirect hemolytic activities. In it, *R. serpentina* plant extract was effectively neutralize all the toxic effects induced by the *Daboia russelli* venom.[26]

In Vivo Studies

In vivo studies of different pharmacological activities based on *R. serpentina* summarized in Table 4 and compiled are as follows:

Hypolipidemic activity

Shamim *et al.* investigated the hypolipidemic activity of root powder of *R. serpentina* when administered to rabbits orally for 12 days. The blood was collected from each group on 1st, 4th, 8th, and 12th day to estimate the serum triglyceride (TG), total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), alanine aminotransferase (ALT), and lactate dehydrogenase, respectively. The test revealed the significant hypolipidemic activity.[27]

Hepatoprotective Activity

Gupta *et al.* investigated the hepatoprotective activity of aqueous ethanolic extract (AET) of the root of *R. serpentina* against paracetamol-induced hepatic damage in rat. The AET has reversal effect on the level of liver glutathione, Na+ K+-ATPase activity, serum marker enzyme, serum bilirubin and thiobarbituric acid, liver glutathione peroxide, glutathione-S-transferase, glutathione reductase, superoxide dismutase, catalase, and glycogen. Hepatoprotective activity was observed due to oxidant effect and normalization of impaired membrane function activity.[28]

Gupta *et al.* investigated the free radical scavenging activity of MREt of *R. serpentina* using CCl_4-induced hepatotoxicity model in albino rats. The extract significantly exhibits free radical scavenging activity by showing an increased level of glutathione peroxide, glutathione-S-transferase, glutathione reductase, superoxide dismutase, catalase, and glutathione and decreased level of lipid peroxidation. The MREt shown prominent antioxidant activity and CCl_4-intoxicated liver recovery.[29]

Hyperglycemic Activity

Azmi *et al.* investigated the effect of MREt of *R. serpentina* on hyperglycemic, hematinic, and antioxidative dysfunctioning with alloxan-induced diabetic mice model for 14 days. Mice are divided into normal, diabetic, treated test, and positive and negative control groups. Considerable decrease was observed on blood glucose level by improving various other mechanisms. MREt restores the liver functions by recovering the protein concentration and normalizing the level of ALT, alkaline phosphatase, and aspartate aminotransferase in test mice.[30]

Antidiabetic Activity

Azmi *et al.* studied the atherogenic dyslipidemia, arteriosclerosis, and glycosylation index of MREt of *R. serpentina* in alloxan-induced type-1 diabetic mice for 14 days. 42 mice were divided into diabetic control, negative, positive, and normal control with three test dose groups. After 14 days of respective treatments, fasting blood glucose, insulin, hemoglobin (Hb), glycosylated HbA1c, TG, TC, LDL-C, very LDL-C, and HDL-C levels were determined with other parameters. A significant reduction in glycosylation, atherogenic, arteriosclerosis, and non-HDL-C was observed. The obtained results highlighting therapeutic potential of MREt in lowering the risk of atherogenic dyslipidemia, arteriosclerosis and glycosylation in alloxane-induced diabetic mice.[31]

Antidiarrheal Activity

Ezeigbo *et al.* evaluated the antidiarrheal property of methanolic extract of leaves of *R. serpentina* in castor oil-induced diarrhea in mice. The dose of 100, 200, and 400 mg kg of extract was administered to the mice. The dose-dependent reduction in intestinal weight and fluids volume was observed which are responsible for antidiarrheal effect of *R. serpentina.*[32]

Antivenom Activity

Rajashree *et al.* reported antivenom activity of the ethanolic extract of *R. serpentina*. Theakston and Reid 1983 method was used for the determination of median lethal dose (LD50) of *N. naja* venom. The plant extract significantly reduced the lethal effect of the *N. naja* venom. About 0.14 mg of *R. serpentina* plant extract was sufficient to neutralize the lethal effect of 2LD50 of *N. naja* venom.[25]

James *et al.* explored the venom neutralizing potential of the aqueous *R. serpentina* extract in mice. In this study, the venom lethality dose of LD of *D. russelli* venom was found to be 0.628 µg/g which effectively neutralized by 10.99 mg/3LD of *R. serpentina* plant extract. The LD of *R. serpentina* plant

extract was >2000 mg/kg. These findings confirmed that *R. serpentina* plant extract possesses some compounds which inhibit the toxins present in *D. russelli* venom.[26]

CLINICAL STUDIES

Antihypertensive Activity

Alka *et al.* evaluated antihypertensive activity of polyherbal compound M - Sarpagandha Mishran on 41 patients of essential hypertension without any comorbid illness. The patients were administered M - Sarpagandha Mishran for 8 weeks and blood pressure was monitored at 2nd, 4th, 6th, and 8th week. Changes in diastolic, systolic, and mean arterial blood pressure were analyzed. A significant fall in blood pressure was found in all the patients.[33]

Coronary Artery Disease

Lewis *et al.* reported the therapeutic spectrum of *R. serpentina* in angina syndrome in accordance with double-blind technique. Fifteen patients of coronary artery disease and angina pectoris were administered the alternatively with alseroxylon fraction of *R. serpentina* and placebo. Alseroxylon revealed prolonged therapeutic effect.[34]

CONCLUSION

The extensive literature survey revealed that *R. serpentina* is being used since pre-Vedic period to treat various ailments including hypertension, insomnia, psychological disorders, gastric disorders, epilepsy, wounds, fever, and schizophrenia. Recent studies also suggest a role of its various constituents for the wide array pharmacological and therapeutic properties. However, detail phytochemical, pharmacological, and clinical studies are required to validate the effect of *R. serpentina* and its constituent.

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