MS.ID-IJPBS-2770
International Journal of Pharmacy and Biological Sciences-IJPBS™ (2025) 15 (2): 144-152
Online ISSN: 2230-7605, Print ISSN: 2321-3272
Review Article | Pharmaceutical Sciences | OA Journal | MCI Approved | Index Copernicus

A Review on *Rauwolfia serpentiana*

V. Asha Jyothi* and S. Jyothirmai Bai

Sarojini Naidu Vanitha Pharmacy Mahavidyalaya, Tarnaka, Hyderabad, India.

Received: 26 Jan 2025 / Accepted: 20 Mar 2025/ Published online: 01 April 2025
***Corresponding Author Email:** ashajyothivadlapudi@gmail.com

Abstract

Many age-old and highly popular plants are well-studied for their medicinal properties, Rauwolfia Serpentina is one such plant. It belongs to the family *Apocynaceae*. It is commonly known as Indian snakeroot or devil pepper It is widely used in Ayurveda and homeopathy. Its roots were traditionally used to treat snakebites, fevers, and insect stings. In the present article, *Rauwolfia Serpentina's* updated research is documented.

Keywords

Rauwolfia Serpentina, Indian snakeroot, Devil pepper, Rauwolfia, Sarpagandha.

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INTRODUCTION

Rauwolfia Serpentina is an important medicinal plant of tropical and subtropical India. Use of Rauwolfia was mentioned in ancient literature of Ayurveda (Charaka Samhita).[1] Rauwolfia serpentina, commonly known as Indian snakeroot or devil pepper, is a flowering under-shrub native to the Indian subcontinent and East Asia. It has spear-shaped leaves (7–10 cm), white-violet flowers that bloom in August and September, and a branched root system. Widely used in Ayurveda and homeopathy, it thrives in acidic to neutral soils.

The plant grows in various Indian states including J&K, Himachal Pradesh, Uttarakhand, Kerala, Tamil Nadu, and across Northeast India, and is also reported in China, Southeast Asia, and other continents. It flourishes in hot, humid climates with monsoon rainfall, growing well in both sun and partial shade, especially in tropical to subtropical regions with temperatures ranging from 10–30°C. The Deccan Plateau is considered particularly favourable for its cultivation.[2]

Rauwolfia, commonly known as devil peppers belongs to the family Apocynaceae has recorded as native to tropical areas of the world with about 110 species of smaller to medium-large sized shrubs/trees. The ethnopharmacologial studies were attempted to prove the medicinal values of several species of Rauwolfia by many researchers. Although, there is poor exploration on information on the account on ethnobotany, phytochemistry and pharmacological values of various species of Rauwolfia.[3]

Figure 1: Sarpagandha whole plant.

Figure-2: Indian snakeroot's leaves and fruits (Rauvolfia serpentina).[9]

HISTORY

Rauwolfia serpentina commonly known as Sarpaghanda, is a medicinal shrub historically used in Indian medicine for over 4,000 years. First referenced by ancient physician Sushruta, its roots were traditionally used to treat snakebites, fevers, and insect stings. It also appears in classical texts like the *Charaka Samhita*. Clinically, it has been used to treat hypertension and is recognized in Ayurveda, Siddha, Unani, and Western medicine. Native to India and parts of Southeast Asia (Bangladesh, Bhutan, Malaysia, Myanmar, Sri Lanka), it grows in moist deciduous forests, especially in the Himalayan foothills, Western Ghats, and Andaman Islands at elevations of 1300–1400 m.[4]

Rauwolfia was included in Hindu manuscripts from 1000 BCE. Sarpagandha was most widely used in India as uterine stimulant, to treat snake bites, insect bites, malaria, dysentery.[5]

Rauwolfia appeared in Ayurvedic Medicine as Sarpagandha which means snake smell and was used to treat snake bites.[6]

CLASSIFICATION

S.NO	KINGDOM	PLANTAE
1.	Clade	Tracheophyte
2.	Clade	Angiosperms
3.	Clade	Eudicots
4.	Clade	Asterids
5.	Order	Gentianales
6.	Family	Apocynaceae
8.	Genus	Rauvolfia
9.	Species	R. serpentina

Table-1: Scientific Classification of Rauwolfia serpentina.

PHARMACOGNOSY ASPECTS

Language	Regional Names
Sanskrit	Vanya Sarpagandha, Sarpanasini
Hindi	Barachandrika, Chandrabhaga
Kannada	Doddachandrike, Naalkele Sarpagandha
English	Wild Snake Root, Devil Pepper, Still Tree
Malayalam	Pampumkolli, Kattamalpori
Telugu	Papataku
Bengali	Bar Chandrika, Gandhanakuli
Oriya	Patalagarudi
Tamil	Pampukaalaachchedi

Table-2: Vernacular names of Rauwolfia serpentina.[7]

Macroscopic Characteristics of Rauwolfia Serpentina

Feature	Description
Root	Long, cylindrical, slightly twisted; 0.5–1.5 cm thick; greyish-brown to pale brown externally; shows transverse wrinkles and longitudinal fissures. Strong, characteristic odour; bitter and acrid taste
Stem	Erect, up to 60 cm tall; branched; green or purplish in color.
Leaves	Simple, in whorls of 3; lanceolate to elliptic; 7–17 cm long, 3–6 cm broad; petiolate; dark green and glabrous on the surface.
Inflorescence	Cymose, terminal or axillary clusters.
Flowers	Small, pink to violet; five-lobed corolla; funnel-shaped.
Fruits	Drupe, ovoid, purplish-black when ripe; often paired.
Latex	Absent.

Table-3: Description of Macroscopic features of parts of Rauwolfia serpentina.[8]

Microscopical Characters of Rauwolfia Serpentina

Anatomical Feature	Description
Cork (Periderm)	Stratified cork with alternating layers: 8–12 layers of smaller, suberized, unlignified cells and remaining layers of larger, lignified cells, giving a spongy and friable exterior.
Phelloderm	Composed of several rows of parenchymatous cells, some filled with starch grains and brown resin masses.
Secondary Cortex	Several rows of tangentially elongated to isodiametric parenchymatous cells containing starch grains and brown resin masses.
Secondary Phloem	Narrow zone consisting of sieve cells, companion cells, and parenchymatous cells containing starch grains, rosette and prismatic crystals of calcium oxalate, and occasionally brown resin masses.
Cambium	Indistinct, narrow, dark, and wavering layer between phloem and xylem.
Secondary Xylem	Comprises vessels, tracheids, xylem parenchyma, and wood fibres traversed by xylem rays; shows one or more annual rings with a dense core of wood at the center.
Medullary Rays	Well-developed, lignified, 1–5 cells wide; uniseriate rays are more prominent; cells filled with starch grains and calcium oxalate prisms.
Starch Grains	Mostly simple, but compound granules also occur with 2 to 4 components; individual granules spherical, about 5 to 15 µm in diameter, with well-marked hilum
Calcium Oxalate Crystals	Present as rosette and prismatic crystals within parenchymatous cells of phloem and medullary rays.
Powder Microscopy	Brownish to reddish-grey powder with slight odor and bitter taste; characterized by spherical, simple, semi-compound and compound starch grains; rosette and prismatic crystals of calcium oxalate; brown resin masses; uniseriate medullary rays; elongated cork cells; pitted vessels with simple perforation; lignified and pitted tracheids; lignified xylem fibers occurring singly or in small groups; parenchymatous cells containing starch grains and brown resin masses.

Table-4: Description of Microscopic features of Rauwolfia serpentina.[8]

Material	Parameter	Standard Value
Root powder	Foreign Matter	Not more than 1.00 % w/w
	Total Ash	Not more than 10.00 % w/w
	Acid insoluble	Not more than 1.00 % w/w
	Alcohol soluble Extractive	Not less than 5.00 % w/w
	Water soluble extractive	Not less than 10.00 % w/w
	Moisture Content (at 105'C)	Not more than 10.00 % w/w

Table-5: Standard values for different parameters of root powder of Rauwolfia serpentina.[8]

PHYTOCHEMISTRY

Rauvolfia contains various phytochemicals such as alkaloids, flavonoids, glycosides, tannins, steroids, phytosterols, and fatty acids. The most significant are indole alkaloids, derived from tryptophan, making up over 50% of the plant's alkaloid content. These compounds share a common nitrogen-containing heterocyclic ring structure. Alkaloid concentrations vary, ranging from 0.7% to 3.3% of the plant's dry weight, with the highest levels found in regenerated roots.[9]

Alkaloids

Alkaloids are nitrogen-containing organic compounds, mainly functioning as defence metabolites against herbivores and pathogens. Isolated or synthetic alkaloids are used medicinally for their analgesic, antispasmodic, and antibacterial properties. Alkaloids from Rauwolfia serpentina

roots affect the central nervous system and help lower blood pressure more effectively than some other agents. The roots contain 0.7–3.0% total alkaloids, including about 0.1% reserpine, a key indole alkaloid. Due to its medicinal value, root biomass has economic significance. Based on structure, alkaloids are classified as weak basic indole alkaloids, intermediate bases, and strong anhydronium bases. Identified alkaloids in Rauwolfia include ajmaline, ajmalicine, reserpine, serpentine, yohimbine, and others.[10]

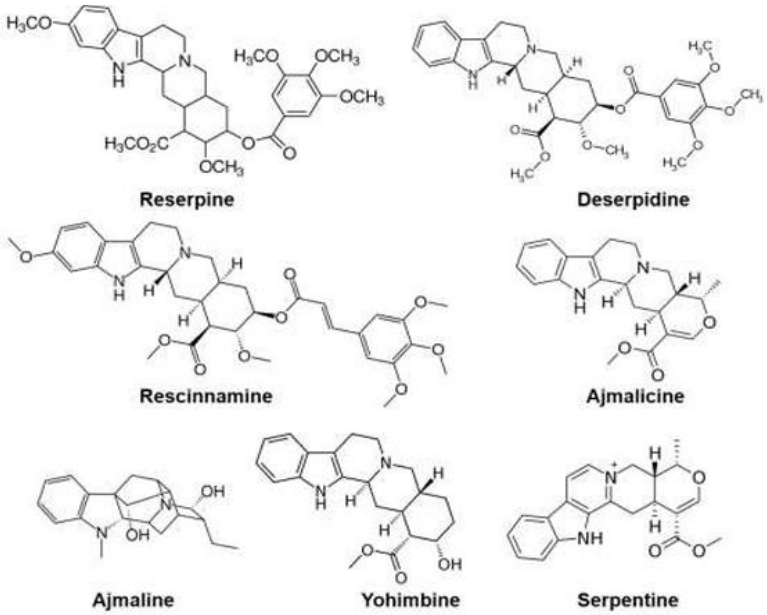

Figure 3 Chemical structures of different alkaloids present in Rauvolfia serpentina. [9]

Reserpine

It is derived from roots of Rauwolfia and is pure crystalline alkaloid which is isolated in 1952.It is most important alkaloid which is mainly used as a tranquillizer. Reserpine is 3,4,5-trimethyl benzoic acid ester of reserpic acid, an indole derivative of 18-hydroxy yohimbine type. Due to its depressant action on Central nervous system (CNS) and peripheral nervous system it also shows antihypertensive action. It also shows other actions like sedation, controls heart rate, cardiac contraction etc.[10]

Ajmaline

Ajmaline, a compound first isolated from Rauwolfia serpentina roots by Salimuzzaman Siddiqui in 1931, was named in honor of Unani medicine expert Hakim Ajmal Khan. It is a class I antiarrhythmic agent, primarily acting as a sodium channel blocker, and is widely used in diagnosing Brugada Syndrome—a hereditary cardiac disorder. Given intravenously, it acts quickly, making it ideal for diagnostic use in the "Ajmaline Test." Ajmaline also stimulates respiration and intestinal movement, with effects on blood pressure similar to serpentine. Antiarrhythmic agents like ajmaline are categorized based on their action on sodium, calcium, or potassium channels, or beta-adrenergic receptors.[11]

Serpentine

Serpentine, a type II topoisomerase inhibitor, possesses antipsychotic effects. The enzyme peroxidase (PER) catalyzes the oxidation of ajmalicine into serpentine by acting on bisindole alkaloids localized within the vacuole.[11]

Yohimbine

Yohimbine is a well-known alkaloid used to treat erectile dysfunction by acting as a selective alpha-adrenergic blocker. It enhances blood flow to the penis by dilating blood vessels. It has also been studied as a potential treatment for diabetes in models with 2A-adrenergic receptor gene variations. Additionally, yohimbine lowers blood pressure, relaxes smooth muscles, and dilates pupils by increasing certain body chemicals.[9]

Phenols

Phenols, common secondary metabolites in herbs and trees, are known for their toxic effects on pests and pathogens. *R. serpentina* contains a high level of polyphenols, contributing to its antidiabetic, hypolipidemic, antimicrobial, and expectorant properties. These compounds also make it useful as an emulsifying agent in medicine.[12]

Tannins

The antioxidant effect of tannins is attributed to gallic acid and diagallic acid. Their astringent nature promotes healing of wounds and inflamed mucous membranes, supporting the traditional use of *R.*

serpentina in treating various ailments in southeastern India. [12]

Saponins

Saponins, found in over 70 plant families, are glycosides of triterpenes and sterols. They are known for forming foam in water, hemolytic activity, cholesterol binding, and bitterness. Saponins can coagulate red blood cells. The high saponin content in *R. serpentina* supports its traditional use in stopping bleeding and treating wounds.[11]

Flavonoids

Flavonoids are powerful water-soluble antioxidants and free radical scavengers that prevent oxidative cell damage and exhibit strong anticancer properties. In the intestinal tract, they help reduce the risk of heart disease. As antioxidants, they also provide anti-inflammatory effects, making them valuable in herbal medicine for treating various diseases. [11]

PHARMACOLOGY

R. serpentina roots are rich in pharmacologically active alkaloids, particularly in the oleoresin fraction. These alkaloids are used to treat cardiovascular conditions like hypertension, arrhythmia, and high blood pressure, as well as psychiatric and neurological disorders including schizophrenia, anxiety, epilepsy, and insomnia. The plant also shows potential against breast cancer and leukaemia

Anti-Hypertensive Activity

Anti-hypertensive activity indicates to reduce elevated blood pressure. They work through various mechanisms to decrease cardiac output, reduce vascular resistance, or alter fluid balance. The goal is to achieve and maintain a target blood pressure, typically less than 140/90 mmHg for most adults. Ranjini et al. evaluated the antihypertensive effect of aqueous *R. serpentina* leaf extract combined with Allium sativum (garlic) cloves on sheep kidney and lung ACE. Using the Hippuryl-Histidyl-Leucine assay and spectrophotometry at 228 nm, they observed a significant reduction in ACE activity, indicating strong antihypertensive potential.[13]

Antioxidant Activity

Antioxidants are molecules that can help your body fight off harmful free radicals, which have been linked to health conditions like diabetes and cancer. They're found in many plant-based foods. Nair et al. assessed the antioxidant potential of methanolic leaf extracts from five *Rauwolfia* species. *R. serpentina* showed the highest total phenolic content, DPPH radical scavenging activity, and vitamin E (tocopherol) levels. R. tetraphylla had the highest flavonoid content, β-carotene, lycopene, and overall nutrient composition, while R. beddomei showed the lowest values across all parameters. [13]

Antivenom Activity

Antivenom, also known as antivenin, venom antiserum, and antivenom immunoglobulin, is a specific treatment for envenomation. It is composed of antibodies and used to treat certain venomous bites and stings. Antivenoms are recommended only if there is significant toxicity or a high risk of toxicity. The specific antivenom needed depends on the species involved. Rajashree et al.: Ethanolic extract of R. serpentina (0.14 mg) completely neutralized the lethal effect of $2LD_{50}$ of Naja naja (cobra) venom.

James et al.: Aqueous extract of R. serpentina effectively countered the procoagulant and hemolytic effects of Daboia russelli (Russell's viper) venom. [13]

Antidiarrheal Activity

Diarrhoea can be defined as alteration in the normal bowel movement, characterized by a situation in which daily stools exceeds 300 gm and contains 60 – 95 % water by frequent, loose bowel movements. It reduces bowel motility, increase water absorption, or bind to toxins in the gastrointestinal tract.[24] Ezeigbo et al. investigated the antidiarrheal effect of methanolic R. serpentina leaf extract in mice with castor oil-induced diarrhoea. Doses of 100, 200, and 400 mg/kg showed a dose-dependent reduction in intestinal weight and fluid volume, indicating effective antidiarrheal properties. [13]

Hepatoprotective activity

Hepatoprotective activity refers to the ability of a chemical substance to prevent damage to the liver. It is the opposite of hepatotoxicity. It plays an important role in the maintenance of internal environment through its multiple and diverse function. It plays a central role in detoxification and excretion of many endogenous and exogenous compounds[25]. A drug having a beneficial effect on the liver is known as a hepatoprotective drug. Gupta et al. studied the protective effects of *R. serpentina* root extracts against liver damage in rats. The aqueous ethanolic extract (AET) reversed paracetamol-induced liver toxicity by restoring liver enzymes, glutathione levels, antioxidant enzymes, and membrane function. In a separate study, the methanolic root extract (MREt) showed strong antioxidant activity in a CCl_4-induced liver damage model, marked by increased antioxidant enzyme levels and reduced lipid peroxidation, promoting liver recovery. [13]

Hypolipidemic activity

Hypolipidemic activity is that it reduces the level of lipids and lipoproteins (lipid-protein complexes) in the blood. Lipoproteins bind cholesterol and can accumulate in blood vessels. High levels of

specific lipoproteins, namely, low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL), have been associated with an elevated risk of certain forms of cardiovascular disease, including coronary artery disease, heart attack, and stroke. Shamim et al. studied the effect of R. serpentina root powder on lipid levels in rabbits over 12 days. Blood samples taken on days 1, 4, 8, and 12 showed significant reductions in triglycerides, total cholesterol, and LDL-C, along with improved HDL-C levels, indicating notable hypolipidemic activity.[13]

Prostate Cancer

Prostate cancer is a growth of cells that starts in the prostate. The prostate is a small gland that helps make semen. It's found just below the bladder. The prostate is part of the male reproductive system. Prostate cancer is a leading cause of cancer-related deaths in men, with limited success from conventional treatments like chemotherapy and radiotherapy. Natural products, particularly from medicinal plants, offer promising alternatives. R. serpentina has long been used in traditional medicine for various conditions. Its root bark contains β-carboline alkaloids, mainly alstonine, which has shown tumor-suppressing effects in mice. Extracts of the plant demonstrated anti-prostate cancer activity in both in vitro and in vivo models, likely by influencing DNA damage response and cell cycle regulation pathways.[6]

Antimicrobial Activity

Antimicrobial activity refers to the ability of an agent to kill microorganisms or stop their growth. Antimicrobial targets can range from preventing the growth of certain types of microorganisms such as bacteria and fungi to inactivating microorganisms, to either reduce the levels and types present or to completely eliminate all microorganisms to reach a sterile level. Antibacterial activity was determined by measuring the diameter of the zone of inhibition for each strain, controls were included that comprised pure solvents instead of the extract[26].

Dry Fruit Extracts: Petroleum ether, chloroform, and ethyl acetate extracts showed broad-spectrum antibacterial activity against eight bacterial species using agar diffusion.[14]

Miscellaneous Uses

Leaf extract used for treating cholera, diarrhoea, dysentery, eye diseases, and fever. Mixed with castor oil for stubborn ailments; bark decoction used for skin diseases and parasite removal. Roots used to stimulate uterine contractions during difficult childbirth.[14]

Clinical Studies

Antihypertensive Activity

Anti-hypertensive activity is to reduce elevated blood pressure. They work through various mechanisms to decrease cardiac output, reduce vascular resistance, or alter fluid balance. The goal is to achieve and maintain a target blood pressure, typically less than 140/90 mmHg for most adults. Alka et al. assessed the effect of the polyherbal formulation M-Sarpagandha Mishran in 41 patients with essential hypertension over 8 weeks. Blood pressure measurements at regular intervals showed a significant reduction in systolic, diastolic, and mean arterial pressure in all patients.[13]

Coronary Artery Disease

Coronary artery disease (CAD), also called coronary heart disease (CHD), or ischemic heart disease (IHD), is a type of heart disease involving the reduction of blood flow to the cardiac muscle due to a build-up of atheromatous plaque in the arteries of the heart. Lewis et al. evaluated the effect of *R. serpentina* in angina using a double-blind study. Fifteen patients with coronary artery disease received either a placebo or the alseroxylon fraction of R. serpentina. The alseroxylon-treated group showed a prolonged therapeutic benefit, indicating its potential in managing angina symptoms.[13]

MEDICINAL VALUE

Rauwolfia serpentina has long been used in the Indian subcontinent in Ayurvedic and Unani medicine to treat various conditions. In Ayurveda, its roots are used for managing hypertension, insomnia, anxiety, mental disorders, gastrointestinal issues, and epilepsy. Siddha medicine also employs it for treating menstrual disorders and hypertension-related symptoms. The plant is listed in multiple national formularies of Ayurvedic and Unani medicine and is commonly used in traditional drug formulations.[15]

Folk Remedies and Traditional Uses

The root of Rauwolfia serpentina is traditionally used to treat conditions such as insanity, hysteria, hypertension, epilepsy, insomnia, bowel pain, dysentery, hypochondria, and nervous system disorders. Applied topically, the bruised root relieves insect bites. A root decoction is used to stimulate uterine contractions and aid childbirth. Combined with Andrographis paniculata, ginger, and black salt, it treats fevers; with Aristolochia indica, it is used for cholera and colic. Leaf juice is applied to the eyes to treat corneal opacities.[15]

Sarpagandha is a cardiodepressant with hypnotic and sedative properties, traditionally used to treat hypertension, insomnia, sexual aggression, vertigo, and schizophrenia. In classical Indian medicine, it is mentioned in texts like Sushruta Samhita as part of

the Aparajit Gana for mental disorders and the Ekasar Gana for treating poisoning, including Musaka Visha (rat poisoning) and Visuchika (cholera). Notably, Sarpagandha became the world's first recognized antihypertensive drug in modern medicine.[6]

MESELLENEOUS:

CATEGORY	DESCRIPTION	REFERENCE
Toxicity	Depression and Mental Health Effects: High doses of R. serpentina can lead to depression and mental health issues, including suicidal tendencies.[16]	Kline NS, Use of Reserpine in a Neuropsychiatric hospital, Journal of American Medical Association, 1954, 156(6): 479–481
	Gastrointestinal Issues: Increased gastrointestinal motility and secretion may aggravate peptic ulcers or ulcerative colitis.	Drugs.com Disease Interactions, 2023
	Veterinary Toxicity: A case of R. serpentina toxicity in a dog showed symptoms like hypotension, bradycardia, and gastrointestinal ulceration.[17]	Good JM, Mandell DC, Rauwolfia serpentina toxicity in a dog, Journal of Veterinary Emergency Critical Care, 2008, 18(6): 654–658.
Allergy	Hypersensitivity Reactions: Some individuals may experience allergic reactions; however, specific studies detailing these reactions are limited.[18]	Hazarika I, Biradar N, Chandy V, Current Insight to the Uses of Rauwolfia: A Review,Journal of Pharmacognosy, 2016, 3(3): 1–4
Drug interactions	Levodopa: Concurrent use may reduce the effectiveness of levodopa in Parkinson's treatment.	Drugs.com Interaction Report, 2023.
	Antipsychotic Medications: Combining with antipsychotics like olanzapine may increase side effects such as dizziness and lightheadedness.	Drugs.com Interaction Report, 2023.
	Arginine: Combined use may enhance vasodilation, potentially leading to hypotension	Drugs.com Interaction Report, 2023.

Table-6: Details on Toxicity, Allergy and Drug interaction possible by Rauwolfia serpentina

MARKET VALUE SUMMARY TABLE

S.NO	Plant Part	Activity	Extract Type	Model	Standard Drug	Dose	Parameters Measured	Mechanism of Action	Stats P value	Author(s) & Year
1.	Root	Antihypertensive & Antihyperlipidemic	Aqueous-Methanolic	Albino Rats	Atenolol	100 & 200 mg/kg	Blood pressure, lipid profile, liver and kidney histology	Vasodilation via catechol-Amine depletion.	p < 0.05	Syed Muhammad Ali Shah et al., 2020. [19]
2.	Whole plant	Anxiolytic	Aqueous	Rats (immobilization stress)	Not specified	30 mg/kg	Behavioral tests, SOD, CAT, corticosterone, leptin, glucose levels	Modulation of HPA axis and antioxidant enzyme levels.	p < 0.05	Erum Shireen et al., 2020. [20]
3.	Root	Hypoglycemic & Hypolipidemic	Methanolic	Alloxan-induced diabetic rats	Not specified	Not specified	Blood glucose, lipid profile	Improvement in glucose and lipid homeo-stasis.	p < 0.05	Qureshi S, Nawaz A, Udani S, Azmi B, 2009. [21]

4.	Root	Hyperlipidemic activity	Aqueous	Rabbits	Not specified	30 mg/kg	Blood glucose, lipid profile	enhance the activity of lipase enzyme that hydrolyzes Trigly-cerides.	p<0.0001	Shamim A. Qureshi & Shamsa K Udani,2009. [22]
5.	Root powder	Hyperglycemic, Haematinic and Antioxidant activity	Methanolic	Wistar male albino mice	Glibenclamide	60mg/kg	Percent glycemic and body weight change	Improvement in glucose and lipid homeo-stasis.	p<0.0001	Muhammad Bilal Azmi & Shamim A. Qureshi, 2013. [23]

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