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RAUWOLFIA SERPENTINA: A REVIEW ON BIOLOGICAL AND MEDICINAL PROPERTIES

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Abstract: Rauwolfia serpentina is a secure and reliable hypertension remedy. In the 1940s, the plant was utilized by several doctors in India. In the 1950s, it was used all over the world, including in the US and Canada. When negative side effects like as depression and cancer were linked to it, its popularity declined. The scientific literature on the application of Rauwolfia in the management of hypertension is reviewed by this author. The author examines the pharmacology, chemistry, and botany of the plant and offers a well-researched and verified mechanism of action for the active components. The author critically examines the plant's toxicity, carcinogenicity, and unpleasant side effects while focusing on the plant's potential for treating high blood pressure. In order to reduce the likelihood of depression, the author disputes the link between the plant and carcinogenicity and emphasizes the significance of patient screening and appropriate dosage. In conclusion, he suggests that individuals who meet the criteria for hypertension should be treated with low dosage Rauwolfia (LDR). The plant offers medical professionals a secure and efficient supplement to medications for the management of hypertension.

Keywords: Rauwolfia, reserpine, tetraphylla, caffra, alkaloids, serpentina, hypertension.

INTRODUCTION

The evergreen plant Rauwolfia (Rauwolfia serpentina) belongs to the Apocynaceae family, which includes dogbane.1. The Rauwolfia genus has more than 100 species that are indigenous to tropical and subtropical regions around the globe, encompassing Europe, Africa, Asia, Australia, Central America, and South America.2 The wet, deciduous woods of southeast Asia, which include Bangladesh, Sri Lanka, India, Burma, and Malaysia, are home to Rauwolfia serpentina.3. The plant typically reaches a height of 60 to 90

cm, with pale green leaves measuring 3.5 to 5.0 cm in width and 7 to 10 cm in length. The leaves are found in whorls of three to five and have an elliptical or lanceolate form. The plant produces a large number of spherical, glossy fruits that are about 0.5 cm in diameter and are either black or purple. It also features little white or pink flowers. The plant has a noticeable soft taproot that is between 1.2 and 2.5 cm in diameter and between 30 and 50 cm in length.



HISTORY AND FOLK USE

For ages, R serpentina was utilized in Indian traditional medicine to cure a broad range of illnesses, such as diarrhea, feverish conditions, malaria, bites from snakes and insects, and stomach discomfort. It was also employed as a febrifuge, uterine stimulant, and insanity cure. The plant, also known as sarpagandha and chandrika, was first recorded in Indian literature as early as 1000 BC. The German physician Dr. Leonhard Rauwolf, who traveled throughout India in the 16th century and researched flora, is honored by the name Rauwolfia. The study of serpentina was chosen because of its long, tapering roots, which resemble snakes. Rauwolfia was reputedly used by Indian political leader Mahatma Gandhi to prepare a tea, which he drank in the evening to help unwind after a demanding, overstimulating day.

Rustom Jal Vakil, an Indian physician, is credited for bringing Rauwolfia to Western medicine. He gathered information on Rauwolfia patients treated during a ten-year period, from 1939 to 1949. His groundbreaking study on the antihypertensive qualities of R serpentina was published in the British Medical Journal in 1949.8 He gave a thorough explanation of the outcomes of his treatment of fifty patients with hypertension with Rauwolfia root. The outcomes were noteworthy and important. In 1949, Rauwolfia was being used to treat hypertension by almost 90% of Indian doctors. Over a hundred scholarly publications were published worldwide following Vakil's first study.8

CHEMICAL COMPOSITION

Numerous phytochemicals, such as alcohols, sugars, glycosides, fatty acids, flavonoids, phytosterols, oleoresins, steroids, tannins, and alkaloids, are found in rauwolfia. More than fifty of the plant's indole alkaloids have been identified, making them the most significant alkaloids present in the plant.9. Tryptophan is the source of a class of nitrogenous chemicals known as indole alkaloids. They have one

nitrogen molecule and a common heterocyclic ring structure with five and six carbons. Although indole alkaloids are present in all sections of the plant, including the stem and leaves, the root bark has the largest concentration of these compounds.11 Ajmalidine, ajmaline, ajmalinine, aricine, canescine, coryanthine, deserpidine, isoajmaline, isoserine, isoserpiline, lankanescine, neoajmaline, papaverine, raubasine, raucaffricine, rauhimbine, rauwolfinine, recanescine, rescinnamine, reserpiline, reserpine, sarpagine, serpentine, serpentinine, thebaine, yohimbine, and yohimbinine are among the identified indole and indole alkaloids.12, 13

Alkaloids' precise concentration varies. According to one research, the plant's dry weight yield of total alkaloids varied from 0.8% to 1.3%.12 According to a different research, the total alkaloids production ranged from 0.7% to 3.0% of the root content.4 In regenerated roots, the highest amount of alkaloid concentration found was 3.3%.Thirteen Rauwolfia vomitoria and Rauwolfia caffra from Africa, as well as Rauwolfia heterophylla and Rauwolfia tetraphylla from Central and South America, are other species of the Rauwolfia genus that have been used in place of R serpentina. Woodson et al. (2012) discovered that species belonging to the same genus might serve as viable substitutes for R serpentina due to their varying levels of indole and indole alkaloids.



Reserpine

One of the plant's main alkaloids is serpine. It has been shown that the root has the highest reserpine concentration whereas the stems and leaves have lesser levels.11 It has been thought by scientists to be the most common indole alkaloid in the plant, although many tests have cast doubt on that claim. It has been shown that the plant's reserpine content ranges from 0.03% to 0.14% of its dry weight.14 The same study discovered that various plants had varying amounts of reserpine in their roots, ranging from 0.038% to 0.14%. In one investigation, each gram of root had 33 mg of reserpine out of 496 mg of total alkaloids.10 Reserpine concentration in Rauwolfia roots was found to be 0.955 mg/g in another investigation.15 Biochemical therapeutic activities of other plant alkaloids, such as canescine, deserpidine, recanescine, and rescinnamine, have also been found.

PHARMACOLOGY

The most extensively researched alkaloid identified in R serpentina is resperpine. Sen and Bose's 1931 Indian Medical Journal article was the first contemporary study on reserpine.7 Robert Wallace Wiggins

was the first to isolate and use it in 1950. The first comprehensive report on reserpine's chemistry and pharmacology was released in 1952 by CIBA Labs (now Novartis) in Switzerland.7 In 1952, the medication Serpasil was introduced, which contained isolated reserpine and was used to treat tachycardia, hypertension, and thyrotoxicosis.7 One category of indole alkaloid is reserpine. It is a powder that is white to yellow in color and turns dark in the presence of light. It has no smell, is soluble in alcohol only slightly, insoluble in water, and freely soluble in acetic acid.

MECHANISM OF ACTION

Reserpine's mode of action has been well studied and recorded. Reserpine attaches itself to protein receptors in the organelle membranes of certain secretory vesicles of presynaptic neurons known as vesicular monamine transporters (VMATs).19, 20 Reserpine inhibits the binding of intracellular neurotransmitters to VMAT proteins as well as the uptake of neurotransmitters by secretory vesicles. Reserpine ultimately ensures that little or no neurotransmitters are produced from the presynaptic cell. As a result, the postsynaptic neuron experiences either no or very little nerve impulse propagation. The vesicular transport proteins have two isoforms: VMAT1 and VMAT2. VMAT1 is mostly present in the neuroendocrine cells of the peripheral nervous system, especially in sympathetic neurons, platelets, and the chromaffin granules of the adrenal medulla. The brain, sympathetic nervous system, mast cells, and histamine-containing cells in the pancreas and intestine are the primary locations of VMAT2. Reserpine has a three-fold higher affinity for VMAT2 than it does for VMAT1.22, 23 It binds practically permanently to some VMAT receptors, especially VMAT2, with a high affinity

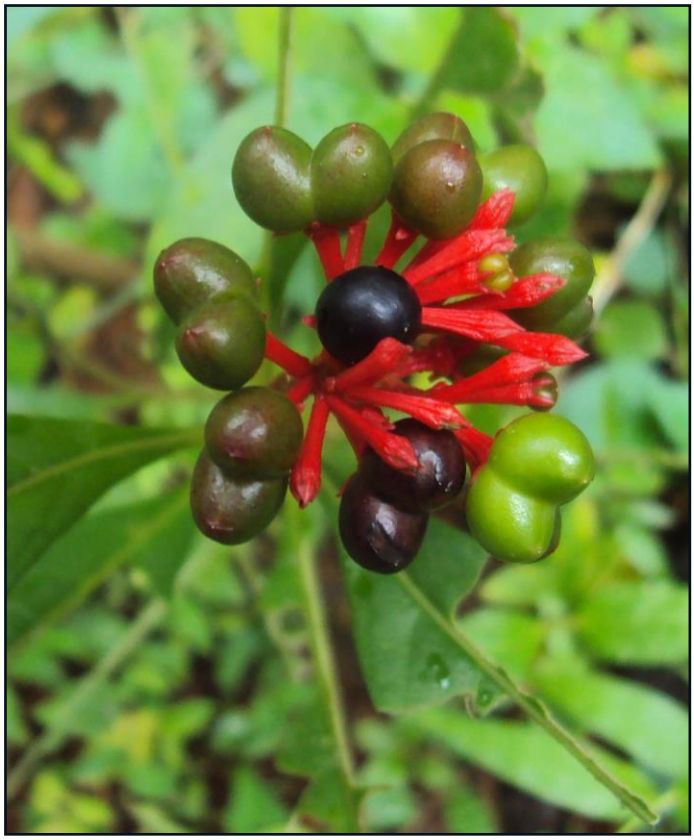
RAUWOLFIA AND HYPERTENSION

Vakil (1949) reported on a trial in which 50 patients receiving Rauwolfia treatment for essential hypertension.26 In that research, systolic blood pressure dropped in 85% of patients and diastolic blood pressure dropped in 81% of patients. Hypertensive individuals had a decrease in blood pressure in 1952, according to Vida in Germany and Austria.26 Of the 50 patients, Arnold and Bach found that 37 of them responded well, with an average reduction in systolic pressure of 30 mm Hg and a diastolic pressure of 15 mm Hg.26 Meissner (1953) stated that Rauwolfia was efficacious in 90% of research participants, resulting in a systolic blood pressure reduction of 15 to 40 mm Hg. 51 hypertensive Swiss workers had a drop in blood pressure in 1953, according to a survey by Loffler in Switzerland.26 Twelve out of fifteen hypertensive patients had decreased blood pressure, according to Goto's 1954 study from Japan.26 Doyle and Smirk in Zealand reported in 1954 that after 4 to 6 hours of dosing, reserpine caused a remarkable drop in blood pressure.26 According to several reports, the most effective hypertension treatment in India during the 1950s was Rauwolfia.26 Ninety percent of doctors nationwide, or over sixty thousand doctors, reportedly utilize it.26 The dried root was shipped to more than 17 nations worldwide, and one company claimed to have sold 94 million pills of it in 1954.2.

OTHER MEDICAL USES

Treatments for mental illnesses such as bipolar disorder and schizophrenia, epilepsy and seizures, insomnia, and sleep issues have all been investigated in relation to rauwolfia. According to one research, Rauwolfia works well for treating anxiety.31 In that study, reserpine, alseroxylon, and the whole root of Rauwolfia were all employed, and they all produced the same outcomes in terms of controlling overt anxiety in patients who were ambulatory.For children with autism, ranging in age from 3.5 to 9 years, rauwolfia has been investigated as a potential therapy.32 It proved to be beneficial in treating delirium tremens in people with alcohol and drug addiction, according to another study.33 In that study, the researchers saw a decline in acute hallucinations, excitation, and agitation. According to one research, rauwolfia efficiently cured migraine headaches, resulting in a marked increase in pain relief and quality of life.34 Another research found a reduction in angina symptoms and a lasting therapeutic benefit when

Rauwolfia was administered to treat angina pectoris in individuals with coronary artery disease.35 Following their participation in the trial, 50% of the patients experienced normal ECGs. Rauwolfia was investigated in another research to see whether it may help with psychogenic and pruritic dermatosis.36 Additionally, it has been believed to help psoriatic breakouts.



SIDE EFFECTS AND TOXICOLOGY

Reserpine side effects include angina-like symptoms, bronchospasm, skin rash, itching, galactorrhea, breast enlargement, sexual dysfunction, hypotension, lethargy, sedation, psychiatric depression, nausea, vomiting, abdominal cramps, gastric ulceration, nightmares, and in one case, withdrawal psychosis. Nasal congestion was the most frequently reported adverse effect among all patients, occurring in 5% to 15% of cases.17 Mental depression may arise and may last for several months after using the product. Convulsions, extrapyramidal responses, and Parkinson-like symptoms can happen at very high dosages. Asthma and other allergic responses to Rauwolfia are uncommon.

RAUWOLFIA AND BREAST CANCER

When three case-controlled studies in the medical literature suggested a possible link between reserpine and rauwolfia and breast cancer, the usage of these medications was drastically cut in the late 1960s and early 1970s.Forty Those results turned out to be incorrect once the original research were reevaluated. Due to their rejection as potential comparison controls, individuals with cardiovascular illness had experienced exclusion bias. Patients who used Rauwolfia or reserpine products did not have a higher incidence of breast cancer, according to further study and analysis that removed exclusion bias.41 In this study, 257 women who had been diagnosed with breast cancer and 257 women who had not were matched with respect to age, date of admission, diagnosis, and race. When those who used Rauwolfia products were compared to those who did not, the chances ratio for getting breast cancer was 1:1. In a another research, the chances ratio

increased to 1:2.5 when 101 women with cardiovascular disease were taken out of the control group. The researchers came to the conclusion that the data pointed to a significant role of exclusion bias in the erroneous correlation between reserpine and breast cancer.

RAUWOLFIA AND DEPRESSION

In an outpatient hypertension clinic in Montreal, the prevalence of depression in patients receiving Rauwolfia and reserpine was investigated between June 1954 and December 1956.44 A total of 296 individuals were watched and compared over the research period; 195 patients used Rauwolfia products either by themselves or in conjunction with other medications, and 101 patients did not use Rauwolfia products at all. Of the 195 individuals who took Rauwolfia products, 134 took reserpine alone, while 61 took either the purified alseroxylon fraction or a whole-root preparation.

CONCLUSIONS

Rauwolfia appears to be a safe and effective therapy for hypertension when taken in relatively low dosages, according to a review of the literature. To treat hypertension, an equivalent dosage of pure Rauwolfia alkaloids—sometimes referred to as alseroxylon extract or pure reserpine—can also be utilized. According to the author's findings, patients who have been deemed to benefit from LDR can be suggested to it without risk. In most circumstances, the daily dosage of Rauwolfia root can be as little as 250 mg, but it should never exceed 500 mg. Purified alkaloid-alseroxylon extract should be taken at a dose of no more than 5 mg per day; in most cases, this is less than 2.5 mg. Less than 500 μg of reserpine should be used daily; in most situations, less than 250 μg. The strength of the tincture should determine an analogous tincture dosage. For example, in a regular dropper, 15 drops would equal 1.0 mL, but in a 1:5 tincture, the dose would be 0.5 mL, or 100 mg of crude root.

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