Rauwolfia vomitoria, R. serpentina

African Snake Root, Indian Snake Root

Traditional Uses

Hypertension and arrhythmia.

Mechanism of Action

Rauwolfia's effects on the heart include decreasing myocardial excitability, inhibiting atrial-ventricular conduction, and extending the refractory period of the heart rhythm.[1]

Much of the medicinal effects of *Rauwolfia serpentina* and *Rauwolfia vomitoria* have been attributed to the hypotensive indole alkaloid reserpine.[2] Additional alkaloids found in *Rauwolfia* roots include the indoles ajmaline, ajmalicine, raubasine, imethylajmaline, methylisoajmaline, hydroxysarpagine, yohimbinic acid, and isorauhimbinic acid.[3] The constituent ajmaline is thought to be antiarrhythmic.[4]

Before the advent of the current pharmaceutical options for hypertension (beta blockers, calcium channel blockers, and angiotensin-converting Inhibitors), reserpine was a mainstay in the management of hypertension. Reserpine acts via the CNS to reduce sympathetic tone, increase parasympathetic activity, and help normalize blood pressure, especially when because of stress and sympathetic nervous responses, as it may partially block adrenaline receptors.[5] Reserpine's ability to block adrenoreception on blood vessels can reduce stress-induced vasoconstriction contributing to hypertension or heart palpitations.

Research suggests that reserpine may deplete peripheral catecholamine stores, contributing to hypotensive effects.[6,7] Reserpine also seems to bind to vesicular monoamine transporters (VMATs) with high affinity, blocking neurotransmitter uptake into the vesicle and ultimately depleting catecholamines from storage vesicles. The actions of reserpine on the VMAT result in an acute catecholamine release, followed by chronic inhibition of catecholamine secretion, as a result of diminished releasable stores of vesicular catecholamine.[8]

Mechanisms involving cellular calcium influx and transport are also involved with the initiation and development of hypertension as a result of constrictive effects on vascular smooth muscle; thus, *Rauwolfia* may elicit vascular relaxation, reducing peripheral resistance and improving blood pressure.[9]

Although *Rauwolfia* can help reduce blood pressure, its effects are more pronounced on the CNS than the peripheral nervous system, through activity at the diencephalon, as reserpine decreases the release and accumulation of noradrenaline.[8] *Rauwolfia* has a mildly sedating effect, making this herb especially indicated for those with concomitant tension, overwork, or poor sleep.

Evidence-Based Research

A review of the few randomized and placebo controlled trials that have been conducted on reserpine in the treatment of hypertension reported that reserpine is an effective tool in managing hypertension but that additional and larger trials are needed.[10] One study that examined 108 elderly patients with II stage hypertensive disease reported that reserpine decreased arterial pressure and peripheral vascular resistance while increasing oxygen saturation in the tissues.[11]

A *Rauwolfia* product called Serpina was given to more than 100 patients for periods of 1 month to 1 year. In the study, a daily dose of one to three Serpina tablets was well tolerated. The product caused sedation and usually improved sleep, and it promoted moderate hypotension, particularly in labile patients with hypertension and tachycardia. It also seemed to have a sympatholytic effect, but did not produce postural hypotension.[12]

A Cochrane meta-analysis of a *Rauwolfia* randomized controlled trial on human hypertension subjects assessed that *Rauwolfia* displayed similar efficacy to first-line antihypertensive drugs, without significant side effects.[10] Much of the medicinal effects have been attributed to the alkaloids reserpine, ajmaline, and ajmalicine.[13]

Safety in Pregnancy and Breastfeeding

Animal studies have shown *R. vomitoria* to have teratogenic effects on rat fetal heart at the higher dosage range.[14] Histological observations of the fetal heart showed marked distortion of the cardiac muscle nuclei and myocardial fibers in the treated groups, particularly those whose mothers received 250 mg/kg of the extracts. These effects were more pronounced in the groups whose mothers received the root extract compared with the control and the groups whose mothers received the leaf extract. Based on these findings, *Rauwolfia* would be best avoided during pregnancy.

General Safety

Rauwolfia has potential side effects of muscle weakness, fatigue, impotence, and depression, so it is not a first-choice therapy for exhausted and lethargic patients. However, *Rauwolfia* is an excellent choice for hypertensive patients with stress, anxiety, insomnia, and muscle tension.

Isolated reserpine use is associated with the so-called extrapyramidal side effects that include dyskinesia and akathisia believed to be a result of depletion of dopamine in the CNS, and the explanation of why the plant is contraindicated in Parkinson's patients.[15]

One confounding factor in evaluating the research on *Rauwolfia* safety involves the widespread use and research on isolated reserpine, which may not equate to the safety of whole plant extracts. Isolated reserpine may deplete dopamine from dopaminergic neurons and be associated with the side effect of depression as well as the therapeutic effects in the treatment of schizophrenia and traditional use in dementia and insanity. Green tea used in tandem with reserpine may modulate some of these effects.[16]

Long-term reserpine therapy is associated with damage to liver and organs, and it is uncertain whether whole *Rauwolfia* extracts carry the same risks. A prudent approach would be to run regular liver function tests and general bloodwork on patients for whom *Rauwolfia* is effective and are to remain on the plant for an extended period. Reserpine may induce damage to hepatocyte cytoplasmic membrane,

nuclear envelope, endoplasmic reticulum, ribosomes, and mitochondria, and green tea extracts have been shown protective and restorative.[16]

A low-probability trend toward breast cancer has been associated with reserpine, whereas this association with whole *Rauwolfia* extracts have not been investigated.[17]

It is best to start off with a small cautious dose of *Rauwolfia* and follow up within 10 days to 2 weeks to make certain the patient tolerates the herb well. In the isolated form of reserpine alone, side effects were frequent, and the drug was abandoned with the advent of other options. Such side effects however are rare when using whole plant extracts, and many practitioners feel the concern in the general medical community over the use *Rauwolfia* is unwarranted and the result of a lack of understanding of how to best use this valuable medicinal plant.

Dosage

A whole extract used in the powdered form may be dosed 50–300 mg daily. Begin with small doses and increase gradually until there is a drop in blood pressure or side effects develop (e.g., nasal congestion, diarrhea, depression).

CNS and cardiovascular effects may be delayed for 2–3 weeks and persist several days to weeks after therapy is discontinued.

This herb has potential for toxicity. Use caution if exceeding up to 600 mg of the powdered whole root per day.

Traditional Uses

Rauwolfia serpentina (Indian Snake Root) is an endangered species and illegal to import. *Rauwolfia vomitoria* (African Snake Root) is widely available and not endangered.

Rauwolfia is an herbaceous plant of Asian and South American tropical forests, and it is in a family known to contain powerful alkaloids and medicinal species. Native to India, *Rauwolfia* has been used as a traditional Ayruvedic medicine for many ailments, including anxiety, headaches, and snakebites and as a general sedative for >1000 years. It is reported that Gandhi regularly drank *Rauwolfia* tea for its calming effect.

Research emerged in the 1930s and 1940s describing the hypotensive effects of *Rauwolfia* and supporting its traditional use as a calming and relaxing agent. A *Rauwolfia*-based medicine for hypertension, Serpasil was released in the 1950s, and several derivatives of this medication remain on the market today.[18] Several reserpine-based medications exist in Russia and are used in the treatment of hypertension.

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