Reversing Hypertension with *Rauwolfia*, *Viscum* and *Piscidia*

Jill Stansbury, ND[a]
Paul Saunders, PhD[b]
David Winston, RH(AHG)[c]
Eugene R. Zampieron, ND[d]

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ABSTRACT

Rauwolfia, Viscum, and *Psicidia* are well known herbs used in the treatment of hypertension. These herbs contain several different bioactive constituents including alkaloids, lectins, rotenones, flavonoids and isoflavones, among others, which research indicates as being cardioprotective, promote vascular health and reduce blood pressure. As the mechanisms of action are different for each herb, due to the varying bioactive compounds present, they can be used alone or in combination for these indications. Patients being treated with the above-described herbs need to be carefully monitored, particularly for interactions with any concomitant antihypertensive medication—and herbal doses individually tailored.

Keywords: Hypertension, Bioactive constituents, *Rauwolfia*, *Viscum*, *Piscidia*

CLINICAL IMPLICATIONS

The use of herbal medicines can be effective in the treatment of hypertension African snake root *(Rauwolfia vomitoria)*, European Mistletoe (*Viscum album)* and Jamaican Dogwood (*Piscidia erythrina)* can normalize blood pressure via different mechanisms, and can synergistically support and tone the cardiovascular system. *Rauwolfia, Viscum* and *Piscidia* (alone or in combination with other herbs) support vascular tone, blood flow and viscosity, stress response, adrenaline and sympathetic nervous tone, and other mechanisms that enhance overall circulatory health and control blood pressure. In some subset of hypertensive patients, herbal medicines can be weaned off totally while patients remain normotensive.

KEY HERBS DISCUSSED

African Snake Root *(Rauwolfia vomitoria)*, European Mistletoe (*Viscum album)* and Jamaican Dogwood (*Piscidia erythrina)*

PRIMARY INDICATIONS

Hypertension

ADJUNCTIVE OR STAND-ALONE TREATMENT

Adjunctive or Stand-Alone

BIOACTIVE CONSTITUENTS

Rauwolfia: Diverse alkaloids including ajmaline, chandrine, deserpidine, reserpine, rescinnamine, sarpagine, serpentinine, and yohimbine

Viscum: Lectins, phenylpropanoids

Piscidia: Isoflavones, rotenoids, piscidin

Rauwolfia whole plant root 200 mg daily containing 300mcg reserpine a day, European Mistletoe up to 2.5 grams daily, Jamaican Dogwood whole plant 50-400 mg a day

[a] Corresponding author: Battle Ground Healing Arts, 408 E Main Street , Battle Ground, WA 98604, USA
[b] Dundas Naturopathic Centre, Dundas L9H 1V6, Canada
[c] David Winston's Center for Herbal Studies, Broadway, NJ 08808, USA
[d] 413 Grassy Hill, Woodbury, CT 06798, USA

CLINICAL IMPLICATIONS (CONTINUED)

SYNERGISTIC HERBAL FORMULA

African Snake Root *(Rauwolfia),* Mistletoe (*Viscum)*, Jamaican Dogwood *(Piscidia)*, Hawthorn *(Crataegus)*, and Motherwort *(Leonorus)*

SIDE EFFECTS (AND CAUTIONS)

This herbal synergistic formula may interact with anti-hypertensive medications in some patients to cause hypotension and bradycardia. While treating patients with the above herbs, it is important to determine any concomitant anti-hypertensive prescriptions, and to closely monitor blood pressure. Because *Rauwolfia* contains reserpine, at high doses it can promote or exacerbate Parkinson's disease. Nasal congestion and diarrhea may occur in patients taking more than 200 mg of *Rauwolfia* daily. While findings are inconclusive, one study found reserpine to cause depression in 10% of the study patients; however, this percentage is not higher than found in the general population. Some researchers cites Reserpine induced depression as a myth.[1,2,4] *Rauwolfia, Viscum* and *Piscidia* are not recommended in pregnancy. At higher doses than 2.5 grams a day, there is some evidence that Viscum is contraindicated in Tuberculosis and Aids.

UNSUBSTANTIATED THEORETICAL CONCERNS

***Rauwolfia*:** There is some theoretical evidence that *Rauwolfia* should not be taken with alcohol, antipsychotics, antidepressants barbiturates, digoxin, monoamine oxidase inhibitors, propranolol, and stimulant drugs.

V*iscum*: There is some theoretical evidence that *Viscum* may decrease effectiveness of immune suppressant drugs.

***Piscidia*:** There is some theoretical evidence this herb should not be taken with central nervous system (CNS) depressant medications.

Editors Note: The first drug studied to be effective in treating depression in a randomized placebo-blind controlled study was reserpine. This study was published in the Lancet in 1955.

DISCUSSION

Hypertension is a very common medical problem commonly treated with prescription antihypertensive drugs;[3, 4] however, these medications are not without side effects.[5-8] Additionally, the patients over time often require increased dosage to control blood pressure and/or additional antihypertensive medications. It is recommended that herbal therapy for hypertension be combined with a healthy lifestyle, low-sodium diet, and reduced stress. Lifestyle modifications and herbal treatments can control blood pressure or be added to an antihypertensive protocol. Some herbs can also support, restore and protect cardiac and vascular health.

RAUWOLFIA AND ITS BIOACTIVE CONSTITUENTS

Rauwolfia (in the *Apocynaceae* family) grows mainly in the tropical forests of Asia and India. The *Apocynaceae* family is rich in alkaloids and other constituents with important medicinal effects. *Rauwolfia* contains a large number of bioactive constituents, though most attention has been directed towards the indole alkaloids. These alkaloids are generally classified as either reserpine-like or yohimbine-like.[9] *R. serpentina* and *R. vomitoria* contain relatively high concentrations of reserpine. *Rauwolfia serpentina* is currently considered an endangered herb; it being replaced with the non-endangered *Rauwolifa vomitoria* in synergistic herbal formulas.

Yohimbine is well known as a selective alpha-adrenergic antagonist in the peripheral blood vessels. Antagonism at these receptors relaxes smooth muscle and lowers blood pressure. Examples of prescription alpha-adrenergic blockers are doxazosin (Cardura) and prazosin (Minipress). Reserpine, on the other hand, acts primarily in the central nervous system at the level of monoamines in the neuronal synapses. Reserpine reduces sympathetic nervous system tone and increases parasympathetic activity via effects on neurotransmittors.

Another principle reserpine-like alkaloid is rescinnamine, which has an antihypertensive effect similar to reserpine.[10] While rescinnamine has a greater hypotensive effect in dogs than reserpine,[11] in humans, it is slightly less potent per gram than reserpine.[12,13] Deserpidine is structurally related to reserpine (11-demethoxyreserpine) and also has anti-hypertensive effects.[14,15] Most clinical trials have used deserpidine in combination with a thiazide drug.[16,17]

Ajmaline (derived from *R. serpentine*) is a class I antiarrhythmic drug that is highly useful in diagnosing Brugada Syndrome (hereditary cardiac disorder), and differentiating between subtypes of patients with this disease. In fact, administration of the *Rauwolfia* alkaloid to patients with this type of arrhythmia is known as the "Ajmaline Test"; EKG results of this test are considered to be the best predictor of patients at risk for sudden death from the condition.[18] Ajmaline is a sodium channel blocker that has a short duration of action when given intravenously, which makes it ideal for diagnostic purposes.[19]

Rauwolfia serpentina

THE MEDICINAL EFFECTS OF *RAUWOLFIA*

Reserpine has been shown to normalize blood pressure, especially in cases of hypertension exacerbated by stress and sympathetic nervous system activity. In fact, prior to the development of beta-blockers, calcium channel blockers, ACE inhibitors, and diuretics, reserpine was a leading therapeutic agent utilized by physicians in the management of hypertension.

Rauwolfia has a mild sedating effect and possible anti-depressant effect; therefore, this herb is especially indicated for those with known concomitant tension or insomnia. However, it is not typically used for exhausted and lethargic patients because it may worsen their fatigue. It is essential to start with a small dose of *Rauwolfia* to determine if the herb is well-tolerated. Due to its significant side effects, the use of isolated alkaloid reserpine was generally abandoned as other antihypertensive medications became available.

Research in the 1930s and 1940s described the hypotensive effects of *Rauwolfia*, and its traditional use as a calming and relaxing agent. A *Rauwolfia*-based medicine for hypertension (Serpasil) was released in the 1950s; several derivatives remain on the market today,[20] and reserpine-based antihypertensive medications are currently used in Russia. A review of randomized, placebo-controlled trials with reserpine concluded that it was an effective tool in the management of hypertension but that additional and larger clinical trials were needed[21].

Rauwolfia reduces peripheral resistance, thereby lowering blood pressure,[22] and decreases arterial pressure and increases tissue oxygen saturation[23]. The isolated *Rauwolfia* component (called Ajmaloon in India, from the Sanskrit name for the plant), has a positive effect on blood pressure through its effect on vascular baroreceptors[24] The reserpine alkaloid may also partially block adrenaline receptors.[25]

THE USE OF *VISCUM*

The *Loranthaceae* family contains several plant genera including *Viscum* or 'Mistletoe'. Several species of *Viscum* are used worldwide as herbal medicines. *Viscum album* contains lectins, phenylpropanoids and flavonoids that inhibit cAMP by inducing phosphodiasterase to break down cAMP. The flavonoids include syringin and conferin which may contract the aorta, while kalopanaxin has a relaxing effect.[26] When used in tandem, they have tonifying effects on vascular muscle tone.

An ethanol extract of *Viscum album* was shown to reduce vascular tension when placed in contact with endothelial tissue. *Viscum* stimulates both the synthesis and release of nitric oxide to enable vasodilation.[27] Nitric oxide is released from the vascular endothelium, and plays a role in local inflammatory processes; it helps to regulate the degree of vasodilation versus vasoconstriction via a mechanism independent of nerve regulation (such as adrenergic innervation).

Viscum album has been used as a blood pressure-regulating agent in Nigeria. Nigerian researchers reported that *Viscum* interfered with calcium ion-driven vascular contraction; both the influx of calcium and mobilization of calcium in intracellular stores were believed to be affected.[28] Researchers in Serbia reported that hydroethanol extracts of *Viscum album* were capable of lowering blood pressure in rats, and that the use of muscarinic receptor blockers diminished or totally abolished the hypotensive effects of *Viscum.* This suggests that *Viscum* may act via muscarinic nerve transmission.[29] Likewise, *Viscum album* has been shown to prevent changes in blood viscosity in a manner that is supportive to maintaining healthy blood pressure.[30] Lectins found in *Viscum* may affect glycoprotein receptors, erythrocytes, lymphocytes and platelets, and contribute to its positive effects on blood viscosity and blood flow.[31]

Besides blood pressure regulation, *Viscum* flavonoids may have other cardio-protective effects; it has been shown to reduce tissue damage by inhibiting platelet activating factor (PAF) response and reducing free intracellular calcium ions[32.] Herbal practitioners usually prescribe *Viscum* as a tincture or tea; few encapsulated products are available on the market. When *Viscum* is used to treat cancer it is prepared by a different extraction method and given by subcutaneous injection.

THE USE OF *PISCIDIA*

The physicians in the early 1900's researched and described *Piscidia's* effects on the cardiovascular system; they stated that *Piscidia* could slow the pulse and briefly increase arterial tension followed by a long reduction in arterial tension.[33] *Piscidia* was sometimes prescribed as a morphine-substitute

to promote restful sleep, because it did not have the numerous side effects associated with morphine.

Piscidia erythrina is a flowering tree in the *Fabaceae* (legume) family, found in Central America, the West Indies and the Caribbean. It is historically used for pain, tension, insomnia, and to control high blood pressure. Its common name is 'Jamaican Dogwood'. The linguistic derivation of *Piscidia* is related to its indigenous historical use as a toxin to stun fish. In fact, the isoflavonoid, sumatrol, and a variety of rotenones are credited with causing fish toxicity and are being investigated as potential chemotherapeutic agents.[34, 35]

Piscidia has powerful effects on the heart, vascular system, respiratory centers and nerve conduction, and is traditionally prescribed in small, doses. Its chemical constituents have not been well-studied; however, it is known to contain the resins, piscidin, jamaicin, and ichthynone. The sum of its chemical constituents are credited with muscle-relaxing effects[36] which could account for its traditional use to treat pain and muscle spasms. Animal studies have also shown an anxiolytic effect that may contribute to its hypotensive actions.[37]

SUMMARY

Rauwolfia, Viscum, and *Psicidia* are well known herbs used in the treatment of hypertension. These herbs contain several different bioactive constituents including alkaloids, lectins, rotenones, flavonoids and isoflavones, among others, which research indicates as being cardioprotective, promote vascular health and reduce blood pressure. As the mechanisms of action are different for each herb, due to the varying bioactive compounds present, they can be used alone or in combination for these indications.

Patients being treated with the above-described herbs need to be carefully monitored, particularly for interactions with any concomitant antihypertensive medication—and herbal doses individually tailored.

DISCLOSURE OF INTERESTS

Dr. Saunders reports personal fees related to employment or seeing patients from CCNM, the Dundas Naturopathic Centre, and from Beaumont Health Systems, Troy Hospital, MI, outside the submitted work. Dr. Winston reports personal fees from Herbalist & Alchemist, Inc, outside the submitted work. Dr. Stansbury and Dr. Zampieron have nothing to disclose.

REVIEW ESSAY

Many nutrients and herbs that have not been the subject of randomized controlled studies are used regularly by clinicians. They have also been used traditionally for hundreds, sometimes thousands of years. Review Essays contain the opinions of professionals and experts in the fields of nutritional and botanical medicine on how to most effectively use herbs and nutrients in clinical practice. The dosages recommended are based on clinical experience. Side effects that are described in "Unsubstantiated Theoretical Concerns" have not been seen in clinical practice or clinical studies but are speculative based on, for example, possible mechanisms of action.

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