

A REVIEW ON: RESERPINE USED IN TREATMENT OF HYPERTENSION

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Abstract- The most frequent modifiable risk factor for death, hypertension is on the rise everywhere. Because it does not manifest until it is very serious, it has become a bigger health concern. Modifying one's lifestyle is the first step, but pharmacological treatment is needed when it becomes difficult to control it. In general, drug therapy consists of diuretic and betablocker medications. The important plant *Rauwolfia serpentina* [L] Kurz ex Benth produces the reserpine alkaloid. As a result of the bioactive indole alkaloids they contain, particularly reserpine, *Rauwolfia* species are significant therapeutic plants. Although reserpine is a potent antihypertensive, its usage in everyday medicine has reduced to the point where it is now unusual. This is predicated in large part on the belief that reserpine induces depression. The primary alkaloid of *Rauwolfia serpentina*, reserpine, is successfully used in therapeutic settings to treat high blood pressure. Reserpine must be taken in much lesser doses to have an antihypertensive effect.

Index Terms- Reserpine, Hypertension, *Rauwolfia*, Blood pressure.

I. INTRODUCTION HYPERTENSION

Chronic disease hypertension (HTN) is a major risk factor for numerous cardiovascular problems. The illness is characterized by chronically elevated blood pressure and clinical lowering blood pressure leads to benefits.^[1] It is a serious health issue that has recently become more prevalent in both emerging and wealthy nations. However, it has contributed increased health burdens.^[2] A number of variables, such as male gender, age, marital status, higher socioeconomic class, lower educational status, cigarette and alcohol consumption, diabetes, kind of activities, and family history of hypertension, all have a direct effect on blood pressure.^[3]

Hypertension Definition

The definition of hypertension is an abnormal increase in diastolic and/or systolic pressure; the condition also causes an increase in mean arterial pressure, which is not typically measured in people. Previously, when evaluating hypertension, the diastolic value was prioritised. However, increases in systolic pressure (also known as "systolic hypertension") are also linked to an increased risk of coronary and cerebrovascular illness (for instance, stroke). Now that we understand this, we can say that it is necessary to note both systolic and diastolic pressure numbers. The newest national policy of the United States.

Types of Hypertension 1. Primary hypertension

- Around 90- 95 percent of cases of high blood pressure are caused by its primary form.
- Is not due to a single, specific cause
- Environmental and genetic factors are possible reasons.

2. Secondary hypertension

- Rare forms of high blood pressure
- Caused by another medical condition or treatment
- Causes include kidney problems (renovascular hypertension), adrenal gland tumors, thyroid disease, and narrowing of the aorta (the main artery that takes blood from the heart to the rest of the body)^[4]

3. Other types of hypertension

Subtypes that fit within the categories of primary or secondary hypertension include: a. Resistant hypertension

- Malignant hypertension
- Isolated hypertension^[5]

Symptoms of Hypertension

- Headache
- Dizziness
- Epistaxis
- Retinopathy
- Nephropathy^[6]

Causes of Hypertension

- Age
- Family history
- Being overweight or obese

- Not being physically active
- Using tobacco
- Too much salt (sodium) in your diet
- Too little potassium in your diet
- Drinking too much alcohol ^[7]

Treatment of Hypertension

1) Nonpharmacological Treatment

- Dietary Salt Restriction
- Weight Loss
- Physical Activity
- Moderate Alcohol Intake- ^[8]

2) Pharmacological treatment

a. Diuretics

Diuretics were once the first line of treatment for mild to moderate hypertension, but the constant development of newer medications and their extensive industry promotion caused physicians to transition away from this practice. Mild hypertension, as well as diuretics of the thiazide type, provide a more effective and less frequent blood pressure decrease comparing the incidence of heart failure and coronary revascularization with additional medicines, such CCB, ACEI, or ARB. The SHEP's data is evidence the value of a low-dose thiazide-type medication is highlighted in a study as beginning treatment for older adults with isolated systolic hypertension patients. Data from clinical trials also show that diuretics are in general, tolerated well.

b. Beta-Blocker

Initially believed to be of clinical significance, these medications reduce cardiac output and cause a lowering of the heart rate, especially in hypertensive patients with tachycardia. The kidney's ability to reabsorb sodium is also improved at the same time as peripheral resistance is slightly raised. In patients with medium or high levels of plasma renin activity, Betablocker's capacity to suppress RAS activity by lessening the release of renin from the kidney's juxtaglomerular cells may contribute to their blood pressure-lowering effects. They gained popularity as a treatment for hypertension over time, and one factor in doctors' acceptance of this drug class was that these agents seemed to be more tolerated than many other medications.

c. Alpha-1 receptor antagonist

Al-1-adrenergic blocking medications lower blood pressure in a manner analogous to that of the majority of other antihypertensive drug groups. In the beginning, for many years, 1- adrenergic antagonists had been thought of as suitable first medications for simple early-stage hypertension. However, recommendations from organizations like the European Society of Hypertension/European Society of Cardiology and the Authors of the JNC 7 no longer recommend using 1-adrenergic antagonists as the first line of treatment for hypertension.

d. TRPV1 antagonists

Momentary Receptor Potential The newest target for the antihypertensive effect is the vanilloid receptor type 1 (VNR1). Anandamide is an endocannabinoid that can act as a depressant and whose synthesis is increased in some pathophysiological conditions. Anandamide's hypotensive effects have been linked to the TRPV1 receptor. Oleamide (cis-9, 10octadecenoamide) is a primary fatty acid amide that developed in sleep-deprived cats and has structural resemblances to anandamide.^[9]

II. RESERPINE

Dogbane, or Apocynaceae, is a family of evergreen shrubs consisting of Rauwolfia (*Rauwolfia serpentina*). The Rauwolfia genus has more than 100 species, all of which are indigenous to tropical and subtropical regions of the world, including Europe, Africa, Asia, Australia, Central America, and South America^[10,11] About 200 alkaloids are present in it, the most significant of which is reserpine, which is found in almost all *R. serpentina* species and can be used as a chemical identifier for the genus.^[12] According to Lopez-Muoz et al. (2004), reserpine, an alkaloid derived from the root of the Rauwolfia Serpentina plant, was first made commercially available in Western medicine in 1952 after being used for millennia in Indian medicine to treat a range of conditions, including schizophrenia. Presently, reserpine is regarded as a second-line treatment^[13] *R. serpentina*, also referred to as Indian snakeroot or Sarpagandha in Sanskrit and Hindi, ^[14,15]

Scientific Classification

- Kingdom: Plantae (plants)
- Subkingdom: Tracheobionta (vascular plants)
- Superdivision: Spermatophyta (seed plants)
- Division: Magnoliophyta (flowering plants)
- Class: Magnoliopsida (dicotyledons)
- Subclass: Asteridae
- Order: Gentianales

- Family: Apocynaceae (dog bane family)
- Genus: Rauwolfia
- Species: serpentina [16]

Chemical structure of Reserpine^[17]

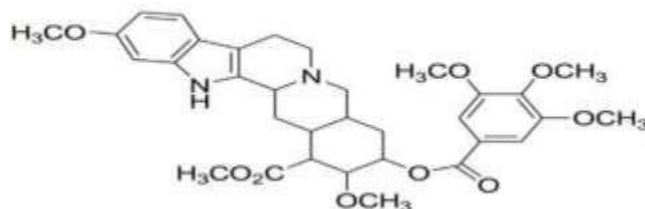


Fig. Structure of reserpine

IUPAC name: - methylester2 α ,11-dimethoxy-3-(3,4,5-Trimethoxybenzoyloxy)-yohimban-1- carboxylic acid

Molecular formula: C₃₃H₄₀N₂O₉ **Molecular weight:** - 608.7 **Melting point:** -264.5 °C

Molecular formula: - C₃₃H₄₀N₂O₉ **Molecular**

Melting point: - 264.5 °C **Boiling point:** - 700.1 °C

Appearance: - Reserpine appears as white, cream, or slightly yellow crystals or crystalline powder. has no smell and a harsh flavor

Solubility: - Freely soluble in glacial acetic acid, methylene chloride, chloroform (about 1 g/6 ml), benzene, and ethyl acetate. Slightly soluble in ether, acetone, methanol, alcohol (1 g/1800 ml), and in aqueous solutions of acetic and citric acids. **Storage:** - Keep in a container that is airtight and chilled.^[18]

Biosynthesis of Reserpine^[19]

Tryptamine and the monoterpene Secologanin produce Glucoalkaloid Strictosidine in the first step of biosynthesis. Then strictosidine enzyme helps in the biosynthesis of Reserpine.

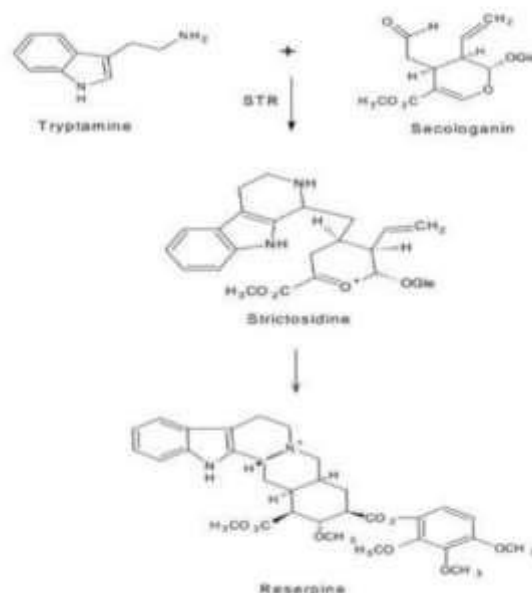


Fig. Biosynthesis of Reserpine

Mechanism of action^[20]

As an adrenergic uptake inhibitor, reserpine serves as a sympatholytic and an antihypertensive drug. Reserpine attaches to the catecholamine storage vesicles that contain dopamine and norepinephrine. Reserpine specifically blocks the adrenergic neurotransmission pathway's VMAT-2 (vesicular monoamine transporter-2) in an irreversible manner. When catecholamine pumps are inhibited, serotonin, norepinephrine, and dopamine cannot enter presynaptic storage vesicles. Cytoplasmic monoamine oxidase will then eliminate them from peripheral and central synapses as a result of this action. Since reserpine is lipid-soluble, it can pass across the blood-brain barrier and reduce nervous system activity. This lowers blood pressure and lowers resistance as well as heart

rate, cardiac output, and resistance. The gastrointestinal tract, the central nervous system, and the cardiovascular system are the key effector areas.

Pharmacology of reserpine ^[21]

The pattern of activity of reserpine is quite intricate. It has also been suggested that it affects the levels of glycogen, acetyl choline, g-amino butyric acid, nucleic acids, and anti-diuretic hormone in addition to the amine concentration in the brain. Reserpine inhibits breathing, promotes peristalsis and myosis, relaxes nictitating membranes, and affects the area of the brain that controls body temperature. The volume and free acidity of gastric output are both increased. In some circumstances, reserpine lowers blood sugar, but the impact is transient. Prothrombin activity is stimulated in certain patients by it. Additionally, reserpine facilitates blood penetration into burn-induced ischemia regions¹. Sedation and a drop in blood pressure are the results. The effects of reserpine when taken orally for hypertension rarely manifest before 3-6 days.

Administration ^[22]

Administration of Reserpine

- **Adults:** -Orally: Begin by taking 0.5 mg once daily, with or without food, for one to two weeks. To maintain, cut back to 0.05 to 0.25 mg each day.
- **Pediatric:** -Not typically advised. When used orally, the recommended starting dose is 20 mcg per day, with a 0.25 mg daily maximum. For psychiatric disorders (not typically used)
- **Orally:** 0.5 mg once daily; however, this dosage may change based on the patient's response to the drug.

> Method of administration of Reserpine ^[23]

Reserpine is available in the form of tablet and injections.

> Hypertension:

• Initial Dosage

Most patients do not get additional antihypertensive medications, and the first dosage is typically 0.5 mg daily for 1 to 2 weeks.

- **Maintenance Dosage** Reduce to 0.1-0.25mg daily for maintenance. Higher dosages should be used with caution as the likelihood of serious mental depression and other side effects may significantly increase. You can take reserpine orally before or after meals. The treating physician's clinical judgement should be used to determine the dosage and length of treatment

Adverse Effects

Common adverse reactions:

- Nasal congestion
- Dizziness
- Drowsiness
- Depression
- Headache Nausea
- Loss of appetite
- Dry mouth • Arrhythmias.

Severe adverse effects:

- Bradycardia
- Chest pain
- Hypotension
- Gastric ulceration

Contraindications

- Active peptic ulcer
- Ulcerative colitis
- Electroconvulsive therapy
- Pregnancy
- Parkinson's disease
- Rauwolfia alkaloid hypersensitivity
- Psychiatric depression
- Pheochromocytoma
- Cardiac arrhythmia
- Myocardial infarction

Drug Interactions of Reserpine

Reserpine's clinically significant medication interactions are briefly listed here.

- **Acebrophylline:** -May enhance the tachycardia effect of Reserpine. Risk C: Monitor therapy
- **Alcohol (Ethyl):** - CNS Depressant may enhance the CNS Depressant effect of Alcohol (Ethyl). Risk C: Monitor therapy

- **Levodopa:** - Containing Levodopa: Containing Products: Blood Pressure Lowering Agents may enhance the hypotensive effect of Levodopa-Containing Products. Risk C: Monitor therapy
- **The Carbidopa:** - This May enhance hypotensive Reserpine. Effect Reserpine of may diminish the therapeutic effect of Carbidopa. Risk X: Avoid combination

Reserpine Uses: -

- Reserpine is an adrenergic neuron blocker, an antihypertensive, and an antipsychotic drug. Reserpine is licensed for the treatment of mental disorders and hypertension
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III. Conclusion

From the above review we concluded that, as a result, identifying, treating, and controlling hypertension is a major issue. The goal of current initiatives is to identify and treat hypertension in middle-aged and elderly people. The disease is prevalent throughout all types of populations. People must now be made aware of the severity of the disease and the best strategies to prevent it. If necessary, the patient should get nonpharmacological treatment initially before developing to pharmacological treatment. Ashwagandha, sarpagandha (*Rauwolfia*), and other herbal plants that are used in herbal medicine are widely produced in India. Reserpine is an alkaloid indole isolated from the Indian plant *Rauwolfia serpentina*. Reserpine is a pure crystalline single alkaloid; it is unable to produce adverse effects from unknown alkaloid in the complete root. Unani therapy may also help reduce high blood pressure. The hypotensive effect of Reserpine can be achieved with much lower doses of the drug.

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