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Studies on Biological Activity and Mechanisms of Action in Alkaloids of *Rauvolia serpentina* (L.) Benth. ex Kurz. for Hypertension Lowering

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Abstract: ***Rauvolfia serpentina, (L.) Benth. ex Kurz.: a perennial South and Southeast Asian plant, is therapeutic. It contains alkaloids, reserpine being the most significant. These alkaloids have been researched to lower blood pressure, and R. serpentina has been used to treat hypertension. Millions worldwide suffer from hypertension or high blood pressure. It increases the risk of heart disease, stroke, and other problems. While there are various pharmaceutical approaches to control hypertension, Rauvolfia alkaloids are the bioactive chemicals responsible for their therapeutic benefits. Reserpine, the most researched antihypertensive alkaloids, is the most prominent. Rauvolfia alkaloids treat hypertension via many routes. One key technique is blocking the sympathetic nervous system, which regulates blood pressure. Rauvolfia alkaloids block nerve terminal reuptake of neurotransmitters including norepinephrine and serotonin. Reduced sympathetic outflow causes vasodilation and cardiac output. Rauvolfia alkaloids also impact the RAAS, another blood pressure regulator. Renin synthesis and release can be modulated to reduce angiotensin II and aldosterone generation. Vasodilation and blood volume reduction reduce blood pressure. The antioxidant effects of Rauvolfia alkaloids protect vascular endothelial cells against oxidative stress and inflammation. Oxidative stress causes endothelial dysfunction and arterial stiffness, contributing to hypertension. Rauvolfia alkaloids may promote endothelial and vascular health by scavenging free radicals and lowering oxidative stress. Rauvolfia alkaloids may also affect vasoactive molecules like NO and ET-1. Increased NO production lowers blood pressure because it dilates blood vessels. ET-1 is a vasoconstrictor, hence blocking its release maintains vasodilation. Rauvolfia alkaloids may also affect pro-and anti-inflammatory cytokines, which may affect hypertension and vascular health. They may lower pro-inflammatory cytokines like TNF-α and IL-6 while increasing anti-inflammatory cytokines like IL-10. Recent research has examined Rauvolfia alkaloids' gut microbiota modulation capability. Hypertension control involves the gut-brain axis and gut bacteria. Rauvolfia alkaloids may indirectly affect blood pressure by affecting gut microbiota makeup and function. Rauvolfia alkaloids are safer than synthetic antihypertensives and have direct modes of action. These substances may cause drowsiness, depression, and gastrointestinal issues, so use them with caution.***

Keywords: *Rauvolfia serpentina*, Hypertension, High blood pressure, Antihypertensive, Reserpine, Alpha-adrenergic blockade

1. Introduction

Rauwolfia (*Rauwolfia serpentina*) is an evergreen plant of the Apocynaceae or dogbane family. (2000) Endress and Bruyns. The *Rauwolfia* genus has about 100 species that are endemic to tropical and subtropical parts of the world, including Europe, Africa, Asia, Australia, and Central and South America. (Vakil (1995) *Rauwolfia serpentina* is endemic to Southeast Asia's wet deciduous woods, including India, Burma, Bangladesh, Sri Lanka, and Malaysia. (U. S. Department of Agriculture. (2014) The plant grows to a height of 60 to 90 cm and has pale green leaves 7 to 10 cm long and 3.5 to 5.0 cm broad. The leaves are elliptical to lanceolate in form and appear in whorls of three to five leaves. The plant produces several lustrous, black, or purple, spherical fruits of about 0.5 cm in diameter. It contains little pink or white blooms as well. The plant has a noticeable tuberous, soft taproot with a length of 30 to 50 cm and a diameter of 1.2 to 2.5 cm.2014 (Brijesh)

History and Folk Use:

In India, *R. serpentine* has a long history of usage in traditional medicine for a wide range of diseases, including but not limited to snake and bug stings, fever, malaria, stomach discomfort, and dysentery. It was also employed as a febrifuge, a treatment for mental issues, and a uterine stimulant. The plant, also known as sarpagandha and chandrika, was first described in Indian literature around the year 1000 BC. (Yarnell and Abascal (2001) In recognition of Dr. Leonhard Rauwolf, a German physician who visited India in the 16th century and conducted botanical research, the species *Rauwolfia* was named after him. Because of its unique, snake-like roots, Serpentina was chosen for this investigation. (Tyler *et al.,* 1988). Indian political leader Mahatma Gandhi allegedly used *Rauwolfia,* brewing tea from the plant's root to unwind at the end of a long day. (Jerie 2007). It was the Indian doctor Rustom Jal Vakil who is credited with bringing Rauwolfia to the attention of Western medicine. For a decade, from 1939 to 1949, he tracked information about patients who were given *Rauwolfia*. His 1949 article in the British Medical Journal on the effectiveness of *R. serpentina* in treating hypertension is considered a landmark in the field. Fifty patients with hypertension were treated with *Rauwolfia* root, and the findings were published in detail (Isharwal *et al.,* 2006). The findings were striking and important. In 1949, almost 90% of Indian doctors were prescribing *Rauwolfia* for hypertension. More than a hundred scholarly publications were published throughout the world after Vakil's initial study.

Chemical Composition

Many various types of phytochemicals may be found in *Rauwolfia*, such as alcohols, sugars and glycosides, fatty acids, flavonoids, phytosterols, oleoresins, steroids, tannins, and alkaloids. More than 50 different alkaloids have been identified from the plant, the majority of which are indole alkaloids. This is supported by (Verma and Verma, 2010). Tryptophan is the building block for a class of nitrogenous chemicals known as indole alkaloids. They both contain 5 or 6 carbons in a heterocyclic ring with 1 nitrogen atom in common. (Leete 1960). Although indole alkaloids are present in all sections of the plant, including the stem and leaves, they are most concentrated in the root bark. R. *et al.* (1991) The identified indole and indole alkaloids include ajmalidine, ajmaline, ajmalinine, ajmalicine, aricine, canescine, coryanthine, deserpidine, isoajmaline, isoserine, isoserpiline, lankanescine, neoajmaline, papaverine, raubasine, raucaffricine, rauhimbine, rauwolfinine, recanescine, rescinnamine, reserpiline, reserpine, reserpinine, sarpagine, serpentine, serpentinine, thebaine, yohimbine, and yohimbinine. According to a study (Woodson *et al.,* 1957). Alkaloids can be found in a wide range of concentrations. Total alkaloid output was estimated to be between 0.8% and 1.3% of the plant's dry weight in a single study. According to a study (Woodson *et al.,* 1957). Another research estimated that the root might provide an alkaloid yield of between 0.7% and 3.0%. In a 2014 study (Brijesh KS. The highest amount of alkaloid found in new root growth was 3.3%. In 2011, (Panwar and Guru). Rauwolfia vomitoria and *Rauwolfia caffra* from Africa, as well as *R. teterophylla* and *R. tetraphylla* from Central and South America, have been substituted for *R serpentina*. In a 1957 study (Woodson *et al.* found that other species in the same genus, which might be used as substitutes for *R serpentina*, had varying amounts of indole and indole alkaloids

Biological Activity:

R. serpentina, commonly known as Indian snakeroot or serpent wood, is a plant that has been used traditionally in Ayurvedic medicine for its potential medicinal properties, including its use in lowering blood pressure due to the presence of alkaloids such as reserpine and raubasine. These alkaloids have been of interest in the treatment of hypertension and related cardiovascular conditions.

1) **Reserpine**: Reserpine is an alkaloid found in *R. serpentina* that has been used historically as an antihypertensive medication. It works by inhibiting the uptake of neurotransmitters such as norepinephrine and serotonin into nerve endings, thereby reducing sympathetic nervous system activity. By doing so, it can lead to a decrease in blood pressure. However, reserpine is rarely used today in clinical practice due to its numerous side effects, including depression and sedation.
2) Raubasine (Ajmalicine): Raubasine is another alkaloid found in *R. serpentina*. It has been investigated for its potential use in lowering blood pressure, although its mechanism of action is not entirely understood. It may act as a vasodilator, helping to relax blood vessels and reduce resistance to blood flow, which can lead to lower blood pressure.

It's important to note that while *R. serpentina* and its alkaloids have been used traditionally for hypertension, the use of these compounds in modern medicine is limited due to their side effects and the availability of more effective and better-tolerated antihypertensive drugs. Medications derived from *R. serpentina* were more commonly used in the past but have largely been replaced by newer, safer options.

If you have hypertension or are considering using natural remedies for blood pressure management, it is essential to consult with a healthcare professional. They can provide guidance on safe and effective treatments and help you make informed decisions about our health. Modern treatments for hypertension often focus on lifestyle modifications (such as diet and exercise) and prescription medications that have been rigorously tested for safety and efficacy.

Mechanism of Action:

The mechanisms of action in *R. serpentina* for lowering hypertension involve a multifaceted interplay of various pharmacological effects. Here are the key mechanisms:

1) **Alpha-Adrenergic Blockade**: One of the primary mechanisms is the inhibition of alpha-adrenergic receptors by alkaloids found in *R. serpentina*, particularly reserpine. Alpha receptors are responsible for vasoconstriction when stimulated by norepinephrine. By blocking these receptors, *Rauvolfia* serpentina causes vasodilation and reduces the resistance in blood vessels, ultimately leading to a decrease in blood pressure.
2) **Calcium Channel Modulation**: *R. serpentina* has been found to modulate calcium channels in vascular smooth muscle cells. By inhibiting calcium influx into these cells, it reduces the contractility of blood vessels, promoting relaxation and vasodilation. This effect contributes to lowering blood pressure by decreasing systemic vascular resistance.
3) **Neurotransmitter Depletion**: Reserpine, a prominent alkaloid in *R. serpentina*, depletes neurotransmitters such as norepinephrine and serotonin from nerve endings. This depletion reduces sympathetic nervous system activity, as these neurotransmitters are involved in transmitting signals that increase blood pressure. By reducing sympathetic tone, *R. serpentina* helps control blood pressure.
4) **Reduced Sympathetic Nervous System Activity**: The overall reduction in sympathetic nervous system activity is a central mechanism. By antagonizing alpha-adrenergic receptors, inhibiting calcium channels, and depleting neurotransmitters, *R. serpentina* collectively reduces the influence of the sympathetic nervous system on blood pressure regulation. This results in a more balanced autonomic nervous system and lower blood pressure.
5) **Vasodilation**: The combined effects of alpha-

adrenergic blockade and calcium channel modulation lead to vasodilation, which is the widening of blood vessels. Vasodilation reduces the resistance within the arteries, making it easier for blood to flow through them. This decreased vascular resistance contributes significantly to the lowering of blood pressure.

6) **Endothelial Function**: *R. serpentina* may also influence endothelial function. Healthy endothelial cells lining blood vessels produce nitric oxide, a molecule that promotes vasodilation. While the exact mechanisms are not fully understood, it is possible that *R. serpentina* affects endothelial function, further enhancing its vasodilatory effects.
7) **Hormonal Regulation**: Some research suggests that *R. serpentina* may influence hormonal pathways involved in blood pressure regulation. It may affect the renin-angiotensin-aldosterone system (RAAS), which plays a role in maintaining blood pressure and fluid balance in the body. By modulating these hormonal pathways, *R. serpentina* may contribute to blood pressure control.

In summary, *R. serpentina* lowers hypertension through a combination of mechanisms that include alpha-adrenergic blockade, calcium channel modulation, neurotransmitter depletion, reduced sympathetic nervous system activity, vasodilation, potential effects on endothelial function, and modulation of hormonal pathways. These mechanisms collectively lead to a decrease in blood pressure, making it a subject of interest in traditional and herbal medicine for the management of hypertension. However, it's essential to consult with healthcare professionals for appropriate and evidence-based treatment options for hypertension.

The mechanism of action of *R. serpentina* in hypertension control primarily involves its influence on the sympathetic nervous system and vascular smooth muscle cells. By targeting alpha-adrenergic receptors and calcium channels, as well as depleting key neurotransmitters, it achieves a multifaceted effect on blood pressure regulation.

2. Conclusion

In conclusion, *Rauvolfia* alkaloids derived from *R. serpentina* demonstrate significant biological activity and multiple mechanisms of action that contribute to their antihypertensive effects. These mechanisms include sympathetic nervous system modulation, RAAS inhibition, antioxidant properties, calcium channel blocking, regulation of vasoactive substances, and potential effects on the gut microbiota. While further research is needed to fully elucidate these mechanisms and optimize their therapeutic potential, *Rauvolfia* alkaloids hold promise as natural agents for lowering hypertension and improving cardiovascular health. Their historical use in traditional medicine, coupled with modern scientific investigations, underscores their importance in the management of hypertension, providing a potential avenue for the development of novel antihypertensive therapies.

References

[1] *Brijesh KS. (2014) Rauwolfia: cultivation and collection. Biotech Articles Web site. http://www.biotecharticles.com/Agriculture-Article/Rauwolfia-Cultivation and-Collection-892.html. Published May 23, 2011. Accessed September 25,*
[2] *Endress ME, Bruyns PV. (2000): A revised classification of the Apocynaceaes. l. BotRev.2000; 66 (1): 1-56.*
[3] *Isharwal S, Gupta S. Rustom Jal Vakil: (2006) his contributions to cardiology. TexHeart Inst J.2006; 33 (2): 161-170.*
[4] *Jerie P. (2007) Milestones of cardiovascular therapy, IV: reserpine [in Czech]. CasLek Cesk.146 (7): 573-577.*
[5] Leete E. (1960): The biogenesis of the Rauwolfia alkaloids, I: the incorporation of tryptophan into ajmaline. *J Am Chem Soc*.82 (24): 6338-6342.
[6] Panwar GS, Guru SK. (2011). Alkaloid profiling and estimation of reserpine in Rauwolfia serpentina plant by TLC, HP-TLC and HPLC. *Asian J Plant Sci*.2011; 10 (8): 393-400.
[7] Ruyter CM, Akram M, Illahi I, Stockigt J. (1991) Investigation of the alkaloid content of Rauwolfia serpentina roots from regenerated plants. *Planta Med*.1991; 57 (4): 328-330.
[8] Tyler VE, Brady LR, Robbers JE. (1988) *Pharmacognosy*.9th ed. Philadelphia, PA: Lea &Febiger; 222-225
[9] US Dept of Agriculture. (2014): Rauvolfia L. Germplasm Resources Information Network Web site. http: //www.ars-grin.gov/cgi-bin/npgs/html/genus. pl?10272. Published March 14, 2003. Accessed August
[10] Vakil RJ. (1995): *Rauwolfia serpentina* in the treatment of high blood pressure: a review of the literature. *Circulation*.1955; 12 (2): 220-229.
[11] Verma KC, Verma SK. (2010): Alkaloids analysis in root and leaf fractions of sarpaghanda (Rauwolfia serpentina). *Agric Sci Dig*; 30 (2): 133-135.
[12] Woodson RE, Youngken HW, Schlittler E, Schneider JE. (1957) *Rauwolfia: Botany, Pharmacognosy, Chemistry and Pharmacology.* Boston, MA: Little, Brown and Company; 1957: 32-33.
[13] Yarnell E, Abascal K. (2001): Treating hypertension botanically. *Altern ComplementTher*.7 (5): 284-290.