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# Phytochemical Composition, Medicinal Applications, and Pharmacological Insights: A Comparative Review of *Rauvolfia serpentina* and *Rauvolfia tetraphylla*

# Sapugaskandage Shenya <sup>a\*</sup>, Dinara Sendanayake <sup>a</sup>, Sohani Medis <sup>a</sup> and Niluka Dlirukshi <sup>b</sup>

 <sup>a</sup> Department of Medical Laboratory Sciences, Faculty of Allied Health Sciences, General Sir John Kotelawala Defence University, Werahera, Sri Lanka.
<sup>b</sup> Department of Medical Laboratory Sciences, Faculty of Health Sciences, Open University, Sri Lanka.

# Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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# ABSTRACT

**Aims:** This review article aims to compare the phytochemical profile, therapeutic potential and pharmacological activities of *Rauvolfia serpentina* and *Rauvolfia tetraphylla*. **Scope of Review:** Review data from published literature and assess about phytochemicals, therapeutic applications and efficacy of *Rauvolfia serpentina* and *Rauvolfia tetraphylla* against

\*Corresponding author: E-mail: shenyags00@gmail.com;

microorganisms and inflammation comparatively.

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**Methodology:** Research papers and review articles on *Rauvolfia serpentina* and *Rauvolfia tetraphylla* were collected and analyzed about phytochemicals, medicinal uses, antibacterial and inflammatory properties.

**Summary of Findings:** *Rauvolfia serpentina* and *Rauvolfia tetraphylla* have many similarities in its phytochemistry such as alkaloids like Reserpine, Ajmaline. They have been used to treat similar diseases and illness conditions like hypertension, psychotic disorders and snake bites. **Conclusion:** According to the findings, due to endangered status of *Rauvolfia serpentina*.

**Conclusion:** According to the findings, due to endangered status of *Rauvoltia serpentina*, *Rauvoltia tetraphylla* can be used as an ideal substitute and can be used for developing novel antimicrobial and anti-inflammatory drugs with mild side effects. Further investigations are necessary to determine their efficacy.

Keywords: Rauvolfia serpentine; Rauvolfia tetraphylla; phytochemistry; antimicrobial activity; antiinflammatory activity; alkaloids.

# 1. INTRODUCTION

The connection between nature and humanity can be defined as a deeply intertwined relationship (Ayele et al., 2024). Humans have been dependents on plants and trees for essential resources such as food, shelter, clothing and also medicine for their survival since time immemorial (Gurib-Fakim, 2006). In fact, plants have been considered as gifts of gods and worshipped by Hindus as a matter of gratitude, since they were vital for the existence of mankind (Wani et al., 2020).

Medicinal plants rich in bioactive are compounds which are produced from either primary or secondary These metabolism. compounds are mainly alkaloids, tannins, terpenoids, carbohydrates, steroids and flavonoids. (Yadav and Agarwala, 2011). These metabolites are known as phytochemicals. Secondary metabolites are non-nutritive to the plant but they enhance the ability of the plant to withstand unfavorable external environment conditions and defense against various pathogenic bacteria, fungi, viruses and insects. However, these phytochemicals also play major healthcare а role in the system in humans in different ways due to its diverse functions that have pharmaceutical value (Bitwell et al., 2023) as well as therapeutic effect on humans (Yadav and Agarwala, 2011).

Antimicrobials (antibiotics, antifungals, antivirals and antiparasitics) are medicines that are utilized to treat and prevent infections in humans and even other animals and plants. Due to misuse and overuse of such drugs antimicrobial resistance has emerged as a global concern affecting the healthcare system and economy (World Health Organization, 2023). Bacterial

resistance is one of the growing issues in the world and has led to rapid increase of multidrug resistant bacteria (MDR). Therefore, finding of novel drugs from plants have become a trend nowadays (Samaraweera et al., 2023).

Inflammation is a crucial reaction that occurs in the body which is a defense mechanism that protects against infections, burn, toxic chemical allergens and various harmful stimuli (Dharmadeva et al., 2018). When inflammation is not controlled properly, it damages the tissue. Anti-inflammatory drugs such as NSAIDs (Nonsteroidal anti-inflammatory drugs) come into play to regulate excessive inflammation and prevent tissue damage but they can cause dangerous side effects such as congestive heart failure and increased blood pressure. Therefore, it is important to discover new anti-inflammatory agents that have minimum side effects. Plants possess phytochemicals like flavonoids, terpenoids and polyphenols that may be effective for inflammation (Senadeera et al., 2021).

Rauvolfia serpentina and Rauvolfia tetraphylla are plants that are classified under the same genus Rauvolfia. They have been utilized as a folklore medicine, since they possess an immense medicinal property that could be a hypertension, cardiovascular treatment for diseases. snakebites, digestive system, metabolic and central nervous system disorders (Kumar et al., 2022). These two species are very important among other species of genus Rauvolfia since they contain crucial active biological compounds within themselves that have certain biological functions. Rauvolfia tetraphylla is often used as a substitute for Rauvolfia serpentina in therapeutic purposes (Mahalakshmi et al., 2019).

# 2. PLANT MORPHOLOGY

# 2.1 *Rauvolfia* serpentina Plant Morphology

*Rauvolfia* serpentina is a small, woody, evergreen shrub that has about 60 cm of maximum height which is identified as a critically endangered species (Kumari et al., 2013; Sulaiman et al., 2020). This plant possesses cylindrical stems and barks are pale in



Fig. 1. Plant Rauvolfia serpentina

appearance. Leaves are lanceolate or elliptical shaped that are pale green in colour and whorls of three. This plant contains light coloured viscous latex. *Rauvolfia serpentina* carries fruits that are small and fleshy which is green in colour that turns into purple-black when ripened. The roots are tuberous and usually 3-7 inches long and they are lens-shaped and clustered (Perera et al., 2023). Roots are greyish to yellow in colour (Fig. 1 and Fig. 2) (Srivastava et al., 2021).



Fig. 2. Flowers and fruits of *Rauvolfia* serpentina



Fig. 3. Plant Rauvolfia tetraphylla

# 2.2 *Rauvolfia tetraphylla* Plant Morphology

Rauvolfia tetraphylla is a small tree shrub that has about 6 feet (~2 meters) of height (Rao et al., 2012). It is whorled in 4, unequally-sized, 5-9 x 3-4 cm, elliptic-ovate shaped leaves. They are dark green in colour and their apex is acute and the base is round. Leaves have a characteristic odor and smooth textured. Both surfaces are pubescent. Stems are round, rough and hairy, green on the outer surface and internally creamy yellow. Roots are sub cylindrical shaped, curved, 8-15 cm long and have about 0.5-2 cm thickness. Outer surface is usually gravish-brown to reddish-brown in colour (Jakaria et al., 2016). Flowers are creamy in colour and flowering can be observed throughout the year. This plant possesses 2 seeded ovoid shaped drupes which turns into purple in colour when ripened (Fig. 3) (Mahalakshmi et al., 2019)

# 3. PHYTOCHEMISTRY

# 3.1 Phytochemistry of *Rauvolfia* serpentina

*Rauvolfia* serpentina is considered an ethnomedicinally valued plant due to its richness of many phytochemicals. Many studies have been conducted extensively and explored various types of chemicals within different parts of the plant. Alkaloids, tannins, flavonoids, phenols are some of the key secondary metabolites found in *Rauvolfia serpentina* (Kumari et al., 2013; Perera et al., 2023).

#### 3.1.1 Alkaloids

More than 50 types of alkaloids have been explored in this plant (Lobay, 2015). They are categorized as; Indole alkaloids, Indolenine alkaloids, Oxindole alkaloids and Pseudo indoxyl alkaloids (Srivastava et al., 2021). Out of these, indole alkaloids are the most crucial type. Reserpine, Ajmaline, Ajmalicine and Yohimbine are some of the identified alkaloids within this plant (Srivastava et al., 2006; Agrawal, 2019).

#### 3.1.1.1 Reserpine

Reserpine is one of the most crucial and prevalent alkaloids present in *Rauvolfia* serpentina. The amount of reserpine in roots are higher compared to leaves and stems of the plant (Lobay, 2015). This alkaloid has a higher neurotherapeutic effect and it is also used as a

natural tranquillizer. It is effective in treating and management of cardiovascular diseases. hypertension and neurological diseases. The antihypertensive effect of Reserpine in central nervous system and peripheral nervous system is demonstrated by binding to catecholamine storage vesicles in nerve cells, disrupting the normal catecholamine and serotonin storage leading to decrease in their levels. This impacts autonomic nervous system to reduce on neurotransmitters from adrenergic neurons and activate the central parasympathetic system (Kumari et al., 2013).

#### 3.1.1.2 Ajmaline

Ajmaline is derived from roots as a class I antiarrhythmic agent utilized in diagnosing "Brugada Syndrome" and to differentiate the subtypes of patients having this syndrome. Ajmaline is given intravenously for such patients during the "Ajmaline test", causing sodium channels to be blocked instantly (Kumari et al., 2013).

#### 3.1.1.3 Ajmalicine

Ajmalicine reduces blood pressure and even prevents strokes by acting on smooth muscles. It maintains the normal cerebral blood flow (Kumari et al., 2013).

#### 3.1.1.4 Yohimbine

It is an alpha blocker that treats erectile dysfunction by dilating the blood vessels and increasing the blood flow to the penis by relaxing the smooth muscles in tunica media (Kumari et al., 2013; Perera et al., 2023).

#### 3.1.1.5 Serpentine

Serpentine is derived from oxidation of Ajmalicine by peroxidase enzyme. It is a type II topoisomerase inhibitor that shows antipsychotic effects. It also possesses antihypertensive activity which is similar to that of Ajmaline (Kumari et al., 2013).

#### 3.1.2 Tannins

Tannins possess stringent properties which speeds up the wound healing and has antiinflammatory properties (Kumari et al., 2013).

#### 3.1.3 Flavonoids

Flavonoids have anticancerous activity and also prevents oxidative damage of cells thanks to its

antioxidative properties and free radical scavenging activity (Kumari et al., 2013). Kaempferol which is a flavonoid isolated in *Rauvolfia serpentina* leaves possesses both antioxidative activity as well as potent antiinflammatory properties (Thors et al., 2008; Gupta and Gupta, 2015).

#### 3.1.4 Phenols

Phenols are secondary metabolites that prevent the growth of pathogens and pests. Hence, it has a potent to be utilized as an antimicrobial agent. *Rauvolfia serpentina* shows antidiabetic and hypolipidemic effects due to presence of total phenolic compounds in higher amounts (Kumari et al., 2013).

#### 3.1.5 Saponins

Saponins are characterized by formation of foams in aqueous solutions, hemolytic activity, bitterness and cholesterol binding properties. They possess the anticoagulating activity of red blood cells therefore, this plant is utilized to treat preventing of bleeding and wound healing due to its higher amounts of Saponins in the plant (Kumari et al., 2013).

# 3.2 Phytochemistry of *Rauvolfia tetraphylla*

*Rauvolfia tetraphylla* contains an innumerous number of phytochemicals especially alkaloids. Most crucial alkaloid found in this plant is also Reserpine. In addition to alkaloids, many phytochemical groups have been discovered such as tannins, phenols, steroids, saponins, flavonoids and terpenoids within different parts of the plant (Mahalakshmi et al., 2019).

#### 3.2.1 Alkaloids

Rauvolfia Root of the plant tetraphylla contains approximately 30 different types of alkaloids. Some of them are Reserpine, Reserpitine Aimalicine, Aimalidine, neo Aimaline, Deserpidine. Sarpagine. Rescinnamine. Corynathine. Serpentine. Allovohimbine. Chandrine, Iscaimaline, Yohimbine, Thambine, Serpinine. Reserpoxidine, Reserpinine, Reserpiline, Rauwolscine, Raunoline, Raunatine and Papaverine (Jakaria et al., 2016).

#### 3.2.1.1 Reserpine

Reserpine is abundantly present in roots whereas leaves and stems contain comparatively lower amounts (Mahalakshmi et al., 2019).

Reduced blood pressure and acts as a tranquilizer (Jakaria et al., 2016).

#### 3.2.1.2 Serpentine

It acts as a weak hypotensive agent (Jakaria et al., 2016).

#### 3.2.1.3 Sarpagine

An alkaloid that has a fleeting effect on blood pressure (Jakaria et al., 2016).

#### 3.2.1.4 Yohimbine

Acts as a hypotensive agent, a cardiovascular depressant and a hypnotic agent. Alphayohimbine ( $\alpha$ -yohimbine) is one of the indole alkaloids that possesses antipsychotic activity (Isoreserpiline and 10-methoxy tetrahydroalstonine are other indole alkaloids that has the antipsychotic activity found in *Rauvolfia tetraphylla*) (Jakaria et al., 2016).

#### 3.2.1.5 Ajmaline

Used in for the treatment of arrhythmic heart diseases. Also used to provoke intestinal movement and respiration (Jakaria et al., 2016).

#### 3.2.1.6 Recanescine

Another alkaloid isolated from *Rauvolfia tetraphylla* that lacks methoxyl group in the C-II position of Reserpine. It possesses sedative and hypotensive properties (Mahalakshmi et al., 2019).

#### 3.2.1.7 Pseudoreserpine

Isolated from roots of the plant that has sedative and hypotensive properties (Mahalakshmi et al., 2019).

#### 3.2.2 Flavonoids

Flavonoids are found in treating acute inflammation. Additionally, it has the inhibition ability against phospholipase A2, protein kinase C and protein Tyrosine kinases (Merlin et al., 2020).

#### 3.2.3 Terpenoids

Influence key signaling pathways which are associated with inflammatory responses such as

nuclear transcription factor – Kappa B activation (NF – Kappa B) (Merlin et al., 2020).

### 3.2.4 Other phytochemical groups

Many studies have been conducted and isolated tannins, saponins, cardiac glycosides, glycosides, steroids, phenols, triterpenoids, coumarin, catechin, fixed oils, fats, gums are mucilages within various parts of the plant (Jakaria et al., 2016; Mahalakshmi et al., 2019).

# 4. MEDICINAL USE

# 4.1 Medicinal Use of *Rauvolfia* serpentina

Rauvolfia serpentina has a wide range of therapeutic effects. It is mainly effective in treatment of hypertension, anxiety, epilepsy, insomnia, psychotic disorders like schizophrenia and insanity. It is also used as a sedative and a hypnotic drug. Root extract of the plant is valued for intestinal disorders like diarrhea, dysentery and also as anathematic. Cholera, cholic and fever have been treated when combined with other plant extracts. It was believed that roots stimulate the uterine contractions and they were recommended during child birth. The juice of the leaves has been utilized as a remedy for the cornea. Gastrointestinal opacity of and circulatory disorders can be treated with juice of Rauvolfia serpentina and extract obtained from the roots. Juice acquired from tender leaves and root extract have been used to treat liver discomfort, stomach pain, dysentery and to eliminate intestinal worms. It is also used for the treatment of cancers (Malviya and Sason, 2016).

# 4.2 Medicinal Use of Rauvolfia tetraphylla

Rauvolfia tetraphylla has a significant therapeutic effect with many medicinal applications. The whole plant is used as a remedy for scorpion bites, snake bites and insect bites and as well as an antidote and sedative agent. This plant is used as a substitute for Rauvolfia serpentina as a treatment for circulatory disorders. It can be also utilized as an antimicrobial agent. Rauvolfia tetraphylla is also utilized to treat skin infections. Leaves are used to treat eye problems, tooth infections, cough, cold, and skin diseases. Root paste with milk or honey is used to treat mental illnesses and hypertension. To increase uterine contractions during labor, roots are used. Stomach aches, diarrhea, diabetes mellitus, malaria and muscle and joint pains are also treated with roots of the plant. Moreover, the roots have the ability to enhance libido and treat impotence (Erectile dysfunction). The resin is used as an antitussive agent. It also accelerates defecation and cures hydropsy. As a remedy for intestinal worms *Rauvolfia tetraphylla* fruits are used (Pandith and Devi, 2024).

# 5. COMPARATIVE ANALYSIS OF ANTIMICROBIAL ACTIVITY BETWEEN Rauvolfia tetraphylla AND Rauvolfia serpentina

# 5.1 Antimicrobial Activity of *Rauvolfia* serpentina

Rauvolfia serpentina aqueous leaf extract (RSALE) and encapsulated gold nanoparticles (R-AuNPs) were utilized to determine its antibacterial activity using disc diffusion method and obtained Minimum Inhibitory Concentration Staphylococcus (MIC) against aureus. coli, Streptococcus Escherichia pvogenes. Bacillus subtilis and Proteus vulgaris. Compared to RSALE and Amoxicillin (control), R-AuNPs gave significantly good antibacterial activity for all tested organisms except Proteus vulgaris. The MIC values that were obtained suggested that lower doses of R-AuNPs were significantly more effective than RSALE and Amoxicillin (Alshahrani et al., 2021).

Methanol extract of Rauvolfia serpentina and few other plant species (Tagetes erecta, Brassica nigra and Ocimum tenuiflorum) were subjected to evaluate the antibacterial activity against Staphylococcus aureus. Escherichia coli. Pseudomonas aeruginosa and Salmonella typhi by disc diffusion method. The test was performed from leaves with different ages. Out of those four plants Rauvolfia serpentina exhibited the best antibacterial activity for the tested strains. However, Salmonella typhi had not shown any inhibition zone for all tested plants. Results demonstrated that along the advancement of age of Rauvolfia serpentina leaves, the antibacterial activity also increased (Rashid et al., 2014).

Antimicrobial activity was determined from methanol, chloroform, hexane and aqueous extract of Rauvolfia serpentina roots against Bacillus subtilis, Enterococcus faecalis, Escherichia Klebsiella coli. pneumoniae, Micrococcus luteus, Pseudomonas aeruginosa, vulgaris, Staphylococcus Proteus aureus, Streptococcus pneumoniae, Aspergillus niger, Candida albicans and Saccharomyces cerevisiae by agar well diffusion method and determined the Inhibitory Concentration Minimum (MIC). Methanol extract showed more effective antimicrobial activity against Bacillus subtilus and Staphylococcus aureus, chloroform extract showed activity against Enterococcus faecalis and Aspergillus niger and aqueous extract demonstrated activity against Streptococcus pneumoniae. Another study demonstrated that methanol extract possessed the best antimicrobial activity against all tested organisms compared to aqueous, chloroform and hexane extracts. Methanol extract also exhibited the lowest MIC against Staphylococcus aureus (Owk and Lagudu, 2016).

# 5.2 Antimicrobial Activity of *Rauvolfia tetraphylla*

Hexane, ethyl acetate, methanolic and 70% ethanol root bark extract of Rauvolfia tetraphylla were tested for its antibacterial activity, comparing with the standard chloramphenicol (30µg/cup) by using cylinder plate assay. All tested extractions at every concentration (50µg/cup, 100µg/cup and 150µg/cup) except hexane, showed significantly good antibacterial against Streptococcus pneumoniae, activity Bacillus cereus, Bacillus pumilis, Staphylococcus aureus. Escherichia coli. Enterobacter aerogenes, Pseudomonas aeruginosa and Streptomyces marienensis. However, hexane extract on dose 50µg/ml had not shown any activity against antibacterial Streptococcus pneumoniae, Enterobacter aerogens and Streptomyces mariensis (Rao et al., 2012).

Leaf and callus extract of Rauvolfia tetraphylla obtained from solvents such as benzene. chloroform, absolute alcohol, methanol and petroleum ether were subjected to test against like bacterial species Bacillus subtilis. Escherichia coli, Pseudomonas solanacearum, Xanthomonas vesicatoria and fungal species like Aspergillus ochreaceous, Aspergillus flavipes, Fusarium verticilloides and Penicillium sp., using broth microdilution method. Out of these solvents both absolute alcohol and chloroform found to be more effective against both bacteria and fungi (Shariff et al., 2006).

Rauvolfia tetraphylla methanolic extract against Salmonella typhimurium, Escherichia coli, Citrobacter freundii, Proteus vulgaris, Enterococcus faecalis and Staphylococcus aureus bacterial strains were tested using well diffusion method and observed for Minimum Inhibitory Concentration (MIC). The highest inhibition zone with lowest MIC was shown by *Staphylococcus aureus* and lowest inhibition zone was shown by *Salmonella typhimurium* whereas highest MIC was shown by *Escherichia coli. Proteus vulgaris* did not show any inhibition zone (Negi et al., 2014).

The ethyl acetate extract of the leaves obtained from *Rauvolfia tetraphylla* were tested against *Shigella dysenteriae* and *Salmonella typhi* using anti-bacterial assay-agar disk diffusion method had shown a good inhibitory activity. The zone of inhibition was increased with the increasing of plant concentration (Krishnasamy et al., 2023).

Evaluation of antimicrobial activity of aqueous and methanolic extracts of *Rauvolfia tetraphylla* leaf against bacteria (*Staphylococcus aureus*, *Streptococcus pyogenes*, *Leuconostoc lactis*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Salmonella typhi*) and fungi (*Aspergillus niger*, *Aspergillus flavus*, *Rhizopus indicus* and *Mucor indicus*) through the well diffusion method. *Streptococcus pyogenes* exhibited the highest zone of inhibition in methanol extract compared to aqueous extract. Except *Mucor indicus*, all other fungal strains showed some antifungal activity for methanolic extraction whereas all four fungal strains did not show any antifungal activity for aquatic extraction (Kavitha et al., 2012).

# 6. COMPARATIVE ANALYSIS OF ANTI-INFLAMMATORY ACTIVITY BETWEEN Rauvolfia tetraphylla AND Rauvolfia serpentina

# 6.1 Anti-inflammatory Activity of *Rauvolfia serpentina*

In the evaluation of chemical composition of Rauvolfia serpentina, flavonoids were found to be present (1.65±0.12 mg/100 g). Since flavonoids act as antioxidants they provide antiinflammatory activity (Bhardwaj and Yadav, 2016). Gupta and Gupta (2015) used Rauvolfia serpentina leaves to isolate and extract flavonoids and determine its antioxidant potential through DPPH-scavenging method (Radical scavenging activity showed 62.5% in leaves of Rauvolfia serpentina). They succeeded in finding the structure of а flavonoid called Kaempferol (3,5,7,4'-tetrahydroxy flavones) using chromatographic and spectrometry techniques. Kaempferol is a natural antioxidant that has antiinflammatory activity (Gupta and Gupta, 2015). It inhibits the activity of fatty amide hydrolase

enzyme (FAAH) acting as a very good antiinflammatory agent (Thors et al., 2008).

# 6.2 Anti-inflammatory Activity of *Rauvolfia teraphylla*

Rao et al. (2012) utilized Carrageenan induced rat paw oedema model, to evaluate the antiinflammatory activity of Rauvolfia tetraphylla by measuring the thickness of rat paws and it was found that the plant has potent anti-inflammatory effect. In this study, root bark extract prepared from solvents; methanol, hexane, ethyl acetate and 70% ethanol were used at several concentrations (200 mg/kg, 400 mg/kg, 800 mg/kg for 70% ethanol; 100 mg/kg, 200 mg/kg, 400 mg/kg for other solvents) to be orally treated for rats. The results showed that all the dose concentration of both hydro-alcoholic (70% ethanol; 200 mg/kg, 400 mg/kg, 800 mg/kg) and methanolic (100 mg/kg, 200 mg/kg, 400 mg/kg) extract exhibited significantly better reduction (P<0.001) compared to drug vehicle treated control group. Also, ethyl acetate and hexane root bark extract exhibited significant reduction activity (P<0.001). This finding supports the folklore use of Rauvolfia tetraphylla as a treatment for inflammations and to further improvements and research in medicine related to inflammations (Rao et al., 2012).

According to Merlin *at al.* (2020) results obtained from aqueous root extract of *Rauvolfia tetraphylla* assessed by heat induced egg Albumin denaturation method carries potentially good anti-inflammatory activity that could provide somewhat relief for inflammation and to be further developed into an efficient antiinflammatory drug, thanks to its synergistic effect of phytochemicals such as flavonoids, phenols and terpenoids (Merlin et al., 2020).

Usina protein (Bovine serum Albumin) denaturation assay, anti-inflammatory activity of crude extracts (Chloroform, hexane, ethyl acetate and methanol) of fruit and leaf Rauvolfia tetraphylla were evaluated and optimized by utilizing Response Surface Methodology (RSM) by Nallasamy et al. (2024), aiming to identify a potential and safer anti-inflammatory drug as an alternative to existing conventional antiinflammatory drugs. Ethyl acetate fruit extract showed the best anti-inflammatory effect and its optimized extract possessed the promising effectiveness to treat inflammations in safer manner instead of using conventional antiinflammatory drugs. This study also validated the

traditional use of *Rauvolfia tetraphylla* for inflammatory conditions (Nallasamy et al., 2024).

# 7. CONCLUSION AND FUTURE DIRECTIONS

From the above study we conclude that Rauvolfia serpentina and Rauvolfia tetraphylla have many similarities in its phytochemistry and they have been used for treating almost same diseases and illness conditions such as hypertension, circulatory disorders, psychotic disorders, skin and eye diseases and elimination of intestinal worms. According to the findings, due to the endangered status of Rauvolfia serpentina, Rauvolfia tetraphylla can be used as perfect substitute candidate. In vitro а antimicrobial properties and anti-inflammatory of both plants suggest that they can be utilized in drug development to address antimicrobial resistance and to produce anti-inflammatory drugs with mild side effects in the future, but further in vitro and in vivo studies are required to evaluate their efficacy.

#### DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

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# **COMPETING INTERESTS**

Authors have declared that no competing interests exist.

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