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## **A REVIEW OF *RAUWOLFIA TETRAPHYLLA* L. : PHOTOCHEMISTRY AND MEDICINAL USES**

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### **ABSTRACT**

Human beings have encountered diseases since ancient times, and natural products were the primary source of treatments. Plants provide humans with a variety of basic needs, such as food, medicine, shelter, paper, and flavorings. *Rauwolfia tetraphylla* L., a genus of over a thousand evergreen trees and shrubs in the Apocynaceae family, is crucial in Indian traditional medicine. It is an important ethnobotanical plant with high therapeutic properties that is widely utilized by South Indian tribes. The plant is rich in secondary metabolites, the most prominent being reserpiline, ajmaline, yohimbine, isoreserpine, lankanescine, alstonine, deserpidine, rauvotetraphyllines, sarpagine, and aricine. The assembled data demonstrated that this plant has essential medicinal properties in snakebites, insecticides, high blood pressure, fever, helminthiasis, wound healing, cough, mental diseases, antioxidants, diabetes, anti-inflammatory, antimicrobial, anticancer, piles, vomiting, etc. The present review focuses on the updated information on the phytochemistry and medicinal use of *Rauwolfia tetraphylla*.

**Keywords:** *Rauwolfia tetraphylla* L., Phytochemicals, Anticancer, Phytochemistry

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### **1. Introduction**

*Rauwolfia tetraphylla*, an endangered evergreen pubescent shrub with a woody stem, is one of the most significant medicinal plants in the family Apocynaceae, growing up to 4-6 feet in height. It is commonly called Devil-Pepper, Wild Snake Root, or Be Still Tree. Leaves are unequal, 5–9 × 3–4 cm, pubescent, and usually found in whorls of 4. Flowers are cream-colored, about 5mm across, and found in terminal corymbose cymes. Fruits are ovoid, 2-seeded, 5–10 mm across, smooth, connected at the top, and purple when ripe. Flowering occurs throughout the year. It is cultivated on a commercial scale in India [1].

Humans have used plants since the beginning for a variety of uses, including food, shelter, dyes, and medicine. Plants have been extensively employed in particular formulations to treat a variety of diseases by traditional practitioners worldwide, as mentioned in Rigveda and Yajurveda, as well as in traditional Chinese medicine [2, 3]. Charles Plumier named the genus *Rauwolfia* in the year 1703. *R. tetraphylla*, a species facing extinction, is commonly known as Milkbush, Devil Pepper, and American serpentwood in English, being native to Mexico, Central America, and the West Indies. It is now grown in many countries, such as Pakistan, India, Sri Lanka, Bhutan, China, and Nepal, and is often cultivated as a medicinal plant. The plant is dispersed throughout India and is known by different vernacular names, such as Chandrabhaga in Hindi, kattamalpori in Malayalam, pampukaalaachchedi in Tamil, papataku in Telugu, patalagarudi in Odia, sarpanasini in Sanskrit, and gandhankuli in Bengali [4]. *R. tetraphylla* is rich in various secondary metabolites, including flavonoids, alkaloids, and terpenoids. The plant is used across the world for different ailments such as snakebite, insecticides, high blood pressure, fever, cough, mental diseases, antimicrobials, and piles, and since ancient times in south India, it has been famous for snake bites [5].

## 2. Ethnobotanical Importance

The Indian traditional medicine system, like the Chinese, Egyptian, and other systems, emphasizes the value of plants in healing numerous diseases. These traditional medicine systems are gaining popularity due to their safety, local availability, accessibility, low toxicity, cost-effectiveness, efficacy, and generally absence of side effects [6, 7]. Over the years, Mahatma Gandhi, the great Indian politician, was known to utilize *Rauwolfia* root to prepare a relaxing herbal tea. *Rauwolfia* is an Ayurvedic herb whose root is used against snake bites, scorpion bites, high blood pressure, insect bites, fever, ulcers, and mental illness, as mentioned in the Hindu sacred book Rigveda [8]. *R. tetraphylla* has significant importance in different traditional medicines worldwide. The plant resin has been claimed to be an antitussive agent, accelerate defecation, and, in addition to being used to cure hydropsy, the fruit juice is utilized as an ink replacement. The juice collected from the leaves is a remedy for eye problems, while the mixture is used to treat tooth infections [8, 9].

In the folk medicine of Kerala, the root is used during labor to increase uterine contractions and facilitate easy fetal ejection. Working women put crying babies to sleep by forcing them to sip breasts covered with root paste [10]. In Madhya Pradesh, root extract is used to treat stomach aches, and in Andhra Pradesh, in solution form, it is used against hypertension. *Rauwolfia* root extract, as a local medicine, is used to treat diarrhea and diabetes mellitus in west Bengal [11, 12, 13]. In Odisha, it is a common treatment for snake and reptile bites, and its roots are a local cure for malaria. In Madumalai, famous for Madumalai National Park in Tamil Nadu, *R. tetraphylla* as a whole plant is used for scorpion bites and its fruits in intestinal worms. In Odisha, Kerala, and Tamil Nadu, it is the local remedy for insect bites. *R. tetraphylla* is used as a substitute for *Rauwolfia serpentina*, which has a common use in circulatory disorders. Moreover, the leaf and root are said to be remedies for piles and sterility in the Eastern Ghats of Tamil Nadu [14, 15, 16, 17, 18, 19, 20].

The Paanar tribe of Kannur district, Kerala, uses the root juice collected from the root to cure muscle and joint pain and leaf solutions for cough, cold, and skin diseases. The Malapadaram tribe of Kerala's Wayanadu district takes root paste with milk or honey twice a day on an empty stomach for 21 days to treat mental illnesses, and for hypertension, it is given 23 times a day [10]. According to the Siddha system, which was prevalent in Tamil Nadu during the Indus Valley civilization, *Rauwolfia* was used as a sedative agent and for high blood pressure, which might be the reason why it is commonly used in Tamil Nadu. The significance of *Rauwolfia* is mentioned not only in Ayurveda but also in Chinese, Unani, Korean, Japanese, Myanmar, and African traditional medicines too [21, 22].

The use of *R. tetraphylla* is most prevalent in south India. *R. tetraphylla*, both as a whole plant and as a root, is used to cure impotence and boost libido in Bangladesh [23]. In Rajshahi district, Bangladesh, the plant is utilized as an antidote [24]. The same plant is used in Bangladesh's Jhenaidah and Chuadanga districts to treat snake bites and repel them [25]. It is also used to treat skin infections in Telangana [26].

## 3. Phytochemical Studies

Plants make a variety of compounds during metabolism that may be classified as primary and secondary metabolites. Secondary metabolites are derivatives of primary metabolites, such as alkaloids, flavonoids, and terpenoids, have multiple health benefits in pharmaceuticals, food additives, and cosmetic ingredients, and shield plants from insects, pathogens, and herbivores. The presence of these metabolites varies from plant to plant. Secondary metabolites are synthesized by four metabolic pathways: shikimic acid, malonic acid, mevalonic acid, and methylerythritol-phosphate [27, 28]. *R. tetraphylla* has a variety of secondary metabolites. Different separation techniques revealed the presence of alkaloids, flavonoids, polyesters, saponins, and phenolic

chemicals in various regions of the plant. *R. tetraphylla* leaf, stem, and root extracts contain a large number of alkaloids; reserpine is a key alkaloid discovered [29].

The roots of *R. tetraphylla* contain two alkaloids: canescine and pseudoyohimbine [30]. Raunescine and isoraunescine are two ester alkaloids uncovered from *R. tetraphylla* [31]. *R. tetraphylla* root contains an alkaloid, pseudoreserpine, which has hypotensive and sedative properties [32]. An alkaloid designated as recanescine with sedative and hypotensive properties was isolated from *R. tetraphylla* [33, 34]. Heterophyllin, an alkaloid, was discovered from *R. tetraphylla* roots [35]. Canembine, an alkaloid, was isolated from *R. tetraphylla* roots [36]. Djerassi et al., elucidated the structures of two alkaloids from the root of *R. tetraphylla*, viz., tetraphylline and tetraphyllicine [37].

Alkaloids such as ajmaline, ajmalieine, arieine, serpiline,  $\alpha$ -yohimbine, sarpagine, and reserpine were identified from *R. tetraphylla* roots and aerial parts [38]. N ( $\alpha$ )-Demethylaccedine, a novel sarpagine-type alkaloid, was isolated from *R. tetraphylla*'s stem bark [39]. A HPTLC examination found ajmalicine and reserpine in *R. tetraphylla* root [40]. Maurya et al. isolated alkaloids like isoreserpiline, 10-methoxytetrahydroalstonine, reserpiline, and  $\alpha$ -yohimbine from *R. tetraphylla* [41]. HPTLC study revealed that *R. tetraphylla* leaves contain quercetin, an important phytochemical [42]. *R. tetraphylla* leaves contain six indole alkaloids, including isoreserpiline, 10-methoxytetrahydroalstonine, 11-demethoxyreserpiline,  $\alpha$ -yohimbine, and reserpiline [43]. Panda et al., found different concentrations of reserpine in *R. tetraphylla*. Reserpine concentrations were found to be highest in the root, then in the stem and leaves [44].

#### 4. Pharmacological Properties

*R. tetraphylla* has unique pharmacological properties due to its diverse phytoconstituents, particularly alkaloids. This article provides a basic overview of the plant's pharmacological properties. The following list includes several reported actions.

##### 4.1 Antimicrobial and Antifungal Activity

*R. tetraphylla*'s root, leaf, and fruit effectively act as antibacterial and antifungal agents. *R. tetraphylla* acetone and ethanol extracts were found to be highly active against *Staphylococcus aureus*, as determined by the disc diffusion method and the fungus *Candida albicans* [45]. The crude extract of *R. tetraphylla* has shown remarkable antibacterial activity [46]. *R. tetraphylla* L. extract had significant antibacterial activity in vitro, as measured on sterile Mueller-Hinton agar plates [47]. The ethanoic leaf and root extracts of Rauwolfia were found to be effective against various pathogenic fungi [48, 49].

##### 4.2 Anti-inflammatory Activity

The anti-inflammatory efficacy of several *R. tetraphylla* root bark extracts provided orally for carrageenan-induced severe inflammation in rats was assessed in vitro and shown to be effective [50]. Another study found that the root bark of *R. tetraphylla* is an excellent anti-inflammatory drug [51].

##### 4.3 Anticancer Activity

Several investigations have demonstrated that *R. tetraphylla* is an effective cytotoxic agent against breast, lung, colon, and cervical cancer cells [52, 53]. *R. tetraphylla* leaf extract has demonstrated significant cytotoxic action against the chick embryo fibroblast cell line [54]. A study isolated and characterized a new labdane diterpene, which was tested for its anticancer activity against various breast cancer cell lines, including MCF-7, MDA-MB-468, MDA-MB-231, HeLa, Hep-2, A549, and leukemic T cells. The labdane diterpene turned out to have great anti-cancer properties [55]. In vitro experiments revealed that the methanolic extract of *R. tetraphylla* and other

examined plants have antioxidant properties. Among all the plants investigated, *R. tetraphylla* showed the highest antioxidant potential [56]. Furthermore, *R. tetraphylla* has demonstrated potent anticancer activity against a cervical cancer cell line [57]. A recent study found substantial cytotoxic effects of *R. tetraphylla* extract against the MCF-7 breast cancer cell line [58].

#### 4.4 Cardiovascular Activity

In a study conducted in 1949, *Rauwolfia* was helpful in reducing both systolic and diastolic blood pressure in hypertension cases [59]. Gadhvi et al., studied *R. tetraphylla*'s antihypertensive activity in rats, finding that methanolic root extract significantly reduced systolic pressure after administering sodium chloride [60]. In another study, *R. tetraphylla* was proven to be an effective cardio-protective agent [61]. Reserpine, the main alkaloid in *Rauwolfia*, is an efficient and secure treatment for hypertension when taken in suitable, low dosages [62].

#### 4.5 Antiparasitic Activity

The methanolic leaf extracts of *R. tetraphylla* reduced the mortality of the target parasite, *Setaria cervi* [63]. According to recent in vitro research, curan-17-oic acid, 18, 19-secoyohimban, and reserpiline are encouraging inexpensive and easily accessible biological options for developing and producing macrofilaricidal medicines [64]. Furthermore, *R. tetraphylla* ethanolic root extract has shown positive anti-trypanosomal activity in Panama [65].

#### 4.6 Antioxidant Activity

The antioxidant capacity of *R. tetraphylla* leaves and fruits was examined. The overall antioxidant capacity was determined to be greatest in leaves compared to fruits [66]. In an in vitro investigation, *R. tetraphylla* demonstrated effective antioxidant activity [67]. Furthermore, leaves from five *Rauwolfia* species from the southern Western Ghats were selected to examine their antioxidant activities by employing different in vitro models like total antioxidant capacity, 1,1-diphenyl-2-picryl hydrazyl (DPPH) radical scavenging activity, superoxide anion scavenging activity, and reducing power. *R. tetraphylla* displayed high antioxidant activity [68].

### 5. Conclusion

The review indicated that *Rauwolfia tetraphylla* contains significant phytochemicals with promising pharmacological applications. The plant's phytoconstituents, including alkaloids, flavonoids, phenols, terpenes, tannins, and triterpenes, have led to its usage in conventional healthcare worldwide. All components of the plant are used to cure various ailments caused by bacteria, fungus, parasites, and cancer. It is also used to treat inflammation, antioxidants, hypertension, and skin problems. Furthermore, it should be noted that *R. tetraphylla* is an endangered species, so efforts should be made to preserve and propagate it. Hence, more investigation should be conducted into the isolation, examination, and pharmaceutical evaluation of *R. tetraphylla*'s isolated pure bioactive constituents.

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