OPEN ACCESS PEER REVIEW
DOI: https://doi.org/10.52756/boesd.2024.e03.002

Chapter- 2

Exploring the Riches of *Rauvolfia serpentina*: Botany, Pharmacology, and Conservation Perspectives

Bishop Debnath[1], Suparna Sanyal Mukherjee[2] and Saikat Kumar Basu[3]*

Keywords: *Rauvolfia serpentina*, Sarpagandha, Palynology, Pharmaceutical, Ethnobotanical, Conservation, Nanobiotechnology, Alkaloids, Reserpine, Serpentina, Traditional medicine

Abstract:

Rauvolfia serpentina (L). Benth. ex-Kurz, commonly known as Sarpagandha, is a vital medicinal plant native to the Indian subcontinent and Southeast Asian countries. This comprehensive review explores the botanical description, palynology, pharmaceutical properties, ethnobotanical practices, applications in nanobiotechnology, *in vitro* propagation, and bioinformatics associated with this plant. Belonging to the Apocynaceae family, *R. serpentine faces endangerment due to the overexploitation of* its bioactive constituents, which prompts the need for sustainable conservation strategies. The Apocynaceae family, distributed worldwide, encompasses approximately 400 genera and 5000 species. Among the six Indian species of the *Rauvolfia* genus, *R. serpentina* and *R. tetraphylla* are particularly valued for their medicinal properties, with R. *serpentina* facing extinction and listed under CITES Appendix II. This study delves into the phytochemical composition of *R. serpentina*, emphasizing the therapeutic virtues of its alkaloids, including the renowned reserpine, ajmaline, ajmalicine, serpentina, rescinnamine, deserpidine and yohimbine. These alkaloids contribute to the plant's efficacy in treating hypertension, mental disorders, and snake bites. Pollen morphology, ayurvedic pharmacodynamics, and ethnoveterinary practices are also discussed, highlighting the plant's diverse applications in traditional medicine. The mineral composition of *R. serpentina* suggests potential therapeutic roles in managing diabetes and aiding blood coagulation. Recent advancements in *in vitro* propagation techniques are explored to address challenges in commercial cultivation. Furthermore, the plant's role in synthesizing nanoparticles and the existence of SerpentinaDB, a structured compilation of plant-derived molecules from *R. serpentina*, provide avenues for future research and development. The present sequel has been emphasized and counteracted with the multifaceted exploration of R. serpentine with its significance as a traditional medicine, pharmaceuticals, and conservation efforts among the society at large**.** Because of overharvesting and habitat destruction, the *Rauvolfia* genus of medicinal plants is experiencing a decline in population, making conservation efforts essential. Protecting habitat and using sustainable farming methods are crucial to maintaining these priceless species and their ecological significance.

Abbreviations used:

AgNPs: Silver Nanoparticles; CITES: Convention on International Trade in Endangered Species of Wild Fauna and Flora; NPACT: Naturally Occurring Plant-based Anti-cancer Compound-Activity; PDMs: Plant-Derived Molecule

Introduction:

[1] **Bishop Debnath**
Agriculture and Food Engineering, IIT Kharagpur, West Medinipur, West Bengal, India 712302
[2]**Suparna Sanyal Mukherjee**
Department of Education, Seacom Skills University, Kendrangal, Bolpur, Birbhum, West Bengal India 731236
Saikat Kumar Basu*
[3]Executive Research Director, PFS, Lethbridge Alberta, Canada T1J 4B3
E-mail: saikat.basu@alumni.uleth.ca; Orcid iD: http://orcid.org/0000-0001-7305-4817
***Corresponding Author**: saikat.basu@alumni.uleth.ca

Nithar Ranjan Madhu, Tanmay Sanyal, Koushik Sen, Biswajit (Bob) Ganguly & Roger I.C. Hansell (eds.), A Basic Overview of Environment and Sustainable Development [Volume: 3]. ISBN: 978-81-969828-3-6, pp:20-55 ; Published online: 08th August, 2024

Rauvolfia serpentina, also known as **Sarpagandha** in Hindi, is a remarkable **Ayurvedic herb** with a rich history of use. Let's explore its fascinating properties:

Botanical Description:

Scientific Name: *Rauvolfia serpentina*

Common Names:

English: Indian Snake Wood, Serpentina Wood

Hindi: Sarpagandha, Chandrabagha, Chota chand

Sanskrit: Sarpagandha, Chandarmar

Habitat: Native to India, Burma, Sri Lanka, China, and Pakistan, it thrives in moist forests.

Plant Features:

An evergreen perennial undershrub.

Grows up to around 2 feet in height.

Oval leaves in whorls of 3, with paler green below and dark green above.

Irregular corymbose white flowers with a violet tinge.

Oval fleshy fruits are around 1 cm long, turning shiny purple-black when ripe.

Milky sap.

Medicinal Parts: The roots of *Rauvolfia serpentina* are used for their medicinal properties.

Medicinal Uses:

Antihypertensive: Used for managing high blood pressure (hypertension).

Sedative and Antianxiety: Helps calm the central nervous system, reducing anxiety and irritability.

Antipsychotic: Used in mental disorders alongside Jatamansi (Spikenard).

Hypnotic: Aids in treating insomnia (sleeplessness).

Rauvolfia serpentina (L). Benth. ex-Kurz., also known as Sarpagandha, is an essential medicinal plant native to the Indian subcontinent and South East Asian countries, generally in the region having annual rainfall of 200 to 250 cm, up to an altitude of 1000 m and in deep fertile soil rich in organic matter (Dey and De, 2010). The plant is distributed worldwide in the region of the Himalayas, the Indian peninsula, Burma, Indonesia, and Sri Lanka belongs to the Apocynaceae family and is commonly known as Sarpagandha, Chandrabagha, Snake root plant, Chotachand, Chandrika, and Harkaya (Ojha and Mishra, 1985). The plant has several characteristics: tuberous roots with pale brown cork; Leaves in whorls of three, with dark green color above and pale green color below; white, pinkish, or red flowers (Figure 1) occurring in whorls; Small, oval fruits (Deshmukh et al., 2012).

Certain plants' roots, leaves, and juice contain various secondary metabolites, including indole alkaloids, which have medicinal properties (Flores et al., 1987). These compounds are essential for maintaining homeostasis and have the potential to produce specialty chemicals (Devi and Sarma, 2021). Alkaloids, a type of secondary metabolite, are found in various plant families and have diverse bioactivities (Islam, 2015).

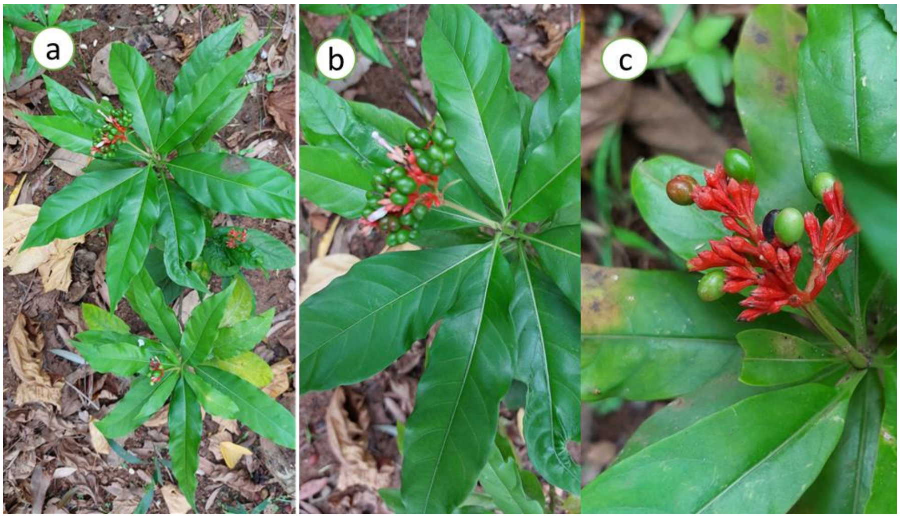

Figure 1. a) Shoot of *R. serpentina*; b) fruit set and fully grown leaves of *R. serpentina*; c) flowering set in the inflorescence of *R. serpentina*. (Photo credit: Saikat Kumar Basu)

Medicinal herbs, which are rich sources of secondary metabolites, have been used in traditional medicine for thousands of years (Sreenivasulu, 2015). Medicinal plant extracts, integral to traditional medicine, exhibit efficacy against diseases, serving as a source for drug discovery; notably, 65% of the Indian population relies on phytomedicines, and approximately 80% of the global population depends on traditional medicines, as per the World Health Organization (Boateng et al., 2016).

Importance of medicinal plants to the ecosystem and from the points of sustainability

Medicinal plants hold significant importance both ecologically and in terms of sustainability. Here are the key points:

Ecological Importance:

Biodiversity: Medicinal plants contribute to biodiversity, supporting various forms of life, from microorganisms to larger animals, by providing food and habitat.

Soil Health: Many medicinal plants help maintain soil health by preventing erosion, improving soil structure, and adding nutrients through leaf litter.

Pollination: These plants attract pollinators such as bees, butterflies, and birds, aiding in the reproduction of numerous plant species and maintaining ecological balance.

Water Cycle: They regulate the water cycle by maintaining moisture levels in the soil and contributing to groundwater recharge.

Sustainability:

Alternative Medicine: Medicinal plants offer an alternative to synthetic drugs, often with fewer side effects and lower costs, promoting health and wellness sustainably.

Economic Benefits: Sustainable harvesting and cultivation of medicinal plants can provide economic opportunities for local communities, reduce poverty, and encourage conservation efforts.

Resource Conservation: Utilizing medicinal plants can reduce the demand for conventional pharmaceuticals, often requiring significant resources and energy.

Cultural Preservation: Many indigenous and local communities have a rich knowledge of medicinal plants, and their sustainable use helps preserve cultural heritage and traditional practices.

Climate Change Mitigation: Medicinal plants can sequester carbon, helping mitigate the effects of climate change. Sustainable practices ensure that these benefits are maintained over the long term.

Medicinal plants play a crucial role in maintaining ecological balance and offer sustainable alternatives for health and economic benefits, supporting both environmental and human well-being.

Why do we need to conserve and protect medicinal plants?

Conserving and protecting medicinal plants is essential for several reasons:

- Biodiversity Preservation: Medicinal plants are a critical component of biodiversity. Protecting them helps maintain ecological balance and the health of ecosystems.
- Medical and Pharmaceutical Value: Many modern medicines are derived from plant compounds. Preserving these plants ensures a continued supply of natural resources for developing new drugs and treatments.
- Cultural and Traditional Importance: Medicinal plants hold significant value in many cultures and traditional medicine systems. Protecting them helps preserve cultural heritage and traditional knowledge.
- Economic Benefits: Medicinal plants contribute to the economy through their use in pharmaceuticals, cosmetics, and natural health products. Sustainable harvesting and conservation can provide ongoing economic benefits to communities.
- Environmental Health: Medicinal plants often play vital roles in their ecosystems, such as soil stabilization, water purification, and providing habitat for other species. Their conservation supports overall environmental health.
- Climate Change Resilience: Diverse plant species can contribute to ecosystem resilience against climate change by maintaining genetic diversity and supporting various ecological functions.

Overall, conserving and protecting medicinal plants is crucial for health, environmental stability, cultural heritage, and economic sustainability.

How can we conserve medicinal plants like *Rauvolfia*?

Conserving medicinal plants like *Rauvolfia* involves several strategies:

- Habitat Protection: Protect natural habitats where *Rauvolfia* grows. This can be done by establishing protected areas like national parks or reserves.
- Sustainable Harvesting: Implement guidelines for sustainable harvesting to ensure that plants are not overexploited. This includes limiting the amount of plant material that can be collected and ensuring that collection methods do not harm the plants.
- Cultivation: Encourage the cultivation of *Rauvolfia* in botanical gardens, farms, and community gardens. This reduces pressure on wild populations.
- Education and Awareness: Raise awareness among local communities and stakeholders about conserving *Rauvolfia* and other medicinal plants. Education programs can help promote sustainable practices and discourage illegal harvesting.
- Research and Documentation: Conduct research on *Rauvolfia* to understand its ecology, distribution, and propagation methods. Documenting traditional knowledge and uses can also aid in conservation efforts.
- Legal Protection: Enforce laws and regulations that protect medicinal plants from overharvesting and habitat destruction. This can include implementing policies at local, national, and international levels.
- Ex-situ Conservation: Establish seed banks and tissue culture facilities to conserve *Rauvolfia* genetic material outside its natural habitat. This can provide a backup in case wild populations are threatened.
- Community Involvement: Engage local communities in conservation efforts by involving them in managing and protecting *Rauvolfia* habitats. Providing incentives for conservation can also be effective.

By combining these strategies, we can help ensure the survival and sustainable use of *Rauvolfia* and other valuable medicinal plants.

Can we create a sustainable environment by conservation of important medicinal plants in India?

Yes, creating a sustainable environment by conserving important medicinal plants in India is possible and highly beneficial. Here are some key ways this can be achieved:

- Biodiversity Preservation: Conserving medicinal plants helps maintain biodiversity, which is crucial for ecosystem stability and resilience. A diverse range of species ensures natural sustainability for all life forms.
- Ecological Balance: Medicinal plants play essential roles in ecosystems, providing habitat and food for various organisms. Protecting these plants supports ecological balance and promotes healthy ecosystems.

- Cultural Heritage: Many medicinal plants have been used in traditional Indian medicine systems like Ayurveda for centuries. Conserving these plants helps preserve cultural heritage and traditional knowledge.
- Sustainable Livelihoods: Conservation initiatives can provide sustainable livelihoods for local communities. By responsibly cultivating and harvesting medicinal plants, communities can benefit economically without depleting natural resources.
- Climate Change Mitigation: Plants, including medicinal ones, act as carbon sinks, absorbing CO2 from the atmosphere. Conservation efforts can mitigate climate change by preserving and restoring plant populations.
- Scientific Research and Medicine: Protecting medicinal plants ensures they remain available for scientific research and potential new drug discoveries, benefiting global health.

➢ To effectively conserve medicinal plants, strategies could include:

- Protected Areas: Establishing reserves and protected areas where medicinal plants can thrive without the threat of habitat destruction.
- Sustainable Harvesting: Implementing guidelines and practices for the sustainable collection of medicinal plants to prevent overexploitation.
- Community Involvement: Engaging local communities in conservation efforts, providing education, and promoting sustainable agricultural practices.
- Legislation and Policy: Enforcing laws and regulations that protect medicinal plants from illegal trade and habitat destruction.
- Research and Documentation: Conducting research to document medicinal plant species, their uses, and conservation status, aiding in informed conservation strategies.

By integrating these approaches, India can create a sustainable environment that supports both ecological health and human well-being by conserving its valuable medicinal plant resources.

What is the scale of commercial needs for *Rauvol*plants in both Indian and international markets, and how do the market dynamics look?

Rauvolfia, particularly *Rauvolfia serpentina*, is a medicinal plant with significant commercial demand due to its therapeutic properties. It is commonly known as Indian Snakeroot or Sarpagandha. Here is a breakdown of its demand in Indian and international markets:

Indian Market

1. Pharmaceuticals: *Rauvolfia* is widely used in traditional Ayurvedic medicine and modern pharmaceuticals for its antihypertensive, sedative, and tranquilizing properties.
2. Herbal Medicine: There is a growing demand for natural and herbal remedies in India, boosting the market for plants like *Rauvolfia*.

3. Research and Development: Various research institutions and pharmaceutical companies are involved in studying *Rauvolfia*'s medicinal properties, driving demand.
4. Government Initiatives: The Indian government promotes the cultivation and export of medicinal plants, including *Rauvolfia*, to support traditional medicine systems and farmers.

International Market

1. Pharmaceuticals: International pharmaceutical companies use *Rauvolfia* alkaloids, particularly reserpine, to treat hypertension and mental disorders.
2. Herbal Supplements: There is a significant market for herbal supplements in the US, Europe, and other regions, where *Rauvolfia* is marketed as a natural remedy.
3. Regulatory Approvals: *Rauvolfia*-based medications are approved and used in many countries, contributing to stable demand.
4. Natural Products: Growing consumer preference for natural and organic products boosts the global demand for medicinal plants like *Rauvolfia*.

Market Dynamics

1. Cultivation and Supply: *Rauvolfia*'s supply depends on its cultivation, which requires specific climatic conditions. Any fluctuation in supply can affect the market.
2. Sustainability Concerns: Overharvesting and habitat destruction threaten *Rauvolfia* populations, prompting the need for sustainable cultivation practices.
3. Regulations and Standards: Different countries have varying regulations for medicinal plants, affecting the export and import dynamics.

Overall, Rauvolfia's commercial need is driven by its medicinal applications, which are in strong demand in both domestic and international markets. Factors like cultivation practices, regulatory frameworks, and consumer preferences for natural and herbal products influence the market.

In terms of sustainability and ecology, medicinal plants are essential. The salient points are as follows:

- Biodiversity: By offering food and habitat, medicinal plants support various life forms, from microscopic creatures to giant animals.
- Soil Health: A variety of therapeutic plants contribute to preserving soil health by reducing erosion, enhancing soil structure, and supplying nutrients through leaf litter.
- Pollination: By drawing pollinators like bees, butterflies, and birds, these plants help to reproduce a wide variety of plant species and preserve ecological equilibrium.
- Water Cycle: They help control the water cycle by preserving soil moisture levels and assisting in groundwater recharge.

- Sustainability: Alternative Medicine: Medicinal plants can sustainably promote health and wellness as a cheaper, more side-effect-free substitute for synthetic medications.
- Economic Benefits: Local populations can benefit economically from the sustainable collection and cultivation of medicinal plants, which lowers poverty and promotes environmental protection.
- Resource conservation: Therapeutic plants can decrease the need for traditional pharmaceuticals- whose pharmaceuticals- whose hose production frequently requires substantial energy and consumption- consumption- can
- Cultural Preservation: The sustainable use of medicinal herbs, which many indigenous and local groups are knowledgeable about, contributes to preserving cultural history and customs.
- Mitigation of Climate Change: By sequestering carbon, medicinal plants can lessen the consequences of climate change. Sustainable methods ensure the long-term sustainable methods ensure long-term maintenance of these benefits.

The plant's propagation is hindered by poor seed viability and low germination rates, leading to its endangerment due to prolonged overexploitation for commercially valuable bioactive constituents. Consequently, *in vitro* propagation is a means to conserve germplasms, sustainably exploit medicinal compounds, and optimize elite genotypes for genetic and phytochemical uniformity, fostering enhanced secondary metabolite production (Pathania et al., 2015). Topics such as botanical description, palynology, pharmaceutical properties, ethnobotanical practices, applications in nanobiotechnology, *in vitro* propagation, and bioinformatics are explored here. The overview of selected research works and their digests is discussed in Table 1.

Table1. Summary of selected research works on *Rauvolfia serpentina*.

Selected research works on *Rauvolfia serpentina*	References
Reserpine is one of many alkaloids in the plant.	(Monachino, 1954)
R. serpentina therapy in high blood pressure states has been reviewed up to the present time.	(Vakil, 1955)
Active chemical and pharmacological interest in *R. serpentina* have resulted in discovering several new alkaloids.	(Phillips and Chadha, 1955)
DNA bar coding provides new perspectives for forensic identification of Indian snakeroot.	(Eurlings et al., 2013)
Nodal cultures of sarpagandha could be maintained for nine months at 25°C by replacing cotton plugs with polypropylene caps as enclosures for culture tubes.	(Sharma and Chandel, 1992)
The Indian government was forced to impose restrictions on its exports to prevent complete extermination.	(Dutta et al., 1963)

Genetic fidelity of the regenerated plants analyzed by 18 ISSR markers. ISSR marker HB-12 showed a polymorphic band among the callus regenerants.	(Saravanan et al., 2011)
Vomilenine and reserpine were characterized from the analysis of the hairy roots of *R. serpentina.*	(Madhusudanan et al., 2008)
The flowers of *Agrobacterium rhizogens* mediated transformed plants were more delicate and less pigmented than the mature normal plants.	(Benjamin et al., 1993)
Major phytochemical constituents of *R. serpentina* are root indole alkaloids	(Pathania et al., 2015)
A portion of membrane proteins extracted from *Rauvolfia serpentina* facilitated the conversion of labeled strictosidine into sarpagan-type alkaloids. The enzymatic activity demonstrated a dependency on NADPH and molecular oxygen, implying that the sarpagan bridge enzyme might belong to the cytochrome P450 family.	(Ruppert et al., 2005)
Key finding proposes a novel biosynthetic pathway in *Rauvolfia*, indicating that the reduction of vomilenineen route to antiarrhythmic ajmaline may proceed through an alternative sequence of biosynthetic steps, thereby expanding the structural diversity within the monoterpenoid indole alkaloid family.	(Geissler et al., 2016)
Enzyme responsible for the formation of N-methylajmaline is found in *Rauvolfia serpentina*.	(Cázares-Flores et al., 2016)
Strictosidine synthase, an enzyme found in the Indian medicinal plant *R. serpentina*, plays a critical role in the indole alkaloid ajmaline biosynthetic pathway.	(Ma et al., 2006)
Reserpine is used as an antihypertensive and sedative agent.	(Srivastava et al., 2021)
In India, *R. serpentina* has been traditionally employed to address snakebites, manage hypertension, and treat mental illnesses. Recognized for its sedative properties, it is utilized to regulate high blood pressure and specific manifestations of mental disorders.	(Glynn, 1955)
R. serpentina has been employed since ancient times, predating the Vedic period, to address various health issues, including snake bites, insect stings, hypertension, insomnia, psychological disorders, gastrointestinal issues, epilepsy, wounds, fever, and schizophrenia.	(Vakil, 1955)
The fibrous roots are more active than the interior of the main taproot.	(Akbar, 2020)

The International Union for Conservation of Nature (IUCN) Red List classifies *Rauvolfia serpentina*, also referred to as Indian snakeroot or sarpagandha, as "Endangered" in several areas, including sections of India. Its endangered status mainly causes habitat damage, overharvesting for medicinal purposes, and a lack of sustainable production methods. Conservation initiatives are required to guarantee the continued existence of this priceless medicinal plant in India and South Asia.

Answer to the "why conservation":

It is crucial to preserve and safeguard medicinal plants for several reasons:

- Preserving Biodiversity: One essential aspect of biodiversity is the presence of medicinal plants. By keeping them safe, we can support the health of ecosystems and ecological equilibrium.
- Medical and Pharmaceutical Value: Plant-based chemicals are the source of many contemporary medications. Keeping these plants alive guarantees a steady supply of natural resources to create novel medications and therapies.
- Cultural and Traditional Importance: Many cultures and traditional medical systems prioritize medicinal herbs. By keeping them safe, traditional knowledge and cultural legacy are preserved.
- Economic Benefits: Medicinal plants used in cosmetics, pharmaceuticals and natural health products boost the economy. Sustainable conservation and harvesting practices can benefit communities economically throughout time.

Key-points to the survival strategies regarding medicinal plants:

Recreating a sustainable ecosystem in India by conserving significant medicinal plants is feasible and advantageous. Here are a few crucial methods for making this happen:

- Preservation of Biodiversity: Medicinal plant conservation contributes to biodiversity preservation, which is essential for the resilience and stability of ecosystems. A wide variety of species guarantees all life forms natural sustainability.
- Ecological Balance: Medicinal plants are vital components of ecosystems, offering food and shelter to various creatures. Preserving these plants helps maintain ecological equilibrium and fosters robust ecosystems.
- Cultural Heritage: For millennia, Ayurvedic and other traditional Indian medical systems have extensively and extensively used various medicinal herbs. The conservation of these plants aids in preserving cultural history and traditional knowledge.
- Sustainable Livelihoods: Local communities may benefit from conservation efforts by obtaining sustainable means of subsistence. By ethically growing and harvesting medicinal plants, communities can profit monetarily without diminishing natural resources.

- Mitigation of Climate Change: Plants, especially medicinal ones, take CO_2 from the atmosphere by acting as carbon sinks. Conservation activities can help mitigate the effects of climate change by preserving and restoring plant populations.
- Scientific Research and Medicine: By safeguarding medicinal plants, we can make sure they are available for future drug discoveries and scientific research, ultimately improving world health.

Among the tactics that could be used to protect medicinal plants successfully are:

1) Reserves and protected areas should be established so medicinal plants can flourish without fear of habitat loss. 2) Sustainable harvesting involves Implementing policies and procedures for the ethical gathering of medicinal plants to avoid overuse.

- Community Involvement: Educating locals, encouraging sustainable farming methods, and involving them in conservation initiatives.
- Law and Policy: Upholding rules and laws that shield medicinal plants from illicit commerce and damage to their ecosystem.
- Research and Documentation: To support well-informed conservation efforts, research is being done to document medicinal plant species, their applications, and their current state of conservation.

By integrating these strategies, India can preserve its priceless medicinal plant resources while fostering a sustainable environment that promotes ecological health and human well-being.

Answer to the "why conservation":

Indian snakeroot is a medicinal plant that requires both in-situ and ex-situ conservation techniques to be conserved and multiplied. Here are a few such tactics:

Conservation in-situ

Create and preserve protected areas where *Rauvolfia serpentina* naturally occurs, such as national parks, wildlife sanctuaries, and biosphere reserves (Surendran et al., 2021).

- Sustainable Harvesting: To avoid overexploitation, policies and procedures for sustainable harvesting should be implemented.
- Community Involvement: Ensure the local people know the value of *Rauvolfia* and reap the rewards of its preservation by involving them in conservation initiatives through educational and incentive programs.

Restoring damaged habitats where *Rauvolfia* thrives typically will increase the species' chances of surviving and proliferating.

In situ Preservation

Establish and preserve botanical gardens and seed banks to preserve ex situ *Rauvolfia* plants and seeds (Singh et al., 2007).

- Tissue Culture and Micropropagation: Use tissue culture and micropropagation procedures to grow many plants in a controlled environment.
- Farm Cultivation: Encourage *Rauvolfia*'s growth by giving farmers the tools and expertise they need to cultivate it sustainably.

Investigation and Creation

1) Genetic Research: Genetic research was needed to comprehend the diversity and adaptability of *Rauvolfia* species and generate more hardy variants.
2) Phytochemical Research: To determine and improve medicinal potential, the phytochemical characteristics must be looked at.

Law and Policy

- Regulatory Framework: Create and implement rules to safeguard *Rauvolfia* against unauthorized trading and overexploitation.
- Intellectual Property Rights: Ensure equitable benefit-sharing and intellectual property rights for traditional knowledge connected to Rauvolfia (Chakrabarti, 2014).

Consciousness and Instruction

- Public Education Campaigns: Hold educational programs to inform the general public about the value of protecting medicinal plants like *Rauvolfia*.
- Educational Initiatives: Incorporate conservation education into school and community initiatives to instill a conservation mindset in children early on.

Global Collaboration

- Collaborative Initiatives: Take part in global cooperative initiatives for the preservation and sustainable utilization of medicinal plants.
- Information Exchange: Provide global conservation networks and organizations with information and best practices.

By collectively implementing these tactics, we may contribute to the long-term preservation and propagation of *Rauvolfia serpentina* and other important medicinal plants for future generations.

The Apocynaceae family and medicinal significance of studied *Rauvolfia* spp.:

Apocynaceae Juss., situated within Gentianales (asterids, lamiids), encompasses approximately 400 genera and 5000 species distributed in tropical and subtropical regions worldwide (Endress, 2004; APG IV 2016). The family is classified into five subfamilies: Rauvolfioideae (cosmopolitan; 10 tribes/83 genera; 915 species), Apocynoideae (cosmopolitan; eight tribes/80 genera; 822 species), Periplocoideae (Old World; 33 genera), Secamonoideae (Old World; eight genera), and Asclepiadoideae (cosmopolitan; four tribes/172 genera) (Endress et al., 2014; Endress and Bruyns, 2000). Numerous taxonomic, evolutionary, and phylogenetic studies have been conducted on Apocynaceae, along with investigations into pollen morphological characteristics (Furness, 2007; Van Der Ham et al., 2001; Van Der Weide and Van Der Ham, 2012). *Rauvolfia* (Rauvolfioideae: Apocynaceae) represents a genus comprising evergreen trees and shrubs, encompassing around 85 species found across Europe, Africa, Asia, Australia, and Central and South America (Mabberley, 2017) varying in their flowering periods (Table 2). Renowned for the phytochemical 'reserpine', these *Rauvolfia* species have been extensively utilized in the treatment of hypertension (Sahu, 1983). The plants' various parts are employed in traditional medicine to address human ailments, as documented in studies by (Dutta and Virmani, 1964; Ebadi, 2007 ; Sihag and Wadhwa, 2011).

This application aligns with the broader use of herbal medicine as a secure and time-honored therapeutic approach for managing diseases and infections. Among the six Indian species within the *Rauvolfia*genus (*R. serpentina*, *R. tetraphylla*, *R. hookeri*, *R. micrantha*, *R. verticillata*, and *R. sumatrana*), only *R. serpentina* and *R. tetraphylla* are found in the Gangetic Plain of Central India and these two species are highly valued for their medicinal properties and are regularly harnessed in the pharmaceutical industry for drug formulation; unfortunately, rampant exploitation has driven them perilously close to extinction in their natural habitats. The population decline of *R. serpentina* has led to its inclusion in Appendix II of the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES). The remaining four *Rauvolfia* species, while outside the focus of our current study, also face limitations in population size.

Table 2. Flowering seasons concerning different *Rauvolfia* species.

Species	*Rauvolfia serpentina* (L.) Benth. ex Kurz	*Rauvolfia tetraphylla* L.	*Rauvolfia hookeri* S.R. Sriniv. & Chitra	*Rauvolfia micrantha* Hook.f.	*Rauvolfiaverticillata* (Lour.) Baill.	*Rauvolfia sumatrana* Jack
Flowering season	October-December	October-December	Whole year	Whole year	June-September	April-December

Interestingly, except the *R. sumatrana* Jack, which is exclusively native to Andaman and Nicobar Islands, all other species are present in Tamilnadu (Sinha, 1999; 2012). *R. tetraphylla* is present in Madhya Pradesh, Uttar Pradesh, Haryana, Orissa, Punjab, and Tamil Nadu (Matthew, 1983). *R. serpentina*, also known as Indian snakeroot or devil pepper, originates from Southeast Asia's moist, deciduous forests, including India, Burma, Bangladesh, Sri Lanka, and Malaysia. Employed in traditional medicine, particularly in Kerala's Ayurveda (Blackwell, 1990), this species is experiencing a rapid decline in its natural habitat due to various ecological and biological factors. These include its limited distribution, small endemic populations, constraints in pollination, poor seed viability, and substantial anthropogenic pressure on forest land.

Consequently, *R. serpentina* is now categorized as rare and endangered (Sihag and Wadhwa, 2011). Despite the challenges, seed propagation is considered the most effective method for commercial cultivation, although it faces low and variable seed production (Bhadwar et al., 1956). *R. tetraphylla*, commonly called still tree or devil pepper (Rao, 1956), is native to Mexico, Central America, the West Indies, and northern South America. It has become naturalized in tropical regions worldwide, including Australasia, Indochina, and India; widely cultivated for ornamental purposes and traditional medicine use; various parts of the plant, such as the root, fruit, and leaves, are utilized in diverse forms like paste, powder, decoction, and juice. *R. tetraphylla* holds significance in traditional medicine, particularly for treating snakebites, with its leaves serving as an anti-venom and blood pressure remedy in Bogota, Colombia (Bussmann et al., 2018). Additionally, the peasants in San Jacinto, Northern Colombia use the leaves to alleviate tension as ethnomedicine (Bonzani, 1999).

Pollen morphology:

Rao and Shukla (1975) explored the pollen morphology of *R. serpentina*, highlighting the distinctive oblate shape as a characteristic feature of the species. Erdtman (1952) attributed the oblate amb of the single species he examined, *R. verticillata*. However, subsequent observations revealed this characteristic in other species of *Rauvolfia*. *R. serpentina* possesses a large pollen size of 47.75 ± 52 mm concerning other members of the Apocynaceae family (Tripathi et al., 2022). The formation of ectocolpi is an essential distinguishing feature for sorting species of *Rauvolfia*. The ectocolpi thickening is longer in *R. serpentina* (15.54 mm), forming a concave margin at either side of the ectocolpi (Erdtman, 1952). In R. *serpentina*, the exine exhibits a broad and thick structure, allowing for clear differentiation into a sexine and a nexine layer. The sexine's tectum presents a smooth surface without ridges and furrows. As it approaches the ectocolpi, the sexine layer appears slightly thinner, forming a wavy structure. The sexine and nexine maintain a consistent thickness, creating a seamless layer. Conversely, in *R. tetraphylla*, the tectum displays a smooth surface, and distinguishing between the sexine and nexine layers is impossible (Tripathi et al., 2022).

Agronomic practices:

For best growth, *Rauvolfia*, also called sarpagandha or Indian snakeroot, needs particular agronomic conditions. The following are essential elements for commercial *Rauvolfia* growth:

- Climate: Warm, humid climates with temperatures between 25 and 30 degrees Celsius. For rainfall, 1500-2500 mm of precipitation must fall yearly. In regions with lower rainfall, supplemental irrigation is required.
- Soil: Fertile, well-drained sandy loam or clay loam soils are ideal for *Rauvolfia* growth, optimal pH ranges from 6.0 to 7.5, which is slightly acidic to neutral. An abundance of organic

matter is desirable in soil. Growth is aided by adding compost or well-decomposed farmyard manure (Sihag and Wadhwa, 2011).

- Propagation: Fresh seeds are recommended for optimal germination. Gibberellic acid (GA_3) pretreatment increases the rate of germination. Both root and stem cuttings are necessary for propagation.
- Season: In rain-fed regions, it is best to plant at the start of the monsoon season.
- Plants should be spaced 30-45 cm apart, and rows should be 60-75 cm apart. Avoid water logging.
- Mulching: Regular weeding is required to reduce competition for moisture and nutrients. Mulching inhibits weed growth and helps the soil retain moisture.
- In the fertilization process, organic fertilizers, such as farmyard manure or compost, should be used. When necessary, balanced NPK fertilizers should be added as a supplement (Saravanan et al., 2019).

Phytochemicals and Therapeutic Virtues of *R. serpentina*:

A renowned medicinal plant in Indian and Chinese traditional medicine, it has a history of use dating back almost 3000 years, known as Sarpagandha (Swami et al., 2022). This tropical shrub, ranging from 15-60 cm in height, is a flowering plant with white and violet flowers, and its medicinal properties stem from diverse phytochemicals present in its root, stem, and leaves; the root, containing the highest concentration of these phytochemicals, is categorized into six major groups, including carbohydrates, lipids, phenolics, terpenoids, alkaloids, and other nitrogen-containing compounds (Pandey et al., 2016).

Extensive research has focused on its alkaloids' chemistry and therapeutic applications, revealing notable pharmacological effects such as blood pressure reduction and sedative actions (Nair et al., 2012). Clinical trials have successfully explored its use in neuropsychiatry, gynecological, and geriatric disorders, particularly in addressing mental health issues like anxiety, schizophrenia, bipolar disorder, epilepsy, seizures, insomnia, and sleep disorders (Singh et al., 2015). Furthermore, *R. Serpentina* demonstrates efficacy in treating diarrhea, dysentery, and gastrointestinal motility disorders and is believed to stimulate uterine contraction during childbirth. The plant exhibits variable hypoglycemic effects in diabetic patients (Arts and Hollman, 2005; Scalbert et al., 2005).

Ayurvedic pharmacodynamics:

Rasa- Tikta, Guna – Ruksha, Virya- Ushna, Vipak – Katu, Doshkarma- Kaphavatsamak (Singh et al., 2015).

Phytochemical constituents:

Rauvolfia serpentina has been a focal point of research for numerous decades, attracting researchers intrigued by its rich phytochemical composition. The plant contains a diverse array of secondary metabolites, including alkaloids, phenols, tannins, and flavonoids (Kumari et al., 2015).

Alkaloids:

Alkaloids, a diverse group of organic molecules characterized by a heterocyclic nitrogen ring, are prevalent in various organisms, with plants exhibiting a vast spectrum of alkaloid diversity. Around 10% of plant species produce alkaloids as secondary metabolites, primarily serving in defense against herbivores and pathogens (Adeyeye et al., 2019). Isolated alkaloids and their synthetic derivatives find applications as medicinal agents, offering analgesic, antispasmodic, and bactericidal effects. In *R. serpentina*, the root extract yields alkaloids that directly impact the central nervous system, reducing blood pressure compared to other antihypertensive agents.

The root is reported to contain 0.7-3.0% of total alkaloids, including approximately 0.1% of the active principle reserpine, an indole alkaloid. The structural classification of alkaloids in *Rauvolfia* encompasses weak basic indole alkaloids, alkaloids of intermediate basicity, and strong anhydronium bases (Pandey et al., 2016). Notable alkaloids identified in *Rauvolfia* include ajmaline, ajmalimine, ajmalicine, deserpidine, indobine, indobinine, reserpine, reserpiline, rescinnamine, rescinnamidine, serpentina, serpentinine, and yohimbine (Srivastava et al., 2021). Among these, reserpine stands out as a principal alkaloid with multiple clinical applications. Notable alkaloids identified in *Rauvolfia* include ajmaline, ajmalimine, ajmalicine, deserpidine, indobine, indobinine, reserpine, reserpiline, rescinnamine, rescinnamidine, serpentina, serpentinine and yohimbine (Srivastava et al., 2021). Reserpine stands out as a principal alkaloid with multiple clinical applications.

Reserpine:

This single alkaloid, known as reserpine, was initially isolated from the roots of *Rauvolfia* in 1952, and it exists in a pure crystalline form (Schlittler et al., 1954). Functioning as a relatively weak tertiary base within the oleoresin fraction of the roots, reserpine has proven efficacy in treating hypertension, cardiovascular diseases, and neurological disorders (Shamon and Perez, 2016). Notably, it is a key contributor to the antihypertensive properties of *Rauvolfia* roots. Reserpine, identified as 3, 4, 5-trimethyl benzoic acid ester of reserpic acid (Figure 2a), belongs to the indole derivative of the 18-hydroxy yohimbine type (Goel et al., 2009; Srivastava et al., 2021). As the most prominent alkaloid, reserpine serves primarily as a natural tranquilizer and has found utility in physiologic and pharmacological studies. Its antihypertensive effects stem from its depressive impact on the central and peripheral nervous systems, achieved by binding to catecholamine storage vesicles in nerve cells (Lobay, 2015).

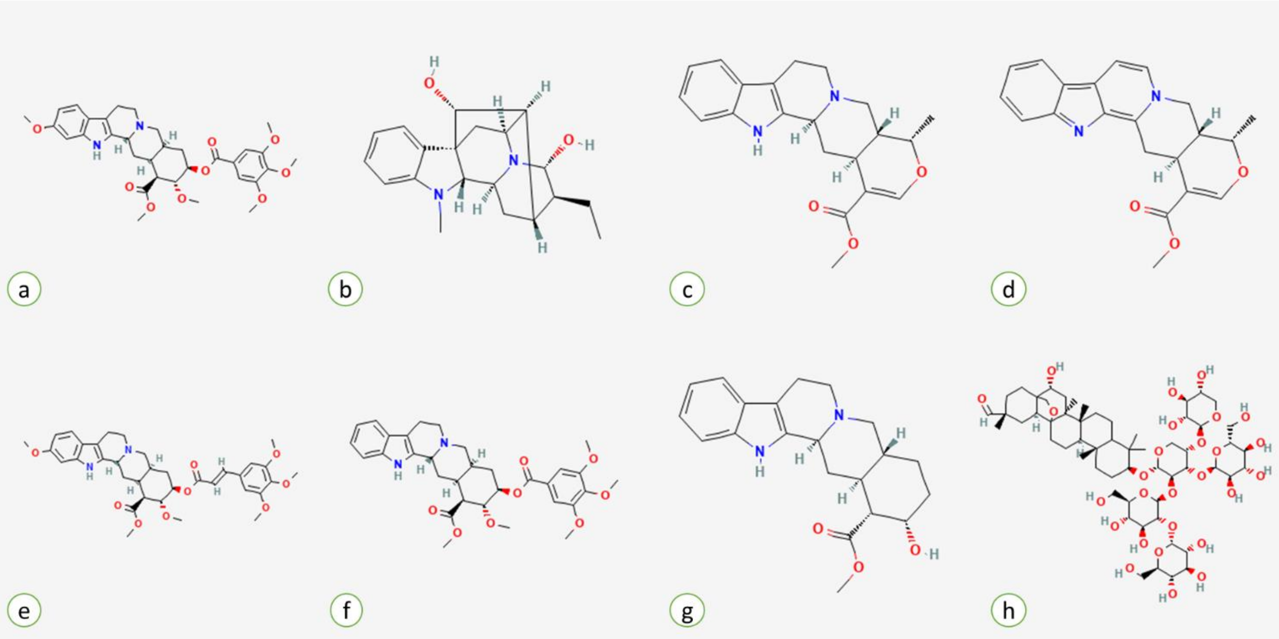

Figure 2. Representative essential phytochemicals present in *Rauvolfia*spp. (a) Reserpine (b) Ajmaline (c) Ajmalicine (d) Serpentina (e) Rescinnamine (f) Deserpidine (g) Yohimbine (h) Saponin. Source: https://pubchem.ncbi.nlm.nih.gov

This action prevents the normal storage of catecholamines and serotonin, resulting in a decline in catecholamine levels. Additionally, reserpine interferes with the autonomic nervous system by depleting transmitter substances from adrenergic neurons and potentially activating the central parasympathetic system. These mechanisms control heart rate, cardiac contraction, and peripheral resistance (Nammi et al., 2005). Furthermore, reserpine induces sedation and reduces blood pressure, particularly in cases of hypertension exacerbated by stress and sympathetic nervous system activity. The alkaloid also prompts the release of 5-hydroxytryptamine from tissues where it is typically stored, leading to increased urinary metabolites (Prusoff, 1961).

Ajmaline:

Isolated from the roots of *R. serpentina* in 1931 by Salimuzzaman Siddiqui, this compound was named Ajmaline in honor of the distinguished Unani medicine practitioner Hakim Ajmal Khan (Roy, 2018). As a class I antiarrhythmic agent derived from *R. serpentina* roots, Ajmaline proves highly valuable in diagnosing Brugada Syndrome, a rare autosomal dominant inherited cardiac disorder, and distinguishing between its subtypes (Rolf, 2003). This compound (Figure 2b), acting as a sodium channel blocker, exhibits rapid effects when administered intravenously, constituting the "Ajmaline Test" for diagnosing this type of arrhythmia (Brugada et al., 2000). Ajmaline's action on blood pressure mirrors that of serpentina. Additionally, its administration has been reported to stimulate respiration and intestinal movements. The categorization of antiarrhythmic agents includes sodium channel blockade, beta-adrenergic blockade, repolarization prolongation, and calcium channel blockade, with Ajmaline falling into the sodium channel blockade category (Liu et al., 2012).

Ajmalicine:

An alkaloid with diverse applications, plays a crucial role in treating circulatory diseases, particularly in promoting normal cerebral blood flow. Its impact on smooth muscle function not only helps prevent strokes but also contributes to lowering blood pressure. Pharmaceutical industries isolate approximately 3500 kg of ajmalicine annually from *Rauvolfia* or *Catharanthus* spp. for circulatory disease treatment (Srivastava et al., 2021). The synthetic pathway commences with geraniol, progressing through iridodial and industrial, synthesizing login. Through oxidation, loganin transforms into secologanin, enabling the formation of ajmalicine via a corynanthe-type nucleus derived from tryptamine. Ajmalicine itself originates from tryptophan, converted to tryptamine through secologanin, strictosidine, and cathenamine (Galan and O'Connor, 2006). The reduction of cathenamine to ajmalicine is facilitated by the enzymes NADPH and tryptophan decarboxylase, with the latter likely playing a key role in the synthesis of ajmalicine in *Rauvolfia*, beyond its blood pressure-lowering properties, ajmalicine restores normal cerebral blood flow by influencing smooth muscle action (Liu et al., 2012). The substantial annual isolation of ajmalicine underscores its significance in therapeutic applications (Figure 2c).

Serpentina:

Serpentina (Figure 2d), a type II topoisomerase inhibitor, demonstrates antipsychotic properties. The enzyme peroxidase plays a crucial role in oxidizing ajmalicine to serpentina, catalyzing the conversion of this bisindole alkaloid localized within the vacuole (Prusoff, 1961).

Rescinnamine:

Rescinnamine (Figure 2e), a refined ester alkaloid derived from the alseroxylon fraction in *Rauvolfia* spp., shares chemical and pharmacological similarities with reserpine, serving similar therapeutic purposes (Iqbal et al., 2013). Initially investigated in the 1950s, it found application as an antihypertensive agent for hypertension treatment. However, clinically, rescinnamine is recognized as a less potent alkaloid than reserpine, displaying lower efficacy in reducing blood pressure (Mashour et al., 1998). This compound functions by inhibiting angiotensin-converting enzyme, a peptidyl dipeptidase catalyzing the conversion of angiotensin I to angiotensin II, a vasoconstrictor substance that stimulates aldosterone secretion by the adrenal cortex (Ahmad et al., 2023). Rescinnamine's action involves the initial inhibition of ACE, followed by the blockade of angiotensin I to angiotensin II conversion. This inhibition results in decreased plasma angiotensin II levels. Given that angiotensin II is a vasoconstrictor and a negative-feedback mediator for renin activity, its reduced concentration contributes to decreased blood pressure. The subsequent stimulation of baroreceptor reflex mechanisms ultimately leads to decreased vasopressor activity and aldosterone secretion (Chen et al., 2010).

Deserpidine:

Deserpidine, an ester alkaloid derived from *Rauvolfia*, distinguishes itself from reserpine solely by the absence of a methoxy group at C-11, a modification synthesized from reserpine (Figure 2f). Its primary applications lie in its antipsychotic and antihypertensive properties (Varchi et al., 2005). Deserpidine regulates high blood pressure by modulating nerve impulses along various nerve pathways, influencing the heart and blood vessels to reduce blood pressure and alleviate psychotic behavior (Kamyab et al., 2020). Additionally, Deserpidine binds to and inhibits angiotensin-converting enzyme, competing with angiotensin I for binding at the enzyme site. This dual action inhibits the conversion of angiotensin I to angiotensin II and contributes to its antihypertensive effects (Li et al., 2014).

Yohimbine:

Yohimbine (Figure 2g) is a thoroughly characterized alkaloid with well-established pharmacological properties and is employed as a selective alpha-adrenergic antagonist or alpha-blocker in blood vessels to treat erectile dysfunction (Goldberg and Robertson, 1983). Its mechanism of action involves dilating blood vessels and enhancing blood flow to the penis, thereby improving erectile function (Andersson, 2001). Additionally, Yohimbine has been investigated as a potential remedy for diabetes, particularly in animal and human models with polymorphisms of the α2A-adrenergic receptor gene (Rosengren et al., 2010). The antagonistic effect at these receptors contributes to the relaxation of smooth muscle and a subsequent reduction in blood pressure. Yohimbine operates by elevating specific chemicals in the body, resulting in dilating the pupils of the eye (Bateman et al., 1998).

Phenols:

Recognized as secondary plant metabolites, they are widely distributed in the plant kingdom, encompassing herbs, shrubs, vegetables, and trees. Their presence serves as a deterrent to the growth of pests and pathogens within the plant, exhibiting notable antidiabetic and hypolipidemic properties, particularly in the case of *R. serpentina*, which contains a high quantity of total polyphenolic compounds (Pastrana-Bonilla et al., 2003). In medicine, phenols find utility as expectorants and emulsifying agents; moreover, the abundance of phenolic compounds signifies their potential application as antimicrobial agents, showcasing their multifaceted roles in plant defense and human health (Nair et al., 2012).

Tannins:

The antioxidative activity of tannins can be attributed to the presence of gallic acid and diagallic acid (Ellong et al., 2015). Tannins exhibit stringent properties, accelerating the healing process of wounds and managing inflammation of mucous membranes. Additionally, flavonoids, recognized as potent water-soluble antioxidants and free radical scavengers, contribute to anti-inflammatory and anticancer activities (Saravanababu et al., 2009). These properties underscore the significance of *R. serpentina* in traditional medicine practices among healers in South Eastern India, who leverage its diverse therapeutic applications in treating various disorders (Prusoff, 1961).

Flavanoids:

These powerful water-soluble antioxidants and free radical scavengers play a crucial role in preventing oxidative cell damage and exhibit robust anti cancerous activity. Additionally, flavonoids in the intestinal tract contribute to a reduced risk of heart disease. As antioxidants, flavonoids offer anti-inflammatory properties that are harnessed in herbal medicine to treat various diseases (Pastrana-Bonilla et al., 2003).

Saponins:

Saponins, glycosides of both triterpenes and sterols, have been identified in over 70 plant families (Figure 2h). Some characteristic features of saponins include the formation of foams in aqueous solutions, hemolytic activity, cholesterol-binding properties, and bitterness. Notably, saponins possess the ability to coagulate red blood cells. The elevated saponin content in *R. serpentina* underscores the use of its extracts for stopping bleeding and treating wounds, highlighting its potential therapeutic applications (Pastrana-Bonilla et al., 2003; Harisaranraj et al., 2009).

Hypertension and mental disorders:

The roots *of R. serpentina*, rich in therapeutically beneficial indole alkaloids, have been historically associated with treating hypertension. Clinical studies conducted in the mid-20th century reported successful hypertension treatment using *R. serpentina* (Dahl, 1972). Cochrane database reviews, encompassing randomized controlled trials, affirmed the effectiveness of reserpine in lowering blood pressure, recommending it as a primary antihypertensive drug (Shamon and Perez, 2016). Beyond hypertension, *R. serpentina* has demonstrated efficacy in mental disorders such as anxiety, schizophrenia, bipolar disorder, epilepsy, seizures, insomnia, and sleep disorders (Glynn, 1955). The plant's sedative properties, attributed to its oleoresin content, have shown promising results in improving the quality of life and reducing pain in migraine patients (Mittal et al., 2012; Agrawal et al., 2013).

Against snake bites:

In vivo assessment of *Naja naja* venom toxicity, including LD_{50} determination using mice (18-20 g) through range finding and median lethal dose assays, revealed a LD_{50} of 0.301 µg/g by the Miller and Tainter method. Additionally, the venom neutralizing potency (ED_{50}) was evaluated using *R. serpentina* root extract, resulting in an ED_{50} of 12.88 µg against *Naja naja* venom, with all animals exhibiting vitality and well-being throughout the acute oral toxicity study, displaying no gross toxicity, antagonistic pharmacological effects, or unusual behavior. supported by LC-MS analysis confirming the presence of bioactive compounds, findings suggest the potential of *R. serpentina* as an alternative and easily accessible antidote for snake bites, warranting further investigation (Sivaraman et al., 2020).

Miscellaneous Uses:

R. serpentina exhibits a broad spectrum of effects, including respiratory inhibition, stimulation of peristalsis, myosis, and potential utility in treating diarrhea, dysentery, and gastrointestinal motility disorders (Ezeigbo et al., 2012). Additionally, it is believed to stimulate uterine contractions, assist in childbirth, and exhibit variable hypoglycemic effects in diabetic patients. The root bark, rich in β-carboline alkaloids, has displayed anti-prostate cancer activity, making it a subject of interest for cancer research (Bemis et al., 2009).

Mineral composition and therapeutic potential:

R. serpentina is a rich source of macro and micro-nutrients, with calcium being the most abundant macro nutrient. The plant's high calcium content may contribute to its hemostatic properties, aiding in blood coagulation. Other essential elements, including zinc, suggest potential roles in managing diabetes. Ascorbic acid, riboflavin, thiamin, and niacin found in *R. serpentina* highlight its significance in herbal medicine for treating various diseases (Lobay, 2015). *R. serpentina* emerges as a valuable therapeutic herb effective in treating hypertension, psychotic disorders, and various ailments. Its ethnobotanical uses extend to circulatory disorders, intestinal issues, cholera, colic, and fever (Figure 3). The plant has demonstrated therapeutic effects in conditions like fever, malaria, eye diseases, pneumonia, asthma, AIDS, headache, skin diseases, and spleen disorders (Britto and Mahesh, 2007; Harisaranraj et al., 2009).

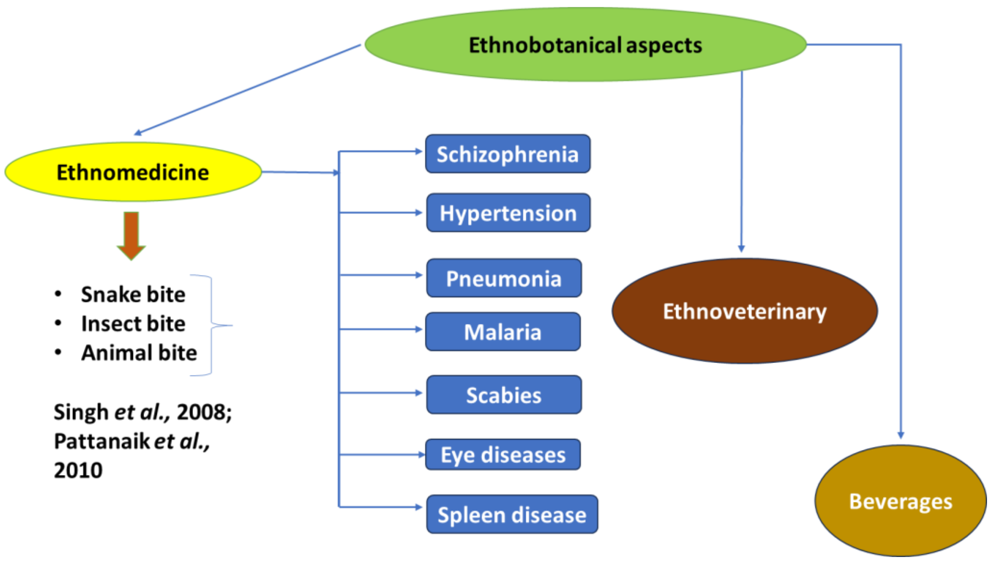

Figure 3. A schematic representation of the various ethnobotanical aspects of *Rauvolfia* spp.

Ethnoveterinary practices:

Certain villages of Madhya Pradesh involve the utilization of a combination of Sarpaganda (*R. serpentina*) roots (20-30 gm) and sugar (50-60 gm) for a period of 2-3 days, exhibiting a 60-70% efficacy in treating loose motion among tribal livestock owners; in the Nawalparasi district of Central Nepal, individuals employ a 10 g root paste or an adjusted dosage to address conditions such as fever, stomach-ache, and menstrual disorders (including heavy menstrual periods and pain during menstrual periods) until the livestock's recovery (Bhattarai et al., 1970).

In beverages:

The root bark of *R. serpentina* plays a key role in introducing bitterness to create Ranu dabai, a crucial component in the preparation of the traditional fermented beverage known as jhara, commonly utilized by rural communities in India; among tribal inhabitants in the tea gardens of Terai in West Bengal, the local use of the plant's root bark, also known as Nagbeli, imparts a bitter taste to rice beer. In cases where R. *serpentina* is abundantly available, it is a substitute for *Coccinia grandis* in the production of starter cultures (Sathe and Mandal, 2016).

In Vitro Propagation and Recent Advancements:

Chemical composition and micropropagation of *R. serpentina*:

R. serpentina is characterized by its rich content of approximately 30 indole alkaloids (0.7-2.4%), phytosterols, unsaturated alcohols, and sugars. Reserpine, renowned for its antihypertensive properties, stands out as the active constituent (Bhatt et al., 2008). Recognized for its high medicinal value and facing endangerment due to overexploitation, this species demands careful conservation efforts (Goel et al., 2009). However, challenges such as poor seed viability, low seed germination rates, and limited success in vegetative propagation through root cuttings impede the widespread commercial cultivation of *R. serpentina* using traditional methods (Bhatt et al., 2008).

In response to the growing market demand and the need for germplasm conservation, this study explores the potential of micropropagation techniques. The objective is to establish a reproducible protocol for *R. serpentina* by investigating the impact of different growth regulators, carbon sources, and light conditions on shoot multiplication. To initiate the micropropagation process, explants were meticulously sterilized using 0.1% (w/v) mercuric chloride ($HgCl_2$) for 20 minutes, followed by thorough washing with distilled water. Trimmed explants were then inoculated into Murashige and Skoog medium. Subsequent bud proliferation and shoot multiplication were facilitated by inoculating the explants in MS medium supplemented with varying concentrations of cytokinins (Table 3).

R. serpentina, in conjunction with various other *Rauvolfia* species, synthesizes a variety of terpene indole alkaloids, including but not limited to ajmaline, yohimbine, and ajmalicine. Due to the sluggish growth and challenging cultivation of *Rauvolfia*, advancements in understanding *Rauvolfia* biosynthesis have been achieved through the establishment of cell suspension and hairy root culture techniques (Stöckigt et al., 2011). The biosynthetic pathway of ajmaline in *R.*

serpentina stands out as one of the most thoroughly characterized terpene indole alkaloid pathways (Galan and O'Connor, 2006).

Table 3. Summary of micropropagation research conducted on *Rauvolfia serpentina*.

Micropropagation of *Rauvolfia serpentina*	References
The protocol demonstrated 96% bud proliferation in 14 days, achieving the highest shoot multiplication (13.3 shoots/explant, 8.2 cm average length) in MS medium+2 mg/l 6-benzylaminopurine+0.25 mg/l 1-naphthaleneacetic acid+3% sucrose, optimal rooting (73.3%) with 1/2 MS+0.5 mg/l indol-3-butyric acid, and a 90% survival rate, confirming genetic uniformity via random amplified polymorphic DNA analysis.	(Senapati et al., 2014)
Axillary bud shoot proliferation exhibited superior performance.	(Pandey et al., 2007)
The most effective rooting of adventitious shoots was observed on half-strength MS medium supplemented with 1.0 mg L-1 each of IBA and IAA.	(Salma et al., 2008)
Rooting was successfully induced in MS medium supplemented with 0.5 mol/L indole-3-butyric acid.	(Alatar, 2015)
The micropropagated, *R. serpentina* plants displayed normal growth in a nursery, with *in vitro* raised plants showing a remarkable 90-95% survival rate under glasshouse and field conditions.	(Goel et al., 2009; Kataria and Shekhawat, 2005)

Biochemical aspects and localization of enzyme:

The biosynthesis of secologanin, a precursor, initiates in the plastid and involves subsequent steps in the cytosol, with distinct enzyme activities associated with specific cellular compartments (Yamamoto et al., 2000). Strictosidine, a key intermediate, is processed in the vacuole and endoplasmic reticulum (De Carolis et al., 1990; Geerlings et al., 2000; Stevens et al., 1993). The branch point for diversification of the strictosidine aglycone occurs following strictosidinede glycosylation, leading to the formation of vindoline (Galan and O'Connor, 2006). Vindoline biosynthesis involves multiple cellular compartments such as the endoplasmic reticulum, chloroplast, and vacuole (De Carolis et al., 1990; Dethier and De Luca, 1993; Sottomayor et al., 1998; St-Pierre and De Luca, 1995).

The intricate subcellular trafficking of biosynthetic intermediates is crucial for terpene indole alkaloid biosynthesis, with some enzymes localized in specialized cells like laticifers and idioblasts (St-Pierre et al., 1999). Vascular cells are considered specialized "terpene factories" (Murata and Luca, 2005). The biosynthesis of vindoline requires at least two distinct cell types and intercellular transport mechanisms for intermediates; additionally, enzyme activity shows spatial restriction within the plant or seedling, with certain enzymes abundant in specific organs, such as roots or leaves (Vazquez-Flota et al., 1997; O'Connor and Maresh, 2006). The final distribution of alkaloids, including vindoline and bisindole alkaloids, varies across plant tissues (Verpoorte et al., 1997; Westekemper et al., 1980). A simplified pathway is presented below (Figure 4).

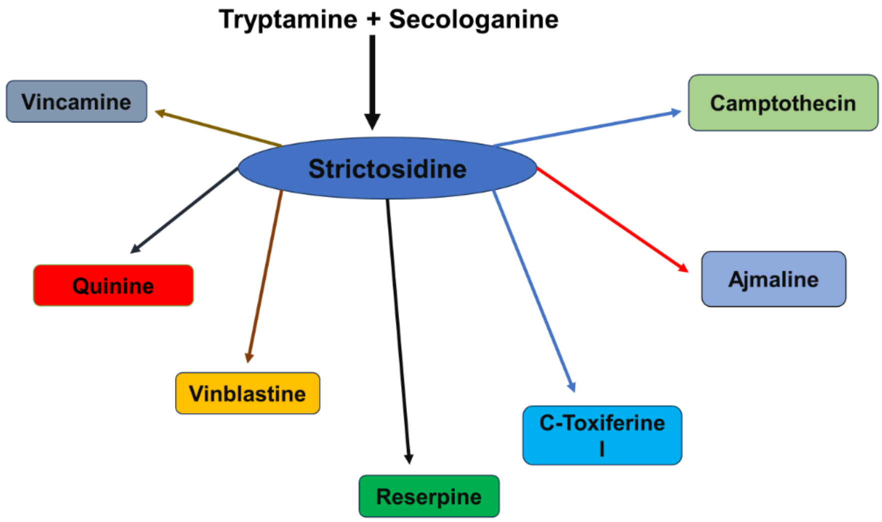

Figure 4. Schematic diagram depicts how the precursors giving rise to valuable secondary metabolites forming a biochemical pathway (a shorter approach)

Application in synthesizing nanoparticles:

Silver Nanoparticles (AgNPs) were synthesized using an eco-friendly and cost-effective method involving the leaf extract of *R. serpentina*. The plant extract served as a reducing and stabilizing agent for the AgNPs. It demonstrated antimicrobial activity against human pathogenic microorganisms, larvicidal activity, and cytotoxicity against HeLa and MCF-7 cell lines suggest that the AgNPs derived from *R. serpentina* have potential applications in various biological activities, making them promising candidates for further research and development (Panja et al., 2016).

SerpentinaDB:

SerpentinaDB is a structured compilation of 147 Plant-Derived molecules (PDMs) from *R. serpentina* (Figure 5b), a medicinally important plant endemic to the Himalayan Mountain ranges of the Indian subcontinent (Pathania et al., 2013, 2015; Varnika et al., 2020). The database provides comprehensive information on the physicochemical properties, plant part source, chemical classification, IUPAC, SMILES, and 3D chemical structures of these molecules, along with associated references (Ye et al., 2011). SerpentinaDB offers a user-friendly web interface for data query and *extraction*, allowing users to search for molecules based on plant part (Figure 5a), chemical class (Figure 5b), or specific physicochemical properties; additionally, the database provides a similarity search option against the ZINC database (http://zinc.docking.org/) to identify analogues of natural molecules at user-defined cut-off values.

The purpose of Serpentina DB is to facilitate the use of natural chemical diversity for drug discovery by providing a comprehensive resource of *R. serpentina* molecules for rational prospection of therapeutic molecules (Pathania et al., 2015). The database has been demonstrated to be helpful in identifying novel aldose reductase inhibitors for the intervention of complications of diabetes (Pathania et al., 2015). Established repositories of natural compounds, including Naturally Occurring Plant-based Anti-cancer Compound-Activity (NPACT) (Mangal et al., 2013), Super Natural (Dunkel, 2006) and Herb Ingredients' Targets (Ye et al., 2011) address various functional dimensions within PDM libraries. While certain databases concentrate on specific diseases or target-compound interactions, others encompass plants from distinct geographical regions (Ntie-Kang et al., 2013). The highly basic anhydronium base serpentina demonstrates both anticancer and anti-malarial properties. Its mode of action, akin to other anhydronium bases, is explained through DNA-intercalation and inhibition of topoisomerase II (Dassonneville et al., 1999).

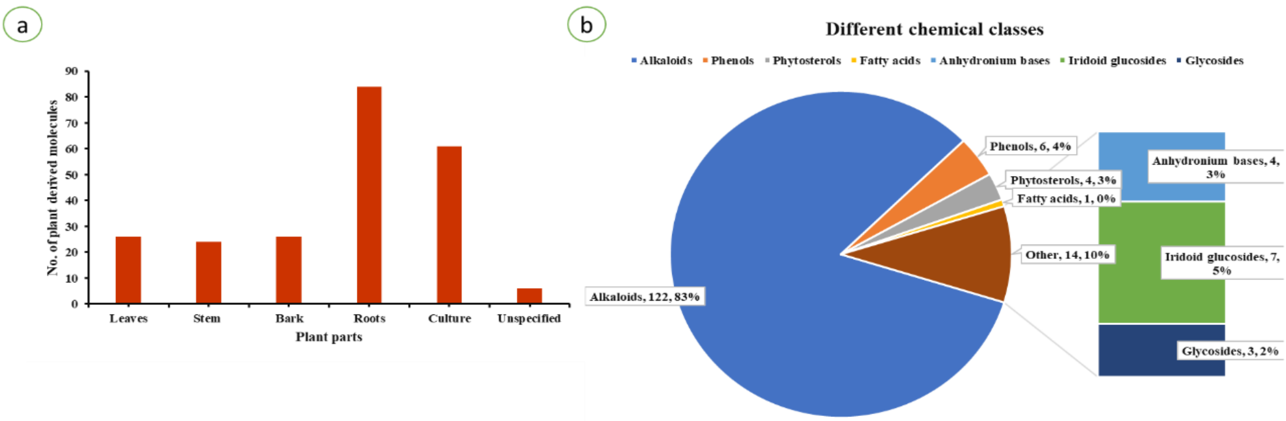

Figure 5. Distribution of different chemical classes and their quantitative presence across various *R. serpentina* plant parts

The value of therapeutic plants from an ecological and sustainability standpoint:

By a variety of means, medicinal plants are essential for preserving ecological balance. They improve biodiversity by offering food and habitat to a diverse spectrum of life forms, ranging from microbes to larger animals. These plants also improve soil health by reducing erosion, enhancing soil structure, and replenishing the soil with nutrients through their leaf litter. Medicinal plants help many plant species reproduce by drawing pollinators such as bees, butterflies, and birds, promoting ecological stability (Ghazoul, 2005). Additionally, by preserving soil moisture levels and promoting groundwater recharge—both critical for the maintenance of ecosystems and agricultural productivity—medicinal plants play a critical role in controlling the water cycle.

When considering alternatives to synthetic pharmaceuticals, medicinal plants provide less expensive and less adverse effects, making them a more sustainable option. Sustainable plant production and harvesting can lower poverty, increase economic opportunities for nearby communities, and support conservation initiatives (Thrupp, 2000). Medicinal plants can lessen the adverse effects that the manufacture and use of conventional drugs have on the environment, which helps conserve resources.

Additionally, the sustainable use of medicinal herbs contributes to the preservation of traditional knowledge and cultural legacy, especially among indigenous and local groups who have an important understanding of these plants. Furthermore, when maintained responsibly, medicinal plants can sequester carbon, aiding in the fight against climate change (Kumar, 2006).

Because of its medicinal qualities, *Rauvolfia* - especially *Rauvolfia serpentina* - is a plant that is in high demand commercially. It is frequently referred to as sarpagandha or Indian snakeroot. The demand for it in Indian and global markets is broken down as follows:

- Indian Market Pharmaceuticals: Due to its sedative, tranquilizing, and antihypertensive qualities, *Rauvolfia* is a common ingredient in both contemporary and traditional Ayurvedic medicine.
- Herbal Medicine: The increasing demand for natural and herbal treatments in India is stimulating the market for plants like Rauvolfia.
- Research and Development: The medical benefits of *Rauvolfia* are being investigated by several academic institutions and pharmaceutical firms, which is fuelling demand.
- Government Initiatives: To support farmers and traditional medical systems, the Indian government encourages the growth and export of medicinal plants, including *Rauvolfia*.
- Pharmaceuticals for the International Market: Reserpine, one of the *Rauvolfia* alkaloids, is used by pharmaceutical companies in other countries to treat mental illnesses and hypertension.
- Herbal Supplements: *Rauvolfia* is sold as a natural cure in the US, Europe, and other places, with a sizable market for herbal supplements (Kumar et al., 2020).
- Regulatory Approvals: Drugs based on *Rauvolfia* are authorized and in use in numerous nations, which helps to maintain a steady demand.
- Natural Products: The market for medicinal plants like *Rauvolfia* is increasing globally due to consumers' growing preference for natural and organic products.
- Cultivation and availability: *Rauvolfia* cultivation, which necessitates particular climatic conditions, determines its availability. Any changes in the supply may impact the market.

- Sustainability Concerns: *Rauvolfia* populations are at risk due to overharvesting and habitat damage, highlighting the need for sustainable production techniques (Sharma and Pandey, 2012).

Conclusions:

R. serpentina emerges as a botanical treasure with profound medicinal significance, encompassing a rich repertoire of phytochemicals and therapeutic virtues. As a member of the Apocynaceae family, *Rauvolfia* species, particularly *R. serpentina* and *R. tetraphylla*, have been integral to traditional medicine practices across the Indian subcontinent. The phytochemical constituents, notably alkaloids such as reserpine, ajmaline, ajmalicine, serpentina, rescinnamine, deserpidine, and yohimbine, underscore its diverse pharmacological applications, ranging from antihypertensive and antiarrhythmic effects to potential remedies for mental disorders, snakebites, and various ailments. The challenges faced by *Rauvolfia* species, including poor seed viability, low germination rates, and overexploitation, necessitate innovative approaches such as *in vitro* propagation for conservation and sustainable exploitation. Beyond its therapeutic applications, *R. serpentina* demonstrates versatile uses, ranging from ethnoveterinary practices to the production of traditional fermented beverages. The plant's mineral composition further adds to its therapeutic potential, with macro and micro-nutrients contributing to its hemostatic properties, antidiabetic potential, and roles in managing various disorders.

The exploration of pollen morphology provides insights into the distinctive features of *R. serpentina*, contributing to its taxonomic characterization. Additionally, advancements in understanding the biosynthetic pathways of key alkaloids, such as ajmaline, offer avenues for targeted research and cultivation practices. In the context of contemporary scientific advancements, the role of synthesizing nanoparticles highlights its potential applications in nanobiotechnology. The eco-friendly synthesis of silver nanoparticles using *R. serpentina* leaf extract showcases its multifaceted contributions to modern research and development. *Rauvolfia serpentina* is a bioactive treasure that requires careful protection and investigation into its possibilities in nanotechnology and medicine. It bridges the gap between traditional wisdom and contemporary science. Its pharmacological components, essential for managing diseases like hypertension, emphasize its health advantages. *Rauvolfia serpentina* is vital to preserving biodiversity, which is in jeopardy due to deforestation and climate change. Preserving it helps support other species that depend on its environment and protects biodiversity and cultural heritage. Beyond conventional medicine, their molecules in pharmacology pique interest since they present a variety of therapeutic possibilities for drug creation. Thus, protecting *Rauvolfia serpentina* symbolizes accountability, fusing conventional knowledge with cutting-edge research for a sustainable future where human health and biodiversity coexist.

References:

Adeyeye, E. I., Adesina, A. J., Olagboye, S. A., & Olatunya, M. A. (2019). Effects of Use and Re-Use of selected vegetable oils on the proximate, minerals, mineral ratios and mineral Safety Index of raw and fried plantain Chips: Note I. *Journal of Agricultural Chemistry and Environment*, *08*(02), 92–106. https://doi.org/10.4236/jacen.2019.82008

Ahmad, H., Khan, H., Haque, S., Ahmad, S., Srivastava, N., & Khan, A. (2023). Angiotensin-Converting Enzyme and Hypertension: A systemic analysis of various ACE inhibitors, their side effects, and bioactive peptides as a putative therapy for hypertension. *Journal of the Renin-Angiotensin-Aldosterone System*, *2023*, 1–9. https://doi.org/10.1155/2023/7890188

Akbar, S. (2020). Rauvolfia serpentina (L.) Benth. ex Kurz (Apocynaceae). In *Springer eBooks* (pp. 1513–1520). https://doi.org/10.1007/978-3-030-16807-0_156

Alatar, A. A. (2015). Thidiazuron induced efficient in vitro multiplication and ex vitro conservation of Rauvolfia serpentina– a potent antihypertensive drug producing plant. *Biotechnology & Biotechnological Equipment*, *29*(3), 489–497. https://doi.org/10.1080/13102818.2015.1017535

Andersson, K. E. (2001). Pharmacology of Penile Erection. *Pharmacological Reviews*, *53*(3), 417–450.

Bateman, J., Chapman, R., & Simpson, D. (1998). Possible toxicity of herbal remedies. *Scottish Medical Journal*, *43*(1), 7–15. https://doi.org/10.1177/003693309804300104

Bemis, D. L., Capodice, J. L., Desai, M., Katz, A. E., & Buttyan, R. (2009). Beta-carboline alkaloid-enriched extract from the Amazonian rainforest tree *Pao pereira* suppresses prostate cancer cells. *Journal of the Society for Integrative Oncology*, *7*(2), 59–65.

Benjamin, B. D., Roja, G., & Heble, M. R. (1993). *Agrobacterium rhizogens* mediated transformation of Rauvolfia serpentina: Regeneration and alkaloid synthesis. *Plant Cell Tissue and Organ Culture (PCTOC)*, *35*(3), 253–257. https://doi.org/10.1007/bf00037278

Bhattarai, S., Chaudhary, R., & Taylor, R. S. (1970). Ethno-medicinal plants used by the people of Nawalparasi district, central Nepal. *Our Nature*, *7*(1), 82–99. https://doi.org/10.3126/on.v7i1.2555

Blackwell, W. H. (1990). *Poisonous and Medicinal Plants*. Prentice-Hall International, Inc.

Brugada, R., Brugada, J., Antzelevitch, C., Kirsch, G. E., Potenza, D., Towbin, J. A., & Brugada, P. (2000). Sodium channel blockers identify risk for sudden death in patients with ST-Segment elevation and right bundle branch block but structurally normal hearts. *Circulation*, *101*(5), 510–515. https://doi.org/10.1161/01.cir.101.5.510

Bussmann, R. W., Zambrana, N. Y. P., Romero, C., & Hart, R. E. (2018). Astonishing diversity—the medicinal plant markets of Bogotá, Colombia. *Journal of Ethnobiology and Ethnomedicine*, *14*(1). https://doi.org/10.1186/s13002-018-0241-8

Cázares-Flores, P., Levac, D., & De Luca, V. (2016). Rauvolfia serpentina N-methyltransferases involved in ajmaline and Nβ-methylajmaline biosynthesis belong to a gene family derived from γ-tocopherol C-methyltransferase. *The Plant Journal*, *87*(4), 335–342. https://doi.org/10.1111/tpj.13186

Chakrabarti, G. (2014). Vulnerable Position of Traditional Knowledge Under IPR: Concern for Sustainable Development. *OIDA International Journal of Sustainable Development*, *7*(3), 67-94.

Chen, L., Kim, S. M., Eisner, C., Oppermann, M., Huang, Y., Mizel, D., Li, L., Chen, M., Lopez, M. L. S., Weinstein, L. S., Gomez, R. A., Schnermann, J., & Briggs, J. P. (2010). Stimulation of Renin Secretion by Angiotensin II Blockade is Gsα-Dependent. *Journal of the American Society of Nephrology*, *21*(6), 986–992. https://doi.org/10.1681/asn.2009030307

Dahl, L. K. (1972). Salt and hypertension. *American Journal of Clinical Nutrition*, *25*(2), 231–244. https://doi.org/10.1093/ajcn/25.2.231

De Carolis, E., Chan, F., Balsevich, J., & De Luca, V. (1990). Isolation and characterization of a 2-Oxoglutarate dependent dioxygenase involved in the Second-to-Last step in vindoline biosynthesis. *PLANT PHYSIOLOGY*, *94*(3), 1323–1329. https://doi.org/10.1104/pp.94.3.1323

Deshmukh, S. R., Ashrit, D. S., & Patil, B. A. (2012). Extraction and Evaluation of Indole Alkaloids from *Rauvolfia serpentina* for their Antimicrobial and Antiproliferative Activities. *Int J Pharm Pharm Sci*, *4*(Suppl 5), 329-34.

Dethier, M., & De Luca, V. (1993). Partial purification of an N-methyltransferase involved in vindoline biosynthesis in Catharanthus roseus. *Phytochemistry*, *32*(3), 673–678. https://doi.org/10.1016/s0031-9422(00)95153-7

Devi, R., & Sarma, M. P. (2021). A review on the plant secondary metabolites with special context with North East India. *International Journal of Advances in Applied Sciences*, *10*(3), 245. https://doi.org/10.11591/ijaas.v10.i3.pp245-250

Dey, A., & De, J. (2010). Rauvolfia serpentina (L). Benth. ex Kurz.-A Review. *Asian Journal of Plant Sciences*, *9*(6), 285–298. https://doi.org/10.3923/ajps.2010.285.298

Dunkel, M., Fullbeck, M., Neumann, S., & Preissner, R. (2005). SuperNatural: a searchable database of available natural compounds. *Nucleic Acids Research*, *34*(90001), D678–D683. https://doi.org/10.1093/nar/gkj132

Dutta, P. K., Chopra, I. C., & Kapoor, L. D. (1963). Cultivation of rauvolfia serpentina in India. *Economic Botany*, *17*(4), 243–251. https://doi.org/10.1007/bf02860133

Ellong, E. N., Billard, C., Adenet, S., & Rochefort, K. (2015). Polyphenols, carotenoids, vitamin C content in tropical fruits and vegetables and impact of processing methods. *Food and Nutrition Sciences*, *06*(03), 299–313. https://doi.org/10.4236/fns.2015.63030

Endress, M. E. (2004). Apocynaceae: Brown and now. *Telopea*, *10*(2), 525-541.

Endress, M. E., & Bruyns, P. V. (2000). A revised classification of the Apocynaceae s.l. *The Botanical Review*, *66*(1), 1–56. https://doi.org/10.1007/bf02857781

Endress, M. E., Liede-Schumann, S., & Meve, U. (2014). An updated classification for Apocynaceae. *Phytotaxa*, *159*(3), 175. https://doi.org/10.11646/phytotaxa.159.3.2

Erdtman, G. (1952). Pollen morphology and plant taxonomy. *Geologiska Foereningan I Stockholm Foerhandlingar*, *74*(4), 526–527. https://doi.org/10.1080/11035895209453507

Eurlings, M. C. M., Lens, F., Pakusza, C., Peelen, T., Wieringa, J. J., & Gravendeel, B. (2013). Forensic Identification of Indian Snakeroot (Rauvolfia serpentina Benth. ex Kurz) Using DNA Barcoding. *Journal of Forensic Sciences*, *58*(3), 822–830. https://doi.org/10.1111/1556-4029.12072

Ezeigbo, I., Ezeja, M., Madubuike, K., Ifenkwe, D., Ukweni, I., Udeh, N., & Akomas, S. (2012). Antidiarrhoeal activity of leaf methanolic extract of Rauwolfia serpentina. *Asian Pacific Journal of Tropical Biomedicine*, *2*(6), 430–432. https://doi.org/10.1016/s2221-1691(12)60070-7

Flores, H. E., Hoy, M. W., & Pickard, J. J. (1987). Secondary metabolites from root cultures. *Trends in Biotechnology*, *5*(3), 64–69. https://doi.org/10.1016/s0167-7799(87)80013-6

Furness, C. A. (2007). Why does some pollen lack apertures? A review of inaperturate pollen in eudicots. *Botanical Journal of the Linnean Society*, *155*(1), 29–48. https://doi.org/10.1111/j.1095-8339.2007.00694.x

Galan, M. C., & O'Connor, S. E. (2006). Semi-synthesis of secologanin analogues. *Tetrahedron Letters*, *47*(10), 1563–1565. https://doi.org/10.1016/j.tetlet.2006.01.009

Geerlings, A., Ibañez, M. M., Memelink, J., Van Der Heijden, R., & Verpoorte, R. (2000). Molecular Cloning and Analysis of Strictosidine β-d-Glucosidase, an Enzyme in Terpenoid Indole Alkaloid Biosynthesis in Catharanthus roseus. *Journal of Biological Chemistry*, *275*(5), 3051–3056. https://doi.org/10.1074/jbc.275.5.3051

Geissler, M., Burghard, M., Volk, J., Staniek, A., & Warzecha, H. (2015). A novel cinnamyl alcohol dehydrogenase (CAD)-like reductase contributes to the structural diversity of monoterpenoid indole alkaloids in Rauvolfia. *Planta*, *243*(3), 813–824. https://doi.org/10.1007/s00425-015-2446-6

Glynn, J. D. (1955). RAUWOLFIA SERPENTINA (SERPASIL) IN PSYCHIATRY. *Journal of Neurology Neurosurgery & Psychiatry*, *18*(3), 225–227. https://doi.org/10.1136/jnnp.18.3.225

Goel, M. K., Mehrotra, S., Kukreja, A. K., Shanker, K., & Khanuja, S. P. S. (2009). In Vitro Propagation of Rauwolfia serpentina Using Liquid Medium, Assessment of Genetic Fidelity of Micropropagated Plants, and Simultaneous Quantitation of Reserpine, Ajmaline, and Ajmalicine. *Methods in Molecular Biology*, 17–33. https://doi.org/10.1007/978-1-60327-287-2_2

Goldberg, M. R., & Robertson, D. (1983). Yohimbine: A pharmacological probe for study of the alpha 2-adrenoreceptor. *Pharmacological Reviews*, *35*(3), 143–180.

Iqbal, M., Alam, A., Wani, T. A., & Khalil, N. Y. (2013). Simultaneous determination of reserpine, rescinnamine, and yohimbine in human plasma by ultraperformance liquid chromatography tandem mass spectrometry. *Journal of Analytical Methods in Chemistry*, *2013*, 1–11. https://doi.org/10.1155/2013/940861

Islam, M.S., Mia, M., Apu, M.I., Halder, J., Rahman, M.F., Islam, M., & Jahan, N. (2015). A Comprehensive Review on Region Based Traditional Ayurvedic Practitioner's Plants Secondary Metabolites and their Phytochemical Activities in Bangladesh. *Journal of Pharmacognosy and Phytochemistry*, *3*, 202-216.

Kamyab, R., Namdar, H., Torbati, M., Ghojazadeh, M., Araj-Khodaei, M., & Fazljou, S. M. B. (2020). Medicinal plants in the Treatment of Hypertension: A review. *Advanced Pharmaceutical Bulletin*, *11*(4), 601–617. https://doi.org/10.34172/apb.2021.090

Kataria, V., & Shekhawat, N. S. (2005). Cloning ofRauvolfia serpentina-An Endangered Medicinal Plant. *Journal of Sustainable Forestry*, *20*(1), 53–65. https://doi.org/10.1300/j091v20n01_04

Kumar, B., Kumar, S., Bajpai, V., & Madhusudanan, K. P. (2020). Phytochemistry of plants of genus Rauvolfia. In *CRC Press eBooks*. https://doi.org/10.1201/9781003014843

Kumar, B. M. (2006). Carbon sequestration potential of tropical homegardens. In *Advances in agroforestry* (pp. 185–204). https://doi.org/10.1007/978-1-4020-4948-4_11

Liu, W., Chen, R., Chen, M., Zhang, H., Peng, M., Yang, C., Ming, X., Lan, X., & Liao, Z. (2012). Tryptophan decarboxylase plays an important role in ajmalicine biosynthesis in Rauvolfia verticillata. *Planta*, *236*(1), 239–250. https://doi.org/10.1007/s00425-012-1608-z

Luthman, H., & Renström, E. (2010). Overexpression of Alpha2A-Adrenergic Receptors Contributes to Type 2 Diabetes. *Science*, *327*(5962), 217–220.

Lobay, D. (2015). *Rauvolfia* in the Treatment of Hypertension. *Integrative Medicine (Encinitas, Calif.)*, *14*(3), 40–46.

Ma, X., Panjikar, S., Koepke, J., Loris, E., & StöCkigt, J. (2006). The Structure of Rauvolfia serpentina Strictosidine Synthase Is a Novel Six-Bladed β-Propeller Fold in Plant Proteins. *The Plant Cell*, *18*(4), 907–920. https://doi.org/10.1105/tpc.105.038018

Mabberley, D. J. (1997). The Plant-book: A Portable Dictionary of the Vascular Plants. *Cambridge university press.*

Madhusudanan, K. P., Banerjee, S., Khanuja, S. P. S., & Chattopadhyay, S. K. (2008). Analysis of hairy root culture of Rauvolfia serpentina using direct analysis in real time mass spectrometric technique. *Biomedical Chromatography*, *22*(6), 596–600. https://doi.org/10.1002/bmc.974

Mangal, M., Sagar, P., Singh, H., Raghava, G. P. S., & Agarwal, S. M. (2012). NPACT: Naturally Occurring Plant-based Anti-cancer Compound-Activity-Target database. *Nucleic Acids Research*, *41*(D1), D1124–D1129. https://doi.org/10.1093/nar/gks1047

Mashour, N. H., Lin, G. I., & Frishman, W. H. (1998). Herbal Medicine for the Treatment of Cardiovascular Disease: Clinical Considerations. *Archives of Internal Medicine*, *158*(20), 2225.

Monachino, J. (1954). *Rauvolfia serpentina*—Its History, Botany and Medical Use. *Economic Botany*, *8*(4), 349–365.

Murata, J., & De Luca, V. (2005). Localization of tabersonine 16-hydroxylase and 16-OH tabersonine-16-O-methyltransferase to leaf epidermal cells defines them as a major site of precursor biosynthesis in the vindoline pathway in Catharanthus roseus. *The Plant Journal*, *44*(4), 581–594. https://doi.org/10.1111/j.1365-313x.2005.02557.x

Nair, V. D., Panneerselvam, R., & Gopi, R. (2012). Studies on methanolic extract of Rauvolfia species from Southern Western Ghats of India – In vitro antioxidant properties, characterisation of nutrients and phytochemicals. *Industrial Crops and Products*, *39*, 17–25. https://doi.org/10.1016/j.indcrop.2012.02.006

Nammi, S., Boini, K. M., Koppula, S., & Sreemantula, S. (2005). Reserpine-induced central effects: pharmacological evidence for the lack of central effects of reserpine methiodide. *Canadian Journal of Physiology and Pharmacology*, *83*(6), 509–515. https://doi.org/10.1139/y05-039

Ntie-Kang, F., Mbah, J. A., Mbaze, L. M., Lifongo, L. L., Scharfe, M., Hanna, J. N., Cho-Ngwa, F., Onguéné, P. A., Owono, L. C. O., Megnassan, E., Sippl, W., & Efange, S. M. (2013). CamMedNP: Building the Cameroonian 3D structural natural products database for virtual screening. *BMC Complementary and Alternative Medicine*, *13*(1). https://doi.org/10.1186/1472-6882-13-88

Ojha, J., & Mishra, U. (1985). Dhanvantari Nighantuh, with Hindi Translation and Commentary, 1st ed., *Deptt. of Dravyaguna, Institute of Medical Sciences, BHU, Varanasi*, *20*.

Pandey, D. K., Radha, N., & Dey, A. (2016). A validated and densitometric HPTLC method for the simultaneous quantification of reserpine and ajmalicine in Rauvolfia serpentina and Rauvolfia tetraphylla. *Revista Brasileira De Farmacognosia*, *26*(5), 553–557. https://doi.org/10.1016/j.bjp.2016.04.002

Pandey, V. P., Kudakasseril, J., Cherian, E., & Patani, G. (2007). Comparison of two methods for in vitro propagation of *Rauwolfia serpentina* from nodal explants. *Indian Drugs*, *44*(07), 514–519. https://doi.org/10.53879/id.44.07.p0514

Panja, S., Chaudhuri, I., Khanra, K., & Bhattacharyya, N. (2016). Biological application of green silver nanoparticle synthesized from leaf extract of Rauvolfia serpentina Benth. *Asian Pacific Journal of Tropical Disease*, *6*(7), 549–556. https://doi.org/10.1016/s2222-1808(16)61085-x

Pastrana-Bonilla, E., Akoh, C. C., Sellappan, S., & Krewer, G. (2003). Phenolic content and antioxidant capacity of muscadine grapes. *Journal of Agricultural and Food Chemistry*, *51*(18), 5497–5503. https://doi.org/10.1021/jf030113c

Pathania, S., Ramakrishnan, S. M., Randhawa, V., & Bagler, G. (2015). SerpentinaDB: a database of plant-derived molecules of Rauvolfia serpentina. *BMC Complementary and Alternative Medicine*, *15*(1), 262. https://doi.org/10.1186/s12906-015-0683-7

Pathania, S., Randhawa, V., & Bagler, G. (2013). Prospecting for Novel Plant-Derived Molecules of *Rauvolfia serpentina* as Inhibitors of Aldose Reductase, a Potent Drug Target for Diabetes and Its Complications. *PLoS ONE*, *8*(4), e61327.

Phillips, D. D., & Chadha, M. S. (1955). The alkaloids of *Rauwolfia serpentina benth*. *Journal of the American Pharmaceutical Association (Scientific Ed)*, *44*(9), 553–567. https://doi.org/10.1002/jps.3030440912

Prusoff, W. H. (1961). Effect of reserpine on the 5-hydroxytryptamine and adenosinetriphosphate of the dog intestinal mucosa. *British Journal of Pharmacology and Chemotherapy*, *17*(1), 87–91. https://doi.org/10.1111/j.1476-5381.1961.tb01107.x

Raja, M. R., & Sreenivasulu, M. (2015). Medicinal plants secondary metabolites used in pharmaceutical importance–An overview. *World Journal of Pharmacy and Pharmaceutical Sciences*, *4*(4), 436–447.

Rolf, S. (2003). The ajmaline challenge in Brugada syndrome: Diagnostic impact, safety, and recommended protocol. *European Heart Journal*, *24*(12), 1104–1112. https://doi.org/10.1016/s0195-668x(03)00195-7

Rosengren, A. H., Jokubka, R., Tojjar, D., Granhall, C., Hansson, O., Li, D., Nagaraj, V., Reinbothe, T. M., Tuncel, J., Eliasson, L., Groop, L., Rorsman, P., Salehi, A., Lyssenko, V., Luthman, H., & Renström, E. (2009). Overexpression of Alpha2A-Adrenergic receptors contributes to type 2 diabetes. *Science*, *327*(5962), 217–220. https://doi.org/10.1126/science.1176827

Roy, P. (2018). Global pharma and local science: The untold tale of reserpine. *Indian Journal of Psychiatry*, *60*(6), 277. https://doi.org/10.4103/psychiatry.indianjpsychiatry_444_17

Ruppert, M., Ma, X., & Stockigt, J. (2005). Alkaloid biosynthesis in rauvolfia- CDNA cloning of major enzymes of the Ajmaline pathway. *Current Organic Chemistry*, *9*(15), 1431–1444. https://doi.org/10.2174/138527205774370540

Sahu, B. N. (1983). *Rauvolfia serpentina*: Sarpagandha: Chemistry and Pharmacology–Vol 4. *Today and Tomorrow's Printers, New Delhi, xiv*, *595*.

Salma, U., Rahman, M., Islam, S., Haque, N., Khatun, M., Jubair, T., & Paul, B. (2008). Mass Propagation of Rauwolfia serpentina L. Benth. *Pakistan Journal of Biological Sciences*, *11*(9), 1273–1277. https://doi.org/10.3923/pjbs.2008.1273.1277

Saravanan, S., Lall, D., Bahadur, V., & Kumar, S. (2019). Response of Different Levels of Plant Spacing on Vegetative Growth and Yield Attributes of Ashwagandha (Withania somnifera) var. Poshita and Sarpagandha (Rauvolfia serpentina. Benth) var. Sheel under

Open Environment and Orchard Conditions. *International Journal of Current Microbiology and Applied Sciences*, *8*(07), 2065–2074. https://doi.org/10.20546/ijcmas.2019.807.248

Sathe, G. B., & Mandal, S. (2016). Fermented products of India and its implication: A review. *Asian Journal of Dairy and Food Research*, *35*(1). https://doi.org/10.18805/ajdfr.v35i1.9244

Scalbert, A., Manach, C., Morand, C., Rémésy, C., & Jiménez, L. (2005). Dietary polyphenols and the prevention of diseases. *Critical Reviews in Food Science and Nutrition*, *45*(4), 287–306. https://doi.org/10.1080/1040869059096

Schlittler, E., Saner, H., & Müller, J. M. (1954). Reserpinin, ein neues Alkaloid ausRauwolfia serpentina Benth. *Experientia*, *10*(3), 133–134. https://doi.org/10.1007/bf02158516

Shamon, S. D., & Perez, M. I. (2016). Blood pressure-lowering efficacy of reserpine for primary hypertension. *Cochrane Library*, *2016*(12). https://doi.org/10.1002/14651858.cd007655.pub3

Sharma, N., & Chandel, K. (1992). Low-temperature storage of Rauvolfia serpentina Benth. ex Kurz.: An endangered, endemic medicinal plant. *Plant Cell Reports*, *11*(4). https://doi.org/10.1007/bf00232533

Sharma, N., & Pandey, R. (2012). Conservation of medicinal plants in the tropics. In *Springer eBooks* (pp. 437–487). https://doi.org/10.1007/978-1-4614-3776-5_18

Sihag, R., & Wadhwa, N. (2011). Floral and reproductive biology of Sarpagandha *Rauvolfia serpentina* (Gentianales: Apocynaceae) in semi-arid environment of India. *Journal of Threatened Taxa*, *3*(1), 1432–1436. https://doi.org/10.11609/jott.o2337.1432-6

Singh, R. K., Singh, A., Rath, S., & Ramamurthy, A. (2015). A review of Sarpgandha – Whole herb vs. reserpine – its alkaloid in the management of hypertension. *International Ayurvedic Medical Journal*, *3*(2), 565–569.

Singh, A. K., Tyagi, R. K., & Kameshwar Rao, N. (2004). Ex-situ approaches for conservation plant genetic resources: achievements and challenges. *Plant genetic resource management (Eds. BS Dhillon, RK Tyagi, A Lal and S Saxena). Narosa Publishing House, New Delhi*, 179-193.

Sivaraman, T., Sreedevi, N. S., Meenachisundharam, S., & Vadivelan, R. (2020). Neutralizing potential of Rauvolfia serpentina root extract against *Naja naja* venom. *Brazilian Journal of Pharmaceutical Sciences, 56*. https://doi.org/10.1590/s2175-97902019000418050

Sottomayor, M., López-Serrano, M., DiCosmo, F., & Barceló, A. R. (1998). Purification and characterization of α-3′,4′-anhydrovinblastine synthase (peroxidase-like) from Catharanthus roseus (L.) G. Don. *FEBS Letters*, *428*(3), 299–303. https://doi.org/10.1016/s0014-5793(98)00551-1

Srivastava, M., Kesharwani, S., Kesharwani, R., Patel, D. K., & Singh, S. N. (2021). A review on potential bioactive chemical from *Rauwolfia serpentina*: reserpine. *International*

Journal of Research in Ayurveda and Pharmacy, *12*(1), 106–109. https://doi.org/10.7897/2277-4343.120123

Stevens, L., Blom, T., & Verpoorte, R. (1993). Subcellular localization of tryptophan decarboxylase, strictosidine synthase and strictosidine glucosidase in suspension cultured cells of Catharanthus roseus and Tabernaemontana divaricata. *Plant Cell Reports*, *12*(10). https://doi.org/10.1007/bf00233063

Stöckigt, J., Antonchick, A. P., Wu, F., & Waldmann, H. (2011). The Pictet–Spengler reaction in nature and in organic chemistry. *Angewandte Chemie International Edition*, *50*(37), 8538–8564. https://doi.org/10.1002/anie.201008071

St-Pierre, B., & De Luca, V. (1995). A Cytochrome P-450 Monooxygenase Catalyzes the First Step in the Conversion of Tabersonine to Vindoline in *Catharanthus roseus*. *Plant Physiology*, *109*(1), 131–139.

St-Pierre, B., Vazquez-Flota, F. A., & De Luca, V. (1999). Multicellular Compartmentation of Catharanthus roseus Alkaloid Biosynthesis Predicts Intercellular Translocation of a Pathway Intermediate. *The Plant Cell*, *11*(5), 887–900. https://doi.org/10.1105/tpc.11.5.887

Surendran, S., Raju, R., Prasannan, P., & Surendran, A. (2021). A Comprehensive review on ethnobotany, phytochemistry and pharmacology of Rauvolfia L. (Apocynaceae). *The Botanical Review*, *87*(3), 311–376. https://doi.org/10.1007/s12229-021-09262-2

Swami, D. V., Anitha, M., Rao, M. C. S., & Sharangi, A. B. (2022). Medicinal Plants: Perspectives and Retrospectives. In *Apple Academic Press eBooks* (pp. 1–28). https://doi.org/10.1201/9781003277408-1

Thrupp, L. A. (2000). Linking Agricultural Biodiversity and Food Security: the Valuable Role of Agrobiodiversity for Sustainable Agriculture. *International Affairs*, *76*(2), 265–281. https://doi.org/10.1111/1468-2346.00133

Tripathi, S., Garg, A., Shukla, A. N., Farooqui, A., Pandey, A., Tripathi, T., & Singh, V. K. (2022). Pollen micro-morphometry of two endangered species of Rauvolfia L. (Apocynaceae) from the Indo-Gangetic Plains of Central India using LM, CLSM and FESEM. *Palynology*, *46*(4), 1–15. https://doi.org/10.1080/01916122.2022.2072966

Vakil, R. J. (1955). Rauwolfia serpentina in the treatment of high blood pressure. *Circulation*, *12*(2), 220–229. https://doi.org/10.1161/01.cir.12.2.220

Van Der Ham, R., Zimmermann, Y., Nilsson, S., & Igersheim, A. (2001). Pollen morphology and phylogeny of the Alyxieae (Apocynaceae). *Grana*, *40*(4–5), 169–191. https://doi.org/10.1080/00173130131723114

Van Der Weide, J. C., & Van Der Ham, R. W. (2012). Pollen morphology and phylogeny of the tribe Tabernaemontaneae (Apocynaceae, subfamily Rauvolfioideae). *Taxon*, *61*(1), 131–145. https://doi.org/10.1002/tax.611010

Varchi, G., Battaglia, A., Samorì, C., Baldelli, E., Danieli, B., Fontana, G., Guerrini, A., & Bombardelli, E. (2005). Synthesis of Deserpidine from Reserpine. *Journal of Natural Products*, *68*(11), 1629–1631. https://doi.org/10.1021/np050179x

Varnika, V., Sharma, R., Singh, A., Shalini, S., & Sharma, N. (2020). Micropropagation and Screening of Phytocompounds Present among in vitro Raised and Wild Plants of Rauvolfia serpentine. *Walailak Journal of Science and Technology (WJST)*, *17*(11), 1177–1193. https://doi.org/10.48048/wjst.2020.6492

Vazquez-Flota, F., De Carolis, E., Alarco, A., & De Luca, V. (1997). Molecular cloning and characterization of desacetoxyvindoline-4-hydroxylase, a 2-oxoglutarate dependent-dioxygenase involved in the biosynthesis of vindoline in *Catharanthus roseus* (L.) G. Don. *Plant Molecular Biology*, *34*(6), 935–948. https://doi.org/10.1023/a:1005894001516

Verpoorte, R., Van Der Heijden, R., & Moreno, P. R. (1997). Chapter 3 Biosynthesis of Terpenoid Indole Alkaloids in *Catharanthus roseus* Cells. In *The Alkaloids. Chemistry and physiology*, pp. 221–299. https://doi.org/10.1016/s0099-9598(08)60017-6

Westekemper, P., Wieczorek, U., Gueritte, F., Langlois, N., Langlois, Y., Potier, P., & Zenk, M. (1980). Radioimmunoassay for the determination of the indole alkaloid vindoline in Catharanthus. *Planta Medica*, *39*(05), 24–37. https://doi.org/10.1055/s-2008-1074900

Yamamoto, H., Katano, N., Ooi, A., & Inoue, K. (2000). Secologanin synthase which catalyzes the oxidative cleavage of loganin into secologanin is a cytochrome P450. *Phytochemistry*, *53*(1), 7–12. https://doi.org/10.1016/s0031-9422(99)00471-9

Ye, H., Ye, L., Kang, H., Zhang, D., Tao, L., Tang, K., Liu, X., Zhu, R., Liu, Q., Chen, Y. Z., Li, Y., & Cao, Z. (2010). HIT: linking herbal active ingredients to targets. *Nucleic Acids Research*, *39*(Database), D1055–D1059. https://doi.org/10.1093/nar/gkq1165

HOW TO CITE

Bishop Debnath, Suparna Sanyal Mukherjee and Saikat Kumar Basu (2024). Exploring the Riches of *Rauvolfia serpentina*: Botany, Pharmacology, and Conservation Perspectives © International Academic Publishing House (IAPH), Dr. Nithar Ranjan Madhu, Dr. Tanmay Sanyal, Dr. Koushik Sen, Professor Biswajit (Bob) Ganguly and Professor Roger I.C. Hansell (eds.), *A Basic Overview of Environment and Sustainable Development [Volume: 3]*, pp. 20-55. ISBN: 978-81-969828-3-6. DOI: https://doi.org/10.52756/boesd.2024.e03.002