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REVIEW ON *SELAGINELLA BRYOPTERIS*: A TRADITIONAL PLANT

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Abstract: Sanjeevani, a mysterious character in Hindu mythology, continues to intrigue as it remains a prominent figure in ancient civilizations. Despite the passage of time, much of the vegetation associated with it persists and holds significance in modern times. Among the various therapeutic plants utilized by indigenous populations, Sanjeevani stands out as the most renowned. This revitalizing herb is believed to possess the power to restore life itself.In the epic Ramayana, Hanuman sought counsel from Sushena before embarking on a quest to locate the elusive plants on Dunagiri Hill. Throughout history, people have often recounted the paranormal effects attributed to such vegetation. Sanjeevani, with its extraordinary value to society, warrants careful exploration.A remarkable species known as *Selaginella bryopteris (L.)* Baker, locally referred to as Sanjeevani, holds a unique place in India. This pteridophytic plant belongs to the Selaginellaceae family and possesses exceptional resurrection abilities. Thriving in the steep tropical regions of the Himalayan Region, this lithophytic plant is commonly known as Sanjeevani booti in Sanskrit. To confirm its botanical identity, plant specimens were collected from the Chamoli valley in the Uttarakhand region.*Selaginella* has a long history of use in treating various ailments, including abnormal menstrual cycles, post-childbirth uterine pain, jaundice, heatstroke, wounds, and internal health issues, among others. Its chemical composition includes alkaloids, phenols, flavonoids, and numerous secondary metabolites, providing it with a broad spectrum of antimicrobial, antifungal, antibacterial, antiviral, and antioxidant properties. Additionally, it serves as a tonic for enhancing overall health and extending lifespan. Current investigations are centered on gaining specific insights into *Selaginella bryopteris* and its diverse pharmacological activities, which have the potential to enhance fitness and well-being.

Keywords: Sanjeevani, Bio Flavonoids, Mountains, Lithophytic Plant, Old Customs, Traditional Knowledge.

I. INTRODUCTION

Plants have played a crucial role in human history, serving various purposes throughout the ages. An increasing number of individuals are recognizing the vital role of plants across different fields, especially in healthcare. Ancient civilizations found relief from aches and pains through remedies crafted from plant extracts. In the early days of botany, physicians in both Europe and America delved into the study of plants as potential treatments for diseases. Many plants discovered by these ancient cultures remain in use today. For instance, Native Americans used willow leaves, which contain a substance remarkably similar to aspirin, to alleviate discomfort. In South America, cinchona trees were employed to combat malaria.[1]Human beings have grappled with sickness and various ailments since long before modern medicine emerged. During those times, people relied on natural remedies made from herbs and spices in the absence of advanced medical treatments. Numerous herbs, including well-known ones like tulsi and neem, played a significant role in these remedies.[2]These herbal treatments continue to be an integral part of daily life, persisting and evolving in various nations and cultures, often retaining their traditional methods. Spices, which are essential components of many culinary dishes, not only enhance flavor but also possess therapeutic qualities that can effectively address mild ailments such as the common cold and cough.[3]In Indian mythology, the term "SANJEEVANI,"

derived from the Sanskrit word "jeeva" meaning life, remains a subject of controversy due to its claimed ability to "resurrect" life. Among a preliminary list of roughly 17 plant species that could represent Sanjeevani, only three have been chosen—*Cressa cretica, Selaginella bryopteris, and Desmotrichum fimbriatum.*The development of traditional and Ayurvedic medicine, coupled with the emergence of Western therapeutic practices, significantly contributed to the discovery, appropriate selection, and processing of raw medicinal materials. Indigenous knowledge, often referred to as traditional knowledge, encompasses the ancient customs, traditions, and wisdom of regional, indigenous, and local communities. This knowledge is usually passed down orally from one generation to the next and is often conveyed through stories, legends, folklore, rituals, songs, and customary laws. Traditional knowledge is closely tied to the local biodiversity and frequently revolves around the therapeutic properties of plants.[4]

Taxanomical classification of *Selaginella bryopteris*

Kingdom*: Plantae*
Division*: Lycopodiophyta*
Class*: Isoetopsida*
Order*: Selaginellales*
Family*: Selaginellaceae*
Genus*: Selaginella*
Species
apoda
asprella
bifida
biformis
bigelovii
braunii
bryopteris
canaliculata
carinata
cinerascens.[5]

Geographical Area of Species:

Particularly, the terrains spanning India's Aravali Mountains from east to west provide an ideal habitat for the growth of Sanjeevani. S. bryopteris is renowned for its ability to thrive as a poikilohydric lithophyte, primarily found in mountainous regions. This unique herb is traded for its distinctive qualities in various Indian markets, with a notable presence in pilgrimage centers like Rishikesh, Haridwar, and Varanasi.The arrival of rains triggers a luxuriant growth of these plants, transforming the environment into a lush, velvety green landscape. Selaginella bryopteris, also known as Sanjeevani booti, is recognized for its exceptional drought resistance, making it capable of enduring extreme desiccation during the summer months. As the fronds undergo dehydration, they curl, dry out, and almost mimic a lifeless state. In this condition, they resemble a closed fist and are occasionally referred to as "punjemariam" or "hathazori" in Unani tradition.

The medicinal applications of this plant include:

1. Providing relief from heat exhaustion and the burning sensation during urination.
2. Regulating irregular menstruation.
3. Assisting expectant mothers in experiencing a more comfortable labor process.
4. Utilized in the treatment of jaundice.[6]

Medicinal Properties:

Natural products have consistently served as a rich source of novel medications, thanks to their diverse chemical composition and their ability to target various biological pathways. Among these natural wonders, Selaginella stands out as a plant deserving thorough exploration to unlock its mythical, multifaceted medical potential.The primary bioactive compounds within Selaginella species are bioflavonoids, with bioflavonoids being the most noteworthy. It's worth noting that all vascular plants contain naturally occurring biflavonoids,[7] compounds with diverse positive biological and pharmacological properties. Reports suggest that Selaginella bryopteris, in particular, boasts exceptional drought resistance, showcasing the ability to endure extended periods of dry conditions without compromising its vitality. This remarkable resilience is attributed to a specific drought-resistant gene.Remarkably, Selaginella bryopteris fronds, when detached, possess a unique capacity to withstand desiccation akin to the whole plant. To gain insights into the mechanisms of desiccation resistance,

proteome analyses were conducted using Selaginella bryopteris fronds, enabling the identification of differentially expressed proteins in response to desiccation stress.[8]

Flavonoids

Flavonoids belong to a class of metabolites renowned for their health-promoting attributes, possessing both antioxidant capabilities and the ability to modulate cellular signaling. These polyphenolic compounds, aptly named flavonoids due to their derivation from the Latin word "flavus," meaning "yellow," are present in trace amounts in various sources such as beer, fruits, flowers, seeds, and vegetables. Remarkably, the current count of distinct flavonoids exceeds 4000.Flavonoids primarily serve as a defense mechanism for plants, shielding them from direct UV light and neutralizing Reactive Oxygen Species (ROS) generated by UV exposure. Their multifaceted sun-protective effects stem from their direct and indirect antioxidant properties, UV-absorbing qualities, and their ability to modulate signaling pathways.[9]

The Terminological Functions of Flavonoids encompass a range of essential roles:

- Flavonoids act as potent antioxidants, safeguarding the body against environmental pollutants and stressors. They regulate cellular processes and combat free radicals responsible for oxidative stress.
- Their biochemical attributes and antioxidant effects have been linked to several health conditions, including cancer, heart disease, and Alzheimer's disease (AD).
- Flavonoids find extensive applications in the realms of medicine, pharmaceuticals, nutraceuticals, and cosmetics. Additionally, they interact with biological enzymes, displaying robust inhibitory effects on enzymes like cyclo-oxygenase (COX), lipo-oxygenase, aldose reductase, and phosphoinositide 3-kinase.

Structurally, flavonoids typically feature a 15-carbon skeleton ring comprising two benzene rings (labeled as 1 and 3) connected by a heterocyclic pyrane ring (labeled as 2). This structural arrangement is derived from an aglycone and underlies the diverse functions and properties of flavonoids.[10]

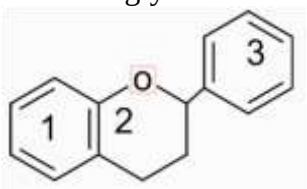

Figure 1: Generic Framework of Flavonoids.

Flavonoid Categories:

Flavonoids are typically classified into three main categories:

I. Flavones:

- Flavones represent one of the most significant subclasses of flavonoids, and they are found as glucosides in various parts of plants, including leaves, flowers, and fruits.
- Foods like celery, parsley, red peppers, chamomile, mint, and *Ginkgo biloba* contain flavones.
- Flavones exhibit a range of beneficial qualities, including anti-inflammatory, antiviral, antiallergic, antioxidative, anticancer, and antitumor properties.[11]

II. Flavonones:

- Citrus fruits such as oranges, lemons, and grapes are prime examples of sources rich in flavonones, a key class of flavonoids.
- Flavonones encompass compounds like eriodictyol, naringenin, and hesperitin.
- Flavonones are known for their ability to neutralize free radicals, which is linked to various health benefits.[12]
- The bitter taste found in citrus juice and peel can be attributed to these compounds.
- Citrus flavonoids have demonstrated anti-inflammatory, antioxidant, and cholesterol-lowering effects within the body.[13]

III. Flavonols:

- Flavonols are flavonoids characterized by the presence of a ketone group and are constituents of proanthocyanins.
- They are abundantly found in numerous fruits and vegetables, including onions, lettuce, tomatoes, apples, grapes, and berries.
- Red wine and tea are also beverages that contain flavonols.
- The consumption of flavonols has been associated with various health benefits, such as their antioxidant potential and a reduced risk of vascular disease.[14]
- It's worth noting that flavonols and flavonones share structural similarities but differ due to the presence of a hydroxyl group at position three and a double bond at carbons 2-3, along with six condensed six-membered rings featuring the benzene ring, namely, -pyrone or dihydroderivative.[15]

IV. Isoflavonoids:

- Isoflavonoids have a limited distribution in the plant kingdom and are primarily found in soybeans and other leguminous plants.
- These compounds hold significant potential in disease treatment, with certain isoflavones like genistein and daidzein often referred to as phytoestrogens due to their estrogenic activity in animal models.[16]
- Isoflavonoids have also been identified in microorganisms and play a crucial role as precursors for phytoalexin production during plant-microbe interactions.
- These distinct categories of flavonoids each offer a spectrum of biological activities and potential health benefits.[17,18]

Pharmacological Activities:

1. Antiplasmodial and Leishmanicidal Effects:

The study focused on evaluating the antiprotozoal properties of a group of eleven biflavonoids derived from the Indian medicinal plant *Selaginella bryopteris*.In vitro assays were employed to assess their activity against the K1 strain of *Plasmodium falciparum, Leishmania donovani, Trypanosoma brucei rhodesiense, and Trypanosoma cruzi*.Among these compounds, 7,40,700-tri-Omethylamentoflavone exhibited the most potent antiprotozoal activity, with an IC50 of 0.26 mM. Importantly, this substance displayed no cytotoxicity (IC50 > 150 mM) when tested on L-6 cells.While 2,3-dihydrohinokiflavone demonstrated high activity against *Leishmania* (IC50 = 1.6 mM), it showed no significant activity against *Trypanosoma* (IC50 > 12.5 mg/mL for the extract).To evaluate the in vivo activity of the most active molecule against *Plasmodium*, researchers synthesized trimethylated flavones from flavone.However, at a dosage of 50 mg/kg, the synthesized combination of trimethylated amentoflavones did not impact female NMRI mice in the *Plasmodium berghei* mouse model.[19]

2. Anticarcinogenic Activity:

In recent years, there has been a significant increase in awareness regarding cancer prevention through dietary interventions. Studies involving mechanistic and molecular epidemiology have highlighted the inverse relationship between flavonoid consumption and cancer risk.The present study delved into the chemopreventive and anticarcinogenic potential of *Selaginella bryopteris*, a traditional Indian plant known as "Sanjeevani" in Ayurvedic medicine.Researchers focused on the flavonoid-rich benzene fraction of the aqueous extract, which exhibited notable cytoprotective activity. This fraction underwent extensive in vitro and in vivo investigations.Various biomarkers of chemoprevention were studied in both human and murine cell cultures, including the proliferation index, cell-cycle regulatory proteins, antioxidant properties, anti-inflammatory effects, reversal of stress-induced senescence, and genoprotective activity.[20]The chemopreventive potential was further evaluated in animal models, including tests related to skin papillomagenesis induced by 7,12-dimethylbenz(a)anthracene and lung carcinogenesis caused by benzopyrene.The findings showcased genoprotective benefits against methyl isocyanate-induced carcinogenicity, inhibition of DNA fragmentation, preservation of normal cell-cycle control, maintenance of intracellular antioxidant defenses, anti-inflammatory actions, protection against stress-induced senescence, and anti-apoptotic effects.Two-stage skin papillomagenesis tests and medium-term anticarcinogenicity testing largely corroborated the in vitro results, confirming the significance of

flavonoids in cancer prevention and unveiling the previously unknown anticarcinogenic and chemopreventive properties of *S. bryopteris*.[21]

3. Wound Healing Activity:

This study aimed to assess the wound-healing potential of the ethanolic extract derived from *Selaginella bryopteris* on rats. The entire plant of *S. bryopteris Linn.* was collected in Andhra Pradesh, India, and ethanol was employed for the extraction process.Active metabolites within the extract were identified through GC-MS analysis, and the levels of total phenolic and flavonoid compounds were quantified.To evaluate the in vivo wound healing capacity of the ethanolic extract, an excision wound model was employed. The extract was topically applied to animals in the form of ointments at two concentrations (5% and 10%), with soframycin (10%) serving as a positive control.The study also investigated the antioxidant activity of the *S. bryopteris* extract by assessing the levels of oxidative enzymes, including Superoxide dismutase (SOD), Catalase (CAT), reduced Glutathione (GSH), and lipid peroxidation (LPO) in animal tissues.Following the trial period, histopathological analyses were conducted on the removed skin. Rats treated with 5% and 10% extract ointments exhibited greater and dose-dependent wound contraction rates compared to the untreated control group.At the conclusion of the study period, the groups treated with the extract were in the recovery phase, showing a higher percentage of healing compared to the 10% concentration.The results provided valuable insights into the wound healing process, demonstrating typical stages of recovery and restored levels of oxidative enzymes. Histopathological analysis indicated positive outcomes, with cellular fibrous tissue and collagen fibers replacing proliferating capillaries and skeletal muscle in the dermis.Overall, the findings underscored the unique potential of the ethanolic extract of *S. bryopteris* as a traditional remedy with remarkable wound healing properties.[22]

4. Anti-Microbial and Photocatalytic Activities:

This study is centered on the eco-friendly synthesis of silver nanoparticles (AgNPs) utilizing an aqueous extract sourced from the extraordinary lithophyte *S. bryopteris.*Characterization of these biologically synthesized nanoparticles was conducted using various techniques, including UV-vis spectrophotometry, X-ray diffraction (XRD), FT-IR spectroscopy, and transmission electron microscopy (TEM).The UV-Visible spectrophotometry analysis, which indicated surface plasmon resonance (SPR) at approximately 420 nm, confirmed the successful formation of AgNPs.TEM images revealed that the nanoparticles were polydispersed, nearly spherical in shape, and ranged in size from 4 to 30 nm.Remarkably, the synthesized AgNPs exhibited robust antibacterial activity and demonstrated the ability to degrade dyes through photocatalysis without the need for chemical reducing agents.The stability of bio-reduced silver nanoparticles was assessed using UV-vis absorption spectra, and their antibacterial effectiveness was tested against various gram-positive bacteria.This investigation showcases the potential of *S. bryopteris*-derived AgNPs as environmentally friendly agents with both antimicrobial and photocatalytic properties.[23]

5. Anti-Fertility Activity:

The global concern of population growth, particularly in colonized nations, has significant implications for economic development.Efforts have been directed towards family planning through various contraceptive methods; however, many contemporary contraceptive methods are associated with undesirable side effects.Consequently, there is a need for potent medications that offer effective contraception with minimal or no adverse effects.This study aimed to evaluate the contraceptive effects of [mention the plant or compound] on female albino mice.Experimental mice were administered methanol extracts of *Actiniopteris radiata* at different doses (175 and 300 mg/kg body weight) and [mention the second substance or compound] at varying doses (250 and 500 mg/kg body weight) orally for a duration of 30 days.The effects of the treatment on the reproductive organs of female mice were assessed using an ECLIA estrogen standard kit.Additionally, quantitative measurements of blood serum levels of protein, cholesterol, and alkaline phosphatase were conducted using a standard kit from Biosystems Diagnostics.The administration of the medication led to a reduction in ovarian weight, a decrease in estrogen levels, and the observation of histopathological abnormalities.The study's overall findings indicated that infertility was induced in *A. radiata* at a low dose of the methanolic extract (175 mg/kg body weight) but not at a high dose (300 mg/kg body weight).Furthermore, female albino mice did not exhibit significant variations in response when compared to the control group.[24]

6. Wound Healing Activity in Diabetic Conditions:

In India, there has been an alarming increase in the prevalence of diabetes and its associated complications, including delayed wound healing.This surge poses a substantial burden on the country's already limited healthcare infrastructure.In response to this growing concern, the current research aims to investigate potential mechanisms and assess the effects of the flavonoid-enriched fraction derived from *Selaginella bryopteris* extract on diabetic wounds induced by streptozocin (STZ) in a male Wistar rat model and human keratinocyte cell lines (HaCaT).Chemical profiling was conducted using an MTT test to identify key bioactive phytoconstituents, which were subsequently confirmed through GC-MS analysis. Notable constituents included amentoflavone, gallic acid, imidazole, palmitic acid, catechine, L-fucitol, lupeol, and myo-inositol.When exposed to *S. bryopteris*, HaCaT cell lines exhibited several responses, including the generation of reactive oxygen species (ROS), chromatin condensation in the nucleus, and alterations in mitochondrial membrane potential.An AO/PI analysis provided evidence of *S. bryopteris*-induced apoptosis-mediated cell death in HaCaT cell lines, with JC-1 staining indicating signs of mitochondrial depolarization.Furthermore, the treatment led to improvements in wound size reduction and epithelialization.Keratinocyte migration displayed dose-dependent inhibition, accompanied by altered expression of genes associated with apoptosis, both pro-apoptotic (p53, caspase-3, caspase-9, and bax) and anti-apoptotic (bcl-2), along with interleukins (TNF-, IL-2, and IL-6).Enhanced migration of keratinocytes was associated with elevated levels of antioxidant enzymes, including catalase (CAT), superoxide dismutase (SOD), malondialdehyde (MDA), and reduced glutathione (GSH).These findings suggest that the mitochondria-mediated apoptotic pathway plays a role in promoting wound healing, representing a promising avenue for the treatment of diabetic wounds.[25]

7. Anti-Coagulant and Anti-Platelet Properties:

Recently, researchers synthesized and characterized silver nanoparticles using *Selaginella bryopteris* (Sanjeevini) Plant Extract (SPE) as reducing and capping agents. Techniques such as PXRD, UV-Vis, FESEM, TEM, and EDX were utilized to analyze the silver nanoparticles produced from the Selaginella bryopteris plant extract (SPEAg-NPs). Evaluation against human pathogens S. aureus, E. coli, and A. niger indicated the high stability of SPEAg-NPs, showing promise as antibacterial and antifungal agents. Moreover, SPEAg-NPs demonstrated anticoagulant properties by prolonging clotting times of citrated human PRP and PPP from 160 s to 220 s and 160 s to 284 s, respectively. They also exhibited modest antiplatelet action by suppressing ADP-induced platelet aggregation by roughly 23% at a dose of 30 g. Notably, despite the higher dosage, SPEAg-NPs did not alter epinephrine-induced platelet function. It's worth mentioning that SPEAg-NPs did not induce edema or hemorrhage in experimental mice, nor did they hydrolyze RBC cells, indicating their safety. Ultimately, it was found that SPEAg-NPs are non-toxic and possess antibacterial, antifungal, anticoagulant, and antiplatelet activities, suggesting their potential in the biomedical field, especially for treating thrombotic diseases.[26,27]

8. Anti-depressant activity: Pteridophytic plant Selaginella bryopteris is a member of the Selaginellaceae family. It is known by the name sanjeevani booti. The focus of the current study was on Selaginella bryopteris's antidepressant efficacy on Albino mice and phytochemical screening. In order to evaluate the medicinal benefits and safety of plants in ethnomedicine, phytochemical analysis was done. The findings of the phytochemical screening indicate the presence of alkaloids, flavonoids, phenols, and tannins. Quantitative estimations showed that the methanolic extract contains the highest concentration of alkaloids relative to flavonoids, phenols, and tannins. According to the findings of the phytochemical estimates, methanolic extract is effective. *Selaginella bryopteris* was put to the test on mice using the Rotarod and Hole Board tests for its antidepressant properties. Diazepam, a depressive and an inducer of depression, is the standard drug used in both tests. The retention time of mice was significantly increased in the Rotarod test with the dose of 250mg/kg (3.960.35) and 500mg/kg (7.230.46) of the methanolic extract of *Selaginella bryopteris*, as compared to the standard of 10mg/kg (1.661.20 at 120min). The results of the Hole Board test demonstrated significant motar performance (head dipping behaviour) with these doses.[28]

9. **Anti- Bacterial Activity:** The goal of the current study was to determine the impact of an extract from *Selaginella bryopteris* fronds on Staphylococcus aureus and Bacillus sp., which were isolated from cow milk with mastitis using the agar well diffusion method. 30, 40, 50, and 100 mg of the methanolic extract of *S. bryopteris* were examined independently along with controls. According to the results, 50 mg methanolic extracts had the strongest inhibitory effects on S. aureus (7.331.03 mm) and Bacillus sp. (50.89 mm) when used in a test tube. The current project is interesting in that it estimates the antibacterial activities of *S. bryopteris*, a significant medicinal pteridophyte that has received the least attention to date.[29,30]

Conclusion

Based on the current article, it is evident that herbs such as Selaginella bryopteris possess numerous medicinal attributes, akin to the legendary Sanjeevani plant referenced in the Indian epic "Ramayana". Due to these properties, the herb is also dubbed the "resurrection plant". Moreover, Selaginella bryopteris holds a revered status among local communities for its magical healing capabilities. Recognized as a plant of profound societal significance, conducting comprehensive research into its therapeutic properties, ethnomedicinal practices, and pharmacological applications could enhance the potential of this herb as a life-saving botanical resource in the future.

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