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A COMPREHENSIVE INTEGRATIVE REVIEW ON *INDIGOFERA TINCTORIA* LINN (*NEELINI*): BRIDGING CLASSICAL AYURVEDIC KNOWLEDGE WITH PHYTOCHEMICAL AND PHARMACOLOGICAL EVIDENCE

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ABSTRACT

Background: *Neelini* (*Indigofera tinctoria Linn.)* is a classical Ayurvedic medicinal plant described in traditional texts for the management of *Kuṣṭha* and *Rakta*-related disorders. Despite its extensive traditional usage and wide geographical availability, its pharmacological potential remains inadequately integrated with contemporary scientific evidence. **Methods:** A comprehensive integrative review was conducted using classical Ayurvedic literature alongside peer-reviewed scientific studies retrieved from PubMed, Google Scholar, and related databases, with emphasis on phytochemistry, pharmacological activities, and toxicological evaluation. **Results:** Classical literature identifies *Neelini* (*Indigofera tinctoria Linn.)* as therapeutically relevant in dermatological and *Rakta*-associated disorders. Phytochemical investigations reveal the presence of indole alkaloids such as indirubin along with flavonoids, phenolic compounds, and terpenoids. These constituents exhibit diverse pharmacological activities including anti-inflammatory, antioxidant, hepatoprotective, antimicrobial, neuropharmacological, and antidiabetic effects. Toxicological studies indicate a favorable safety profile within experimentally studied dose ranges. **Conclusion:** The available evidence demonstrates a significant convergence between

classical Ayurvedic indications and mechanistically supported pharmacological findings. However, lack of clinical validation, standardization, and pharmacokinetic data limits its translational applicability.

INTRODUCTION

Medicinal plants have historically constituted the backbone of traditional systems of medicine and continue to serve as an indispensable source of therapeutic agents in modern drug discovery. The increasing global burden of chronic inflammatory, metabolic, and degenerative disorders has intensified the search for bioactive compounds derived from natural sources that exhibit multi-targeted actions with improved safety profiles. In this context, plant-derived secondary metabolites, characterized by their structural diversity and biological specificity, have gained considerable attention for their potential to modulate complex cellular and molecular pathways involved in disease pathogenesis.[1]

Ayurveda, as a comprehensive and holistic system of medicine, offers a well-established framework for understanding the pharmacological behavior of medicinal plants through principles such as *Rasa*, *Guṇa*, *Vīrya*, and *Vipāka*. These classical concepts, although rooted in traditional knowledge, demonstrate significant parallels with modern pharmacodynamic and pharmacokinetic principles when interpreted through contemporary scientific approaches.[2] The increasing efforts to validate Ayurvedic drugs using modern experimental models have further emphasized the relevance of integrative research in bridging traditional wisdom with evidence-based medicine.[3]

Within this framework, *Indigofera tinctoria* Linn., commonly referred to as Neelini, occupies a distinct position due to its wide distribution, therapeutic versatility, and historical usage in classical Ayurvedic literature. The plant is extensively found in tropical and subtropical regions and has been traditionally utilized for a variety of therapeutic purposes owing to its accessibility and pharmacological potential.[4] Classical texts such as *Bhāvaprakāśa Nighaṇṭu* describe its application in *Kuṣṭha* and *Tvak vikāra*, while *Dhanvantari Nighaṇṭu* highlights its role in disorders associated with vitiation of *Rakta*, thereby indicating its relevance in inflammatory and dermatological conditions.[5] The classical indications of Neelini reflect an empirical understanding of disease processes that are now recognized to involve complex interactions between inflammatory mediators, immune responses, and oxidative stress pathways. Such correlations underscore the importance of re-evaluating traditional medicinal plants through modern pharmacological perspectives to elucidate their mechanisms of action

and therapeutic applicability.[6] Phytochemical investigations have revealed that *Indigofera tinctoria* is rich in a diverse array of bioactive constituents, including indole alkaloids such as indirubin and indigotin, along with flavonoids, phenolic compounds, terpenoids, and glycosides. These compounds are known to exhibit a wide range of biological activities through interaction with multiple molecular targets, thereby contributing to the plant's broad pharmacological profile.[7]

Among these, indirubin has emerged as a compound of significant pharmacological interest due to its ability to inhibit cyclin-dependent kinases and modulate NF-κB signaling pathways. These mechanisms are critically involved in the regulation of inflammatory responses, cell proliferation, and immune function, thereby providing a scientific basis for its traditional therapeutic applications.[8] In addition to its anti-inflammatory potential, *Indigofera tinctoria* has been shown to exhibit significant antioxidant activity, primarily attributed to its flavonoid and phenolic content. These compounds play a crucial role in scavenging reactive oxygen species and protecting cellular components from oxidative damage, which is a key factor in the progression of various chronic diseases.[9]

Despite the availability of such evidence, the existing literature on *Indigofera tinctoria* remains fragmented and lacks a comprehensive integrative analysis that correlates classical Ayurvedic descriptions with modern pharmacological findings. Therefore, the present review aims to systematically compile and critically evaluate the available evidence to provide a coherent understanding of its therapeutic potential and relevance in contemporary healthcare systems.

MATERIALS AND METHODS

A comprehensive literature survey was conducted using classical Ayurvedic texts and scientific databases including PubMed, Google Scholar, and ScienceDirect. Only peer-reviewed research articles and experimentally validated studies were included in the analysis.

RESULTS

Classical Ayurvedic Review

Neelini is described in classical Ayurvedic texts such as *Bhāvaprakāśa Nighaṇṭu* in the context of *Kuṣṭha* and *Tvak vikāra*, indicating its significant role in dermatological disorders.[10] Also, *Dhanvantari Nighaṇṭu* describes its indication in *Rakta doṣa*, suggesting

its therapeutic importance in conditions associated with vitiation of blood and inflammatory processes.[11]

Phytochemical Profile

Phytochemical investigations have demonstrated that *Indigofera tinctoria* contains a wide spectrum of bioactive constituents, including indole alkaloids such as indirubin and indigotin, along with flavonoids, phenolic compounds, terpenoids, and glycosides.[12]

These phytoconstituents are known to exert biological activity through interaction with multiple molecular targets involved in inflammatory pathways, oxidative stress mechanisms, and cellular signaling cascades.[13]

Pharmacological Activities

The pharmacological activities of *Indigofera tinctoria* reflect a multi-target and multi-mechanistic mode of action. Anti-inflammatory effects are primarily mediated through inhibition of NF-κB signaling pathways and downregulation of pro-inflammatory cytokines, which play a central role in inflammatory disorders.[14]

The antioxidant activity of the plant is attributed to its rich content of flavonoids and phenolic compounds, which neutralize reactive oxygen species and enhance endogenous antioxidant defense systems, thereby protecting against oxidative stress–induced cellular damage.[15]

Hepatoprotective activity has been demonstrated through reduction of lipid peroxidation and restoration of altered hepatic enzyme levels, indicating its protective role against toxin-induced liver injury.[16]

Antimicrobial activity further supports its traditional use in dermatological conditions, with studies demonstrating inhibitory effects against a range of bacterial and fungal pathogens.[17]

Neuropharmacological investigations have indicated anticonvulsant activity, suggesting its potential interaction with central nervous system pathways.[18]

The antidiabetic activity of *Indigofera tinctoria* has been associated with improved glucose metabolism, enhancement of insulin sensitivity, and reduction of oxidative stress, thereby indicating its role in metabolic regulation.[19]

Toxicity Studies

Toxicological evaluations have demonstrated that *Indigofera tinctoria* is non-toxic up to a dose of 2000 mg/kg (oral**)** in acute toxicity studies, indicating a wide margin of safety.[20]

Sub-acute toxicity studies further reveal that doses ranging from **200–400 mg/kg** are well tolerated without significant alterations in hematological, biochemical, or histopathological parameters, thereby supporting its safety profile.[21]

DISCUSSION

The present integrative review elucidates a significant convergence between the classical Ayurvedic understanding and modern pharmacological evaluation of *Indigofera tinctoria*. The traditional indications of Neelini in *Kuṣṭha* and *Rakta*-related disorders demonstrate an empirical recognition of disease conditions that are now understood to involve dysregulated inflammatory pathways and oxidative stress mechanisms. This alignment highlights the depth of traditional knowledge and its potential relevance in contemporary biomedical research.[22]

A critical aspect of this correlation lies in the identification of indirubin as a key bioactive constituent. Indirubin has been extensively studied for its ability to inhibit cyclin-dependent kinases and modulate NF-κB signaling pathways, both of which play a central role in the regulation of inflammation, immune responses, and cellular proliferation. The inhibition of these pathways results in suppression of pro-inflammatory mediators, thereby providing a mechanistic explanation for the anti-inflammatory effects of *Indigofera tinctoria* and supporting its traditional use in inflammatory conditions.

In addition to its anti-inflammatory effects, the antioxidant activity of *Indigofera tinctoria* plays a vital role in its pharmacological profile. The presence of flavonoids and phenolic compounds enables the scavenging of reactive oxygen species, thereby reducing oxidative stress–induced cellular damage. Considering that oxidative stress is a major contributing factor in the pathogenesis of chronic diseases, including metabolic and degenerative disorders, this property enhances the clinical relevance of the plant.[23]

The hepatoprotective activity observed in experimental studies suggests its ability to restore altered biochemical parameters and protect hepatic tissue from toxin-induced damage. Similarly, its antimicrobial activity against various pathogens supports its traditional application in dermatological conditions.[24] The neuropharmacological effects, including

anticonvulsant activity, further indicate its interaction with central nervous system pathways, while its antidiabetic activity reflects its potential role in metabolic regulation.[25]

These findings collectively indicate that *Indigofera tinctoria* functions as a multi-target therapeutic agent, acting on multiple physiological systems simultaneously. This multi-dimensional mode of action is consistent with the holistic principles of Ayurveda, where a single medicinal substance is understood to exert systemic effects rather than targeting a single molecular pathway.

However, despite these promising findings, several limitations hinder its clinical translation. The majority of available studies are confined to in vitro and animal models, with limited clinical trials available to validate its efficacy in human populations. Additionally, variability in extraction methods and lack of standardized formulations result in inconsistencies in experimental outcomes.

Another significant limitation is the lack of comprehensive pharmacokinetic and pharmacodynamic data. Understanding the absorption, distribution, metabolism, and elimination of active constituents is essential for determining optimal dosing, safety, and therapeutic efficacy. The absence of such data restricts the development of evidence-based therapeutic formulations.

Therefore, while the current evidence strongly supports the pharmacological potential of *Indigofera tinctoria*, there is a need for systematic and multidisciplinary research approaches to bridge the gap between traditional knowledge and modern clinical application.

CONCLUSION

Indigofera tinctoria Linn. (Neelini) emerges as a therapeutically significant medicinal plant with substantial support from both classical Ayurvedic literature and modern pharmacological research. The alignment between traditional indications and experimentally validated biological activities highlights its potential as a multi-target therapeutic agent capable of modulating key pathways involved in inflammation, oxidative stress, and metabolic regulation.

The presence of bioactive constituents such as indirubin, along with flavonoids and phenolic compounds, provides a strong mechanistic basis for its pharmacological actions. These

findings not only validate its traditional usage but also emphasize its potential for further scientific exploration and therapeutic application.

However, the current body of evidence remains predominantly preclinical, and the lack of well-designed clinical studies limits its integration into evidence-based medicine. Furthermore, issues related to standardization, quality control, and pharmacokinetic profiling remain inadequately addressed, thereby restricting its translational applicability.

In order to fully realize its therapeutic potential, it is essential to adopt a rigorous and systematic research approach that integrates classical Ayurvedic principles with modern scientific methodologies. Such an approach will facilitate the development of safe, effective, and scientifically validated formulations, thereby strengthening the role of *Indigofera tinctoria* in contemporary healthcare systems.

Future Scope

Future research on *Indigofera tinctoria* should focus on a comprehensive and integrative approach aimed at bridging the gap between traditional knowledge and modern scientific validation. The development of standardized extracts and identification of bioactive marker compounds are essential to ensure consistency, reproducibility, and quality control in pharmacological studies.

Well-designed clinical trials are required to establish its safety and efficacy in human populations, thereby facilitating its translation into clinical practice. In addition, detailed pharmacokinetic studies should be conducted to elucidate the absorption, distribution, metabolism, and elimination of its active constituents, while pharmacodynamic evaluations are necessary to determine dose-response relationships and therapeutic targets.

The application of network pharmacology offers a promising platform to explore the multi-target interactions of its phytoconstituents and their involvement in complex biological pathways. Integration of this approach with advanced techniques such as molecular docking, metabolomics, and systems biology can provide deeper insights into its mechanism of action and therapeutic potential.

Such a multidisciplinary and integrative strategy will not only enhance the scientific understanding of *Indigofera tinctoria* but also contribute to the development of novel

phytopharmaceutical formulations, thereby strengthening its role in evidence-based healthcare systems.

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