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Polyherbal Transdermal Strategies for Sleep Management: Therapeutic Potential of Valerian (*Valeriana Officinalis*), Jatamansi (*Nardostachys Jatamansi*), Chamomile (*Matricaria Chamomilla*), And Tomato Peel-Derived Biopolymeric Forehead Sheets

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ABSTRACT

Sleep disorders represent a growing global health challenge, affecting millions of individuals and contributing to impaired cognitive performance, reduced quality of life, and increased risk of chronic diseases. Although conventional hypnotic medications remain the primary therapeutic option for insomnia and related sleep disturbances, their long-term use is often associated with adverse effects including tolerance, dependence, residual sedation, and impaired daytime functioning. Consequently, increasing attention has been directed toward plant-based interventions that offer favorable safety profiles and multimodal pharmacological actions. Among medicinal plants traditionally employed for sleep promotion, *Valeriana officinalis*, *Nardostachys jatamansi*, and *Matricaria chamomilla* have attracted substantial scientific interest due to their sedative, anxiolytic, neuroprotective, and sleep-enhancing properties. The bioactive constituents of these plants, including valerenic acid, valepotriates, jatamansone, apigenin, flavonoids, and volatile terpenoids, have been reported to modulate neurotransmitter systems involved in sleep regulation, particularly γ-aminobutyric acid (GABA), serotonin, melatonin, and related neurochemical pathways. The integration of these botanicals into a polyherbal formulation may provide synergistic therapeutic benefits through complementary mechanisms of action targeting multiple aspects of sleep physiology. Recent advances in transdermal drug delivery have created new opportunities for the administration of herbal bioactives through non-invasive and patient-friendly dosage forms. Simultaneously, growing emphasis on sustainable pharmaceutical development has encouraged the exploration of renewable biomaterials as functional carriers. Tomato peel, an abundant agro-industrial by-product, represents a promising source of natural polymers including pectin, cellulose, and hemicellulose, which possess excellent film-forming and biodegradable characteristics suitable for pharmaceutical applications. This review critically examines the neurobiological basis of sleep regulation, the pharmacological evidence supporting the sleep-promoting activities of valerian, jatamansi, and chamomile, and the scientific rationale underlying polyherbal therapeutic approaches. Furthermore, the potential application of tomato peel-derived biopolymers in the development of herbal serum-loaded forehead sheets is discussed, with particular emphasis on formulation design, transdermal delivery, sustainability, and future research directions. The convergence of phytotherapy and biodegradable polymer technology may offer an innovative strategy for developing safe, eco-friendly, and patient-centric interventions for sleep support.

Keywords: Sleep Disorders, Insomnia, Polyherbal Therapy, Valeriana officinalis, Nardostachys jatamansi, Matricaria chamomilla, Transdermal Drug Delivery, Tomato Peel Biopolymers , Forehead Sheets, Herbal Formulations

1. Introduction

Sleep is a fundamental biological process that plays a crucial role in maintaining physical health, cognitive performance, emotional well-being, and overall quality of life. Adequate sleep is essential for memory consolidation, immune regulation, metabolic homeostasis, and neurological restoration. However, the prevalence of sleep disorders, particularly insomnia, has increased significantly in recent decades due to factors such as psychological stress, sedentary lifestyles, excessive screen exposure, irregular work schedules, and underlying medical conditions. Insufficient or poor-quality sleep has been associated with numerous adverse health outcomes, including cardiovascular diseases, metabolic disorders, depression, anxiety, impaired cognitive function, and reduced productivity.

Conventional pharmacological treatments for sleep disorders primarily include benzodiazepines, non-benzodiazepine hypnotics, antidepressants, and melatonin receptor agonists. Although these medications can provide short-term relief, their prolonged use may be associated with adverse effects such as tolerance, dependence, daytime sedation, cognitive impairment, and withdrawal symptoms. These limitations have stimulated growing interest in alternative and complementary therapeutic approaches that offer improved safety profiles and long-term suitability. Medicinal plants have been used for centuries in traditional healthcare systems to promote relaxation and improve sleep quality. Among the various herbal remedies investigated, Valeriana officinalis (Valerian), Nardostachys jatamansi (Jatamansi), and Matricaria chamomilla (Chamomile)

have received considerable scientific attention due to their sedative, anxiolytic, neuroprotective, and antioxidant properties. Valerian is widely recognized for its ability to modulate gamma-aminobutyric acid (GABA)-mediated neurotransmission, thereby facilitating sleep initiation and maintenance. Jatamansi, an important medicinal herb in Ayurvedic medicine, exhibits adaptogenic and stress-reducing properties that may help alleviate sleep disturbances associated with anxiety and psychological stress. Chamomile contains bioactive flavonoids, particularly apigenin, which interact with GABA receptors and contribute to relaxation and improved sleep quality [1-5].

The concept of polyherbal therapy has gained increasing importance in modern phytopharmaceutical research because combinations of medicinal plants may produce synergistic therapeutic effects through multiple biological pathways. Sleep disorders are multifactorial conditions involving neurochemical imbalance, stress responses, oxidative damage, and circadian rhythm disruption. Therefore, a polyherbal formulation containing Valerian, Jatamansi, and Chamomile may provide broader therapeutic coverage than individual herbal preparations by simultaneously targeting several mechanisms involved in sleep regulation.

In addition to the selection of appropriate herbal ingredients, the effectiveness of a therapeutic formulation is strongly influenced by its delivery system. Traditional oral dosage forms often face challenges such as poor bioavailability, gastrointestinal degradation, and extensive first-pass metabolism. Transdermal drug delivery systems have emerged as promising alternatives because they enable controlled release of active compounds, improve patient compliance, avoid [6-10] gastrointestinal complications, and bypass hepatic first-pass metabolism.

Recent advances in pharmaceutical technology have expanded the application of transdermal systems to herbal bioactives, creating new opportunities for developing innovative sleep-support formulations. Simultaneously, increasing emphasis on environmental sustainability has encouraged the exploration of renewable natural materials for pharmaceutical applications. Tomato peel, a major agro-industrial by-product generated during food processing, contains valuable biopolymers such as pectin, cellulose, and hemicellulose that exhibit excellent film-forming, biodegradable, and biocompatible properties. The utilization of tomato peel-derived polymers not only supports sustainable pharmaceutical development but also contributes to waste valorization and circular economy principles.

The integration of Valerian, Jatamansi, and Chamomile into a tomato peel-derived transdermal forehead sheet represents a novel approach that combines herbal therapeutics, advanced drug delivery technology, and sustainable biomaterials. Such a formulation has the potential to provide controlled release of sleep-promoting phytochemicals while offering a patient-friendly, non-invasive, and environmentally responsible alternative for sleep management. Therefore, this review aims to critically examine the therapeutic potential of these medicinal plants, recent advances in herbal transdermal delivery systems, and the emerging role of tomato peel-derived biopolymers in the development of innovative sleep-supportive healthcare products.

Sleep Physiology and Neurobiology

Sleep is a complex and highly regulated physiological process that is essential for maintaining overall health and normal biological functioning. It is characterized by reversible unconsciousness, reduced responsiveness to external stimuli, and distinct patterns of brain activity. Sleep plays a critical role in memory consolidation, learning, tissue repair, immune regulation, hormonal balance, and metabolic homeostasis. Disruptions in normal sleep patterns can negatively affect both physical and mental health, increasing the risk of numerous chronic diseases.

Sleep is broadly divided into two major states: non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep. NREM sleep accounts for approximately 75–80% of total sleep time and is further divided into three stages: N1, N2, and N3. Stage N1 represents the transition from wakefulness to sleep and is characterized by reduced muscle activity and slowed eye movements. Stage N2 is considered a light sleep stage during which heart rate and body temperature decrease. Stage N3, also known as slow-wave sleep or deep sleep, is associated with physical restoration, tissue repair, growth hormone secretion, and immune system strengthening.

REM sleep accounts for approximately 20–25% of total sleep duration and is characterized by rapid eye movements, vivid dreaming, increased brain activity, and temporary muscle paralysis. This stage plays a crucial role in emotional regulation, learning processes, memory consolidation, and cognitive performance. A healthy sleep cycle typically alternates between NREM and REM sleep multiple times throughout the night. The regulation of sleep and wakefulness involves complex interactions among several neurotransmitters and neural pathways. Gamma-aminobutyric acid (GABA) is the primary inhibitory neurotransmitter involved in sleep initiation and maintenance. Activation of GABAergic neurons suppresses arousal systems within the brain, facilitating the transition from wakefulness to sleep. Many conventional hypnotic medications and several medicinal plants exert their effects by enhancing GABA-mediated neurotransmission[11-15].

Other neurotransmitters also contribute significantly to sleep regulation. Serotonin influences mood, emotional stability, and sleep architecture, while melatonin, produced by the pineal gland, regulates circadian rhythms and sleep timing. Adenosine accumulates during prolonged wakefulness and promotes sleep pressure, encouraging the body to rest. In contrast, orexin (hypocretin) functions as a wake-promoting neurotransmitter that helps maintain alertness and prevents inappropriate sleep episodes.

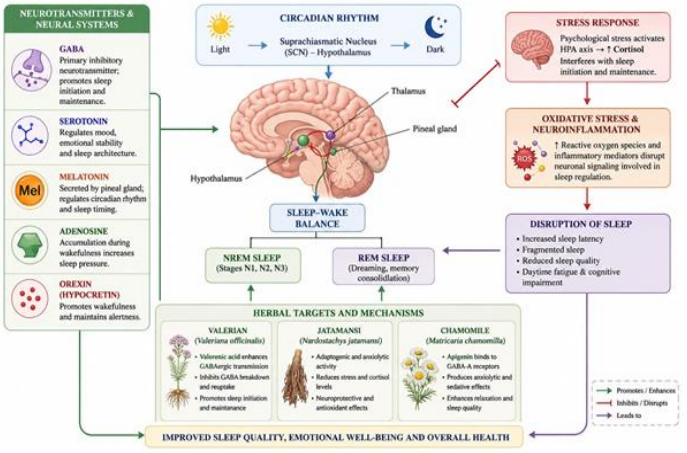
The circadian rhythm is another critical component of sleep regulation. This internal biological clock is controlled by the suprachiasmatic nucleus (SCN) located within the hypothalamus. The SCN synchronizes physiological functions with environmental light-dark cycles and regulates melatonin secretion. Exposure to natural light during the daytime promotes wakefulness, whereas darkness stimulates melatonin production and facilitates sleep onset. Disturbances in circadian rhythm caused by shift work, jet lag, or excessive nighttime exposure to

electronic devices can significantly impair sleep quality. Psychological stress is one of the major contributors to sleep disturbances. Stress activates the hypothalamic-pituitary-adrenal (HPA) axis, resulting in increased secretion of cortisol and other stress hormones. Elevated cortisol levels may interfere with normal sleep initiation and maintenance, leading to insomnia and fragmented sleep patterns [20-24]. Chronic stress can further contribute to anxiety, depression, and other mental health conditions that adversely affect sleep quality.

Oxidative stress and neuroinflammation have also been implicated in the pathogenesis of sleep disorders. Accumulation of reactive oxygen species and inflammatory mediators may disrupt neuronal signaling pathways involved in sleep regulation. Consequently, compounds possessing antioxidant and neuroprotective properties may provide therapeutic benefits in sleep management by protecting neural tissues and reducing inflammation-related disturbances.

Understanding the neurobiological mechanisms underlying sleep regulation provides a scientific basis for the development of effective therapeutic interventions. Medicinal plants such as Valerian, Jatamansi, and Chamomile exert their sleep-promoting effects through modulation of GABAergic neurotransmission, reduction of stress responses, antioxidant activity, and neuroprotective mechanisms. These complementary actions support their potential use in polyherbal formulations designed to improve sleep quality and overall well-being [25-30].

Figure 1. Mechanism of Sleep Regulation and Herbal Targets



Therapeutic Potential of Valerian, Jatamansi, and Chamomile: Medicinal plants have been utilized for centuries as natural remedies for sleep disorders, anxiety, and stress-related conditions. Among the numerous botanicals investigated for sleep support, Valeriana officinalis (Valerian), Nardostachys jatamansi (Jatamansi), and Matricaria chamomilla (Chamomile) have demonstrated significant pharmacological potential. These herbs contain diverse bioactive compounds capable of modulating neurotransmitter systems, reducing stress responses, and promoting relaxation, thereby contributing to improved sleep quality.

Valeriana officinalis (Valerian)

Valerian is one of the most extensively studied medicinal plants for the management of insomnia and sleep disturbances. The roots and rhizomes of the plant contain several bioactive constituents, including valerenic acid, valerenol, iridoids, alkaloids, and flavonoids. These compounds are believed to influence the central nervous system primarily through modulation of gamma-aminobutyric acid (GABA) neurotransmission.

Valerenic acid enhances GABA signaling by inhibiting the breakdown and reuptake of GABA within the brain. Increased GABA activity suppresses neuronal excitability, promotes relaxation, and facilitates sleep initiation. Clinical studies have reported that valerian supplementation may reduce sleep latency, improve sleep quality, and decrease nighttime awakenings without causing significant morning drowsiness. In addition to its sedative properties, valerian exhibits mild anxiolytic and neuroprotective [31-35] effects that may further contribute to its therapeutic value in individuals experiencing stress-related sleep disturbances. Due to its favorable safety profile and long history of traditional use, valerian remains one of the most popular herbal sleep aids worldwide.

Nardostachys jatamansi (Jatamansi)

Jatamansi is a highly valued medicinal plant in Ayurvedic medicine and has traditionally been used to promote mental calmness, enhance cognitive function, and improve sleep. The rhizomes of the plant contain sesquiterpenes, jatamansone, nardostachone, and various phenolic compounds that contribute to its pharmacological activities. Research suggests that Jatamansi possesses sedative, adaptogenic, anxiolytic, antioxidant, and neuroprotective properties. Its adaptogenic activity helps the body cope with physical and psychological stress by modulating stress-related hormonal responses. Since chronic stress is a major factor contributing to insomnia, the stress-reducing effects of Jatamansi may significantly improve sleep quality. Furthermore, antioxidant constituents present in Jatamansi help protect neuronal tissues from oxidative damage, while its neuroprotective actions may support healthy brain function. These combined properties make Jatamansi a promising herbal candidate for managing stress-induced sleep disturbances and enhancing overall neurological well-being [36-40].

Matricaria chamomilla (Chamomile)

Chamomile is one of the oldest medicinal herbs used for relaxation and sleep promotion. The flowers contain several biologically active compounds, including apigenin, luteolin, quercetin, bisabolol, and chamazulene. Among these, apigenin is considered the primary constituent responsible for chamomile's sleep-supportive effects. Apigenin binds to benzodiazepine-sensitive GABA-A receptors within the central nervous system, producing mild sedative and anxiolytic effects. Through this mechanism, chamomile promotes relaxation, reduces anxiety, and facilitates sleep onset. Clinical investigations have demonstrated that chamomile supplementation may improve subjective sleep quality and reduce symptoms associated with generalized anxiety. Chamomile also possesses anti-inflammatory and antioxidant properties that may contribute to overall neurological health. Its excellent safety profile and widespread acceptance make it a valuable component of herbal formulations intended for sleep support[41-2].

Comparative Therapeutic Significance

Although each herb possesses distinct pharmacological characteristics, they share several complementary mechanisms relevant to sleep management. Valerian primarily enhances sleep initiation through GABA modulation, Jatamansi reduces stress and promotes neuroprotection, while Chamomile supports relaxation and emotional stability through anxiolytic effects. The combination of these botanicals offers a comprehensive therapeutic approach capable of targeting multiple pathways involved in sleep regulation. Such complementary actions provide a strong scientific rationale for developing polyherbal formulations designed to improve sleep quality, reduce anxiety, and enhance overall well-being. The diverse pharmacological activities of these medicinal plants highlight their potential as natural alternatives or complementary therapies for sleep disorders. Continued research is warranted to further elucidate their mechanisms of action, optimize dosage strategies, and evaluate their effectiveness within advanced delivery systems such as transdermal formulations.

Table 1: Comparative Pharmacological Profile of Selected Herbs

Herbs	Major Active constituents	Main Mechanism	Sleep Benefits
Valerian	Valerenic acid, valerenol	GABA modulation	Sleep initiation
Jatamansi	Jatamansone, sequiterpenes	Adaptogenic and anxiilytic activity	Stress reduction
Chamomile	Apigenin, flavonoids	GABA-A receptor interaction	Relaxation and sleep quality

Polyherbal Synergy in Sleep Management

The concept of polyherbal therapy has gained considerable attention in modern phytopharmaceutical research due to its ability to provide enhanced therapeutic efficacy through the combined action of multiple medicinal plants. Unlike single-herb formulations, polyherbal preparations utilize the synergistic interactions among various bioactive compounds to target multiple physiological pathways simultaneously.

This approach is particularly beneficial in the management of sleep disorders, which are multifactorial conditions influenced by neurological, psychological, hormonal, and environmental factors. Sleep disturbances often arise from a combination of stress, anxiety, neurotransmitter imbalance, oxidative stress, and circadian rhythm disruption. Therefore, therapeutic strategies focusing on a single mechanism may not provide optimal outcomes for all individuals. Polyherbal formulations offer a broader spectrum of activity by addressing several underlying causes of sleep disorders concurrently. The combination of Valerian, Jatamansi, and Chamomile represents an example of a rationally designed polyherbal approach for sleep support.

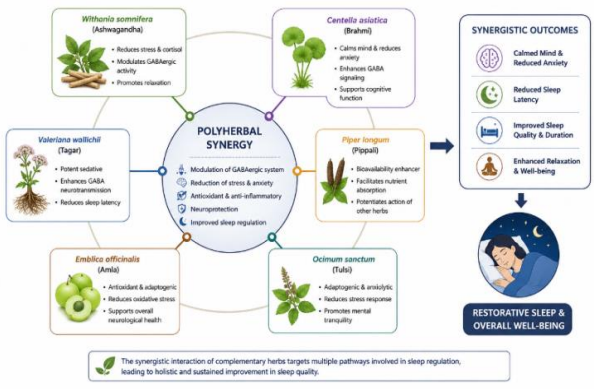
Valerian primarily acts through enhancement of GABAergic neurotransmission, thereby promoting sleep initiation and reducing neuronal excitability. Jatamansi contributes adaptogenic, anxiolytic, and neuroprotective activities that help alleviate stress-related sleep disturbances and support emotional well-being. Chamomile complements these effects by inducing relaxation, reducing anxiety, and improving sleep quality through interaction with GABA-A receptors. The integration of these distinct yet complementary mechanisms may result in greater therapeutic benefits than those achieved by individual herbs alone.

In addition to their neuropharmacological effects, these medicinal plants possess antioxidant and anti-inflammatory properties that may contribute to improved neurological health. Oxidative stress and neuroinflammation have been implicated in the pathogenesis of insomnia and other sleep disorders. Therefore, the combined antioxidant activities of Valerian, Jatamansi, and Chamomile may provide additional protection against sleep-related physiological disturbances. Polyherbal formulations may also improve the consistency and reliability of therapeutic outcomes. Variations in the concentration of active constituents within individual herbs can sometimes affect treatment efficacy. By combining multiple medicinal plants with complementary actions, the overall formulation may achieve a more balanced and robust pharmacological response. Furthermore, lower concentrations of individual herbs may be used within a polyherbal system, potentially minimizing adverse effects while maintaining therapeutic effectiveness.

Scientific evidence increasingly supports the concept of herbal synergy, whereby multiple phytochemicals interact at molecular, cellular, and physiological levels to enhance biological activity. Such interactions may improve receptor binding, increase bioavailability, optimize pharmacokinetic profiles, and influence multiple signaling pathways simultaneously. These advantages are particularly relevant in sleep management, where successful treatment often requires modulation of several interconnected neurobiological processes.

The combination of Valerian, Jatamansi, and Chamomile therefore provides a strong scientific foundation for the development of innovative sleep-support formulations. By simultaneously targeting sleep initiation, stress reduction, relaxation, neuroprotection, and antioxidant defense, this polyherbal system may offer a comprehensive approach for improving sleep quality and overall well-being. The growing interest in natural and complementary healthcare solutions further highlights the importance of polyherbal strategies. As consumers increasingly seek safer alternatives to conventional hypnotic medications, scientifically validated polyherbal formulations may emerge as valuable options for long-term sleep management. Future research should focus on standardization, mechanistic investigations, and clinical validation to fully establish the therapeutic potential of these synergistic herbal combinations[43-46].

Figure 2. Polyherbal Synergy in Sleep Management



Transdermal Delivery of Herbal Bioactives

Transdermal drug delivery systems (TDDS) have emerged as innovative pharmaceutical platforms capable of delivering therapeutic agents through the skin and into systemic circulation. Compared with conventional oral dosage forms, transdermal systems offer several advantages, including avoidance of gastrointestinal degradation, elimination of hepatic first-pass metabolism, sustained drug release, improved bioavailability, and enhanced patient compliance. These characteristics have stimulated increasing interest in the application of transdermal technologies for herbal therapeutics, particularly in the management of chronic conditions requiring prolonged treatment.

The skin serves as an effective protective barrier against external environmental factors. Although this barrier function limits drug penetration, appropriately designed transdermal formulations can facilitate the controlled transport of active compounds across the stratum corneum and into deeper skin layers. Successful transdermal delivery depends on several factors, including molecular size, lipophilicity, concentration gradient, formulation characteristics, and the presence of permeation-enhancing agents.

In recent years, transdermal systems have gained considerable attention for the delivery of herbal bioactive compounds. Many phytochemicals possess valuable therapeutic properties but often suffer from poor oral bioavailability due to instability within the gastrointestinal tract, enzymatic degradation, or extensive first-pass metabolism. Transdermal administration provides an alternative route that may enhance the effectiveness of these natural compounds while minimizing gastrointestinal side effects.

Various transdermal dosage forms have been developed, including patches, films, gels, creams, microneedles, and sheet-based delivery systems. Among these approaches, polymeric films and sheets are particularly attractive because they allow sustained release of active ingredients, maintain prolonged contact with the skin, and provide convenient, non-invasive administration. Such systems can be designed to achieve controlled release profiles that ensure continuous delivery of therapeutic agents over extended periods.

The application of transdermal technology to sleep-support formulations offers several unique advantages. Sleep disorders often require consistent therapeutic effects throughout the night to maintain normal sleep architecture. Controlled-release transdermal systems can provide prolonged exposure to sleep-promoting phytochemicals, thereby reducing fluctuations in drug concentration and enhancing therapeutic efficacy. Additionally, transdermal administration may improve patient adherence because it eliminates the need for repeated dosing and simplifies treatment regimens.

Herbal bioactives derived from Valerian, Jatamansi, and Chamomile possess physicochemical characteristics that make them suitable candidates for incorporation into transdermal delivery systems. The sustained release of these phytochemicals through a transdermal platform may facilitate prolonged modulation of GABAergic neurotransmission, stress responses, and relaxation pathways. Furthermore, the localized application of herbal formulations may enhance patient acceptance, particularly among individuals seeking non-pharmacological or complementary approaches for sleep support.

Recent advances in pharmaceutical formulation technologies have enabled the development of novel biodegradable and biocompatible polymeric matrices for transdermal applications. Natural polymers derived from plant sources have attracted particular interest because of their sustainability, low toxicity, and favorable mechanical properties. These materials provide suitable platforms for the incorporation and controlled release of herbal extracts while supporting environmentally responsible pharmaceutical development.

Despite their promising potential, several challenges remain in the development of herbal transdermal systems. Factors such as variability in herbal extract composition, limited skin permeability of certain phytochemicals, formulation stability, and standardization requirements must be carefully addressed. Continued research focusing on formulation optimization, permeation enhancement strategies, and clinical evaluation will be essential for maximizing the therapeutic benefits of herbal transdermal technologies.

Overall, transdermal delivery represents a promising strategy for improving the administration of herbal bioactives used in sleep management. By combining sustained release characteristics, patient convenience, and improved bioavailability, transdermal systems may facilitate the development of next-generation herbal formulations capable of providing effective and safe support for individuals experiencing sleep disturbances.

Table 2. Advantages of Polyherbal Transdermal Delivery

Parameter	Oral Formulations	Transdermal Forehead Sheet
First-pass metabolism	Present	Avoided
Drug release	Rapid	Controlled
Patient compliance	Moderate	High
Dosing frequency	Repeated dosing	Sustained release
Gastrointestinal irritation	Possible	Minimal
Administration	Oral	Non-invasive
Bioavailability	Variable	Improved
Environmental sustainability	Moderate	High

Tomato Peel-Derived Biopolymers as Sustainable Pharmaceutical Carriers:

The growing demand for environmentally sustainable pharmaceutical materials has encouraged researchers to explore renewable natural resources as alternatives to synthetic polymers. Agricultural by-products and food-processing wastes have emerged as valuable sources of biodegradable biomaterials with potential pharmaceutical applications. Among these resources, tomato peel represents an abundant agro-industrial waste generated during the production of tomato-based products such as sauces, juices, and pastes. Traditionally discarded as waste, tomato peel contains several biologically important components that can be utilized for the development of eco-friendly drug delivery systems.

Tomato peel is rich in structural polysaccharides, including pectin, cellulose, and hemicellulose, which possess desirable physicochemical properties for pharmaceutical applications. These natural polymers exhibit excellent film-forming ability, biodegradability, biocompatibility, and moisture-retention characteristics. Such properties make tomato peel-derived materials suitable candidates for the fabrication of transdermal films, patches, and sheet-based delivery systems. Furthermore, their renewable nature supports sustainable manufacturing practices and contributes to the reduction of environmental pollution associated with agricultural waste disposal.

Pectin is one of the major polysaccharides present in tomato peel and plays an important role in the formation of flexible and stable polymeric films. Due to its non-toxic and biodegradable nature, pectin has been extensively investigated as a pharmaceutical excipient in controlled drug delivery systems. Cellulose contributes mechanical strength and structural integrity to polymeric matrices, while hemicellulose enhances flexibility and film-forming performance. The synergistic interaction among these components facilitates the production of durable yet biodegradable pharmaceutical films suitable for transdermal applications.

In addition to structural polysaccharides, tomato peel contains several bioactive compounds, including lycopene, flavonoids, carotenoids, and phenolic substances. Lycopene is a potent natural antioxidant that protects biological tissues from oxidative damage caused by reactive oxygen species. Flavonoids and phenolic compounds possess antioxidant and anti-inflammatory activities that may contribute to improved stability and biocompatibility of pharmaceutical formulations. These naturally occurring compounds may provide supplementary functional benefits when incorporated into transdermal delivery systems.

The utilization of tomato peel-derived polymers aligns with the principles of green chemistry and the circular economy. By converting agricultural waste into value-added pharmaceutical materials, researchers can reduce environmental burdens while simultaneously creating sustainable healthcare products. Such approaches support resource conservation, waste minimization, and environmentally responsible pharmaceutical development. These advantages have become increasingly important as industries seek innovative solutions to address both healthcare and sustainability challenges[47].

Recent advances in biomaterials science have demonstrated the feasibility of extracting and processing tomato peel polysaccharides for the preparation of biodegradable films and pharmaceutical carriers. Studies have reported favorable mechanical properties, satisfactory moisture retention, and good compatibility with various active pharmaceutical ingredients. These findings suggest that tomato peel-derived polymers possess significant potential as alternative excipients for next-generation drug delivery systems.

The application of tomato peel-based biomaterials in sleep-support formulations represents a particularly innovative area of research. When combined with polyherbal extracts such as Valerian, Jatamansi, and Chamomile, these biodegradable polymers may serve as effective carriers capable of providing controlled release of sleep-promoting phytochemicals. Such systems integrate natural therapeutics with sustainable biomaterials, creating environmentally responsible healthcare solutions that address both therapeutic and ecological objectives.

Despite encouraging progress, several research challenges remain. Further investigations are required to optimize extraction techniques, improve polymer characterization, evaluate long-term stability, and assess large-scale manufacturing feasibility. Comprehensive toxicological and clinical studies will also be necessary to ensure safety and effectiveness in pharmaceutical applications.

Overall, tomato peel-derived biopolymers represent a promising class of sustainable pharmaceutical materials with considerable potential for transdermal drug delivery. Their biodegradability, biocompatibility, film-forming properties, and environmental advantages make them attractive candidates for the development of innovative herbal formulations aimed at improving sleep quality and overall well-being.

Table 3: Pharmaceutical Significance of Tomato Peel Components

Component	**Pharmaceutical Function**
Pectin	Film formation and controlled release
Cellulose	Mechanical strength and stability
Hemicellulose	Flexibility and elasticity
Lycopene	Antioxidant activity
Flavonoids	Anti-inflammatory activity
Phenolic compounds	Free radical scavenging
Carotenoids	Protective and antioxidant effects

Polyherbal Serum-Loaded Tomato Peel Forehead Sheets

The integration of herbal therapeutics, transdermal drug delivery technology, and sustainable biomaterials has created new opportunities for the development of innovative healthcare products. Among emerging approaches, the concept of a polyherbal serum-loaded tomato peel forehead sheet represents a novel strategy for sleep management. This system combines the therapeutic potential of Valerian (Valeriana officinalis), Jatamansi (Nardostachys jatamansi), and Chamomile (Matricaria chamomilla) with the advantages of transdermal delivery and environmentally sustainable biomaterials. The proposed formulation consists of a biodegradable polymeric sheet prepared from tomato peel-derived polysaccharides, including pectin, cellulose, and hemicellulose. These polymers serve as the structural matrix for the incorporation of a polyherbal serum containing standardized extracts of Valerian, Jatamansi, and Chamomile. The resulting formulation is designed to be applied to the forehead, where it remains in close contact with the skin and facilitates the gradual release of sleep-promoting phytochemicals [48].

The therapeutic rationale for this formulation is based on the complementary pharmacological actions of the selected medicinal plants. Valerian promotes sleep initiation through enhancement of GABAergic neurotransmission, Jatamansi provides adaptogenic and stress-reducing effects, and Chamomile contributes relaxation and anxiolytic activity

through interaction with GABA-A receptors. The combination of these herbs creates a multi-target therapeutic system capable of addressing several physiological factors associated with sleep disturbances.

The transdermal delivery platform offers several advantages over conventional oral formulations. Following application, active phytochemicals are gradually released from the polymeric matrix and diffuse across the skin surface. This controlled-release mechanism may help maintain consistent therapeutic concentrations throughout the night, thereby reducing fluctuations in pharmacological activity and improving overall sleep support. Additionally, transdermal administration avoids gastrointestinal degradation and hepatic first-pass metabolism, potentially improving the bioavailability of herbal constituents.

Application of the formulation as a forehead sheet may provide additional practical benefits. The forehead is easily accessible, allows convenient application, and is generally well tolerated by patients. The sheet-based system is non-invasive, comfortable, and suitable for prolonged overnight use. Such characteristics may enhance patient compliance and acceptance, particularly among individuals seeking natural alternatives to conventional sleep medications.

Another unique aspect of this approach is its emphasis on sustainability. The utilization of tomato peel-derived polymers transforms agricultural waste into a value-added pharmaceutical material. This strategy supports waste reduction, resource conservation, and environmentally responsible product development while simultaneously providing a functional carrier system for herbal bioactives. Consequently, the formulation aligns with contemporary principles of green pharmacy and circular economy practices.

In addition to transdermal delivery, volatile aromatic compounds present in Valerian and Chamomile may contribute to relaxation through aromatherapeutic mechanisms. The simultaneous combination of transdermal phytochemical delivery and aromatic stimulation may further enhance the overall sleep-supportive effect of the formulation. Such dual-action functionality distinguishes the proposed system from many conventional herbal dosage forms.

Despite its promising potential, the concept remains at an early stage of development and requires extensive scientific validation. Future investigations should focus on formulation optimization, physicochemical characterization, skin permeation studies, mechanical property evaluation, stability testing, and clinical assessment of therapeutic efficacy. Standardization of herbal extracts and quality-control parameters will also be essential for ensuring reproducibility and product consistency.

The development of a polyherbal serum-loaded tomato peel forehead sheet represents an innovative convergence of phytotherapy, biomaterials science, and transdermal drug delivery technology. By combining natural sleep-promoting agents with sustainable pharmaceutical materials, this emerging platform may provide a safe, effective, patient-friendly, and environmentally responsible approach for supporting healthy sleep and overall well-being [49].

Figure 3. Preparation of Polyherbal Serum-Loaded Tomato Peel Forehead Sheet

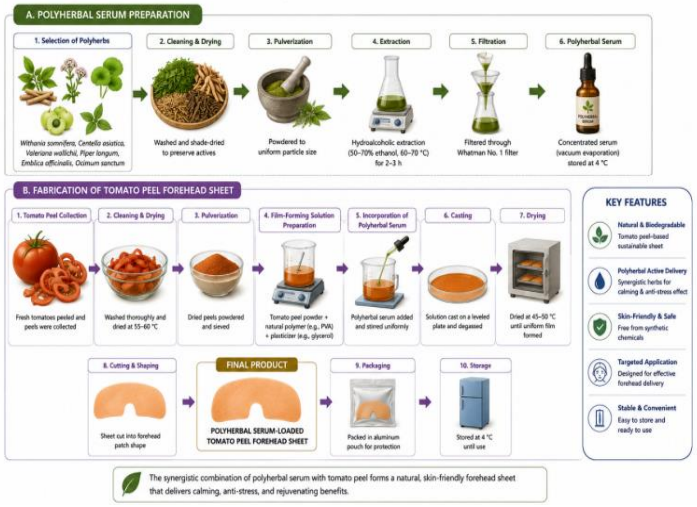
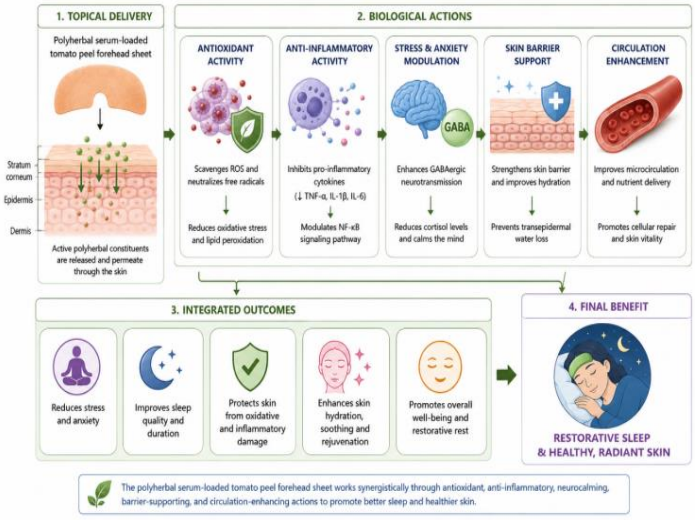


Figure 4. Proposed Mechanism of Action



Future Perspectives and Research Gaps

The growing interest in herbal therapeutics, transdermal drug delivery systems, and sustainable biomaterials has created significant opportunities for the development of innovative sleep-support formulations. The concept of a polyherbal serum-loaded tomato peel forehead sheet represents a promising interdisciplinary approach that combines phytotherapy, pharmaceutical technology, and environmental sustainability. However, despite encouraging scientific evidence supporting the individual components of this formulation, several important research gaps remain that must be addressed before successful clinical translation and commercialization can be achieved. One of the major limitations within the current literature is the lack of comprehensive clinical studies evaluating polyherbal formulations specifically designed for sleep management. While numerous investigations have reported the sleep-promoting properties of Valerian, Jatamansi, and Chamomile individually, limited information is available regarding their combined therapeutic efficacy in standardized formulations. Future randomized controlled clinical trials are necessary to establish the effectiveness, safety, and optimal dosage combinations of these herbal extracts.

Another important challenge involves the standardization of herbal materials. Variations in geographical origin, cultivation practices, harvesting conditions, extraction methods, and storage procedures can significantly influence the concentration of bioactive constituents. The development of validated quality-control protocols and marker-based standardization strategies will therefore be essential to ensure batch-to-batch consistency and reproducibility of therapeutic outcomes. The transdermal delivery of herbal bioactives also requires further investigation. Although transdermal systems offer several advantages over conventional oral dosage forms, limited information is available regarding the skin permeation behavior of many phytochemicals present in Valerian, Jatamansi, and Chamomile. Detailed permeation studies, diffusion kinetics analyses, and formulation optimization strategies are needed to maximize delivery efficiency and therapeutic performance.

Research on tomato peel-derived polymers remains relatively limited compared with other natural biomaterials. Additional studies focusing on extraction techniques, polymer purification, physicochemical characterization, mechanical properties, moisture retention behavior, biodegradation profiles, and compatibility with herbal extracts are required. Such investigations will provide a stronger scientific foundation for the utilization of tomato peel biopolymers in pharmaceutical applications.

Long-term safety evaluation represents another critical area requiring attention. Although the selected medicinal plants possess favorable safety profiles and tomato peel-derived polymers are generally considered biocompatible, comprehensive toxicological assessments are necessary to evaluate potential skin irritation, sensitization, allergenicity, and long-term exposure effects. These studies will be particularly important for products intended for regular or prolonged use.Future research should also focus on understanding the molecular mechanisms underlying polyherbal synergy. Advanced pharmacological and systems biology approaches may help elucidate interactions among bioactive compounds and identify the specific signaling pathways responsible for sleep-promoting effects. Such knowledge could facilitate the rational design of more effective polyherbal formulations.

Recent advances in digital health technologies present additional opportunities for innovation. The integration of wearable sleep-monitoring devices with transdermal herbal delivery systems may enable personalized sleep management approaches. Smart delivery platforms capable of adjusting release profiles according to individual sleep patterns could represent an important future direction in phytopharmaceutical research. Furthermore, commercialization studies and industrial-scale manufacturing assessments are required to evaluate economic feasibility, regulatory requirements, production scalability, and market acceptance. Successful translation from laboratory research to commercial healthcare products will depend on interdisciplinary collaboration among pharmacologists, formulation scientists, biomaterials researchers, clinicians, and industry partners. Overall, the convergence of herbal medicine, sustainable biomaterials, and advanced transdermal technologies offers exciting prospects for the future of sleep management. Continued scientific investigation and technological innovation may facilitate the development of next-generation herbal healthcare products that are effective, safe, environmentally sustainable, and accessible to a growing global population seeking natural solutions for sleep-related disorders.

Table 4. Research Gaps and Future Research Priorities

Research Gap	Gap Future Research Requirement
Limited polyherbal clinical studies	Large-scale randomized clinical trials
Lack of standardized formulations	Development of validated quality standards
Insufficient transdermal permeation data	Detailed skin permeation investigations
Limited tomato peel polymer research	Advanced biomaterial characterization
Inadequate long-term safety data	Extended toxicological studies
Poor understanding of synergistic mechanisms	Molecular and mechanistic investigations
Limited personalized approaches	Smart and wearable-integrated delivery systems
Lack of commercialization studies	Scale-up and industrial feasibility assessments

Conclusion

Sleep disorders continue to represent a significant global health challenge, affecting millions of individuals and contributing to adverse physical, psychological, and socioeconomic consequences. Adequate sleep is essential for maintaining cognitive performance, emotional stability, immune function, metabolic regulation, and overall quality of life. Although conventional pharmacological therapies remain important treatment options, concerns regarding tolerance, dependence, residual sedation, and long-term safety have stimulated increasing interest in alternative and complementary approaches for sleep management.

Medicinal plants have emerged as promising candidates owing to their long history of traditional use, favorable safety profiles, and diverse pharmacological activities. Among the various herbal remedies investigated, Valeriana officinalis (Valerian), Nardostachys jatamansi (Jatamansi), and Matricaria chamomilla (Chamomile) possess substantial scientific evidence supporting their sleep-promoting potential. These medicinal plants exert sedative, anxiolytic, neuroprotective, antioxidant, and stress-reducing effects through multiple biological pathways, particularly through modulation of GABAergic neurotransmission and regulation of stress responses. Their complementary mechanisms provide a strong rationale for the development of polyherbal formulations capable of addressing the multifactorial nature of sleep disturbances[50].

The concept of polyherbal therapy offers several advantages over single-herb interventions by simultaneously targeting multiple physiological processes involved in sleep regulation. The synergistic combination of Valerian, Jatamansi, and Chamomile may enhance therapeutic efficacy through integrated effects on sleep initiation, relaxation, stress reduction, emotional balance, and neurological protection. Such multi-target approaches are particularly valuable for managing complex sleep disorders influenced by both physiological and psychological factors. Recent advances in transdermal drug delivery systems have created new opportunities for improving the administration of herbal bioactive compounds. Compared

with conventional oral dosage forms, transdermal systems provide several benefits, including avoidance of first-pass metabolism, improved patient compliance, sustained release of active constituents, and non-invasive administration. These characteristics make transdermal platforms attractive options for sleep-support formulations intended for prolonged and convenient use.

The exploration of tomato peel-derived biopolymers introduces an additional dimension of innovation and sustainability to pharmaceutical development. Rich in pectin, cellulose, hemicellulose, and antioxidant compounds, tomato peel represents a renewable and biodegradable biomaterial capable of supporting the fabrication of pharmaceutical films and transdermal sheets. The utilization of agricultural waste as a functional pharmaceutical excipient aligns with modern principles of green chemistry, circular economy, and environmentally responsible healthcare product development.

A polyherbal serum-loaded tomato peel forehead sheet represents an innovative convergence of herbal medicine, biomaterials science, and transdermal delivery technology. This novel formulation concept combines the therapeutic benefits of Valerian, Jatamansi, and Chamomile with the controlled-release capabilities of a biodegradable tomato peel-derived polymeric matrix. Such an approach has the potential to provide effective sleep support while simultaneously addressing sustainability challenges associated with pharmaceutical manufacturing. Despite the promising potential of this emerging platform, several challenges remain to be addressed before clinical implementation can be achieved. Future research should focus on formulation optimization, herbal standardization, permeation studies, advanced biomaterial characterization, toxicological evaluation, and large-scale clinical trials. Comprehensive scientific validation will be essential to establish efficacy, safety, and commercial feasibility. In conclusion, the integration of polyherbal therapeutics with sustainable transdermal delivery systems represents a promising future direction in sleep management. The combination of Valerian, Jatamansi, and Chamomile within a tomato peel-derived forehead sheet offers a unique strategy that addresses therapeutic effectiveness, patient convenience, and environmental sustainability simultaneously. Continued interdisciplinary research may facilitate the development of next-generation herbal healthcare products capable of providing safe, effective, and eco-friendly solutions for improving sleep quality and overall well-being.

Conflict of Interests

The authors declare no conflict of interest

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Ai Tool Declaration

The authors declare that no AI and related tools are used to write the scientific content of this manuscript.

Data Availability

Data will be available on request

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