Review Paper

ISSN: 3139-3683

JOURNAL OF HEALTH SYNAPSE (JHS)

Peer Reviewed Refereed Open Access International Multidisciplinary Journal

Publisher: *Scientistic Era Private Limited*
Journal Hompage: *https://healthsynapse.org*

Herbal Microsphere-Based Topical Gel for Treating Bacterial Infections: A Review

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ARTICLE INFO

KEYWORDS:
Herbal microspheres, topical gel, antibacterial activity, controlled drug delivery, herbal formulation, bacterial infections.

ARTICLE HISTORY
Received Date: 05 August 2026
Revised Date: 15 August 2026
Accepted Date: 30 August 2026
Published Date: 09 September 2026

CITATION
Qureshi, S. A., 2026 Herbal Microsphere-Based Topical Gel for Treating Bacterial Infections: A Review. *Journal of Health Synapse (JHS), 1(3), 51-56. https://doi.org/10.67529/jhs.v1i3.5*

A B S T R A C T

Herbal microsphere-based topical gels represent a promising approach for the localized treatment of bacterial skin infections by combining the therapeutic potential of medicinal plants with controlled drug-delivery technology. This review focuses on the design, formulation, and evaluation of herbal microsphere-based topical gels intended for antibacterial applications. Microspheres can enhance drug stability, improve controlled release, prolong residence time at the infection site, and potentially reduce dosing frequency. The review discusses commonly used herbal antibacterial agents, microsphere preparation techniques, gel-forming polymers, formulation variables, and important evaluation parameters such as particle size, entrapment efficiency, pH, viscosity, spreadability, drug release, stability, and antibacterial activity. Overall, herbal microsphere-based topical gels offer a promising and potentially effective platform for improving the localized delivery and therapeutic performance of herbal antibacterial agents.

I. Introduction

Bacterial skin infections are among the most common dermatological disorders affecting people of all age groups worldwide [1, 2]. These infections are caused by pathogenic microorganisms such as Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, and Streptococcus pyogenes, which invade the skin through cuts, burns, wounds, surgical incisions, or weakened skin barriers [3]. The prevalence of bacterial infections has increased significantly due to poor hygiene conditions, environmental pollution, rising antibiotic resistance, diabetes, immunological disorders, and prolonged hospitalization [4]. Conventional treatment methods generally involve oral or topical antibiotics; however, continuous and irrational use of synthetic antimicrobial drugs has led to several limitations including drug resistance, skin irritation, allergic reactions, toxicity, reduced therapeutic effectiveness, and recurrence of infection [5]. These challenges have created a strong demand for safer, more effective, and sustained drug delivery systems capable of enhancing antimicrobial activity while minimizing adverse effects [6].

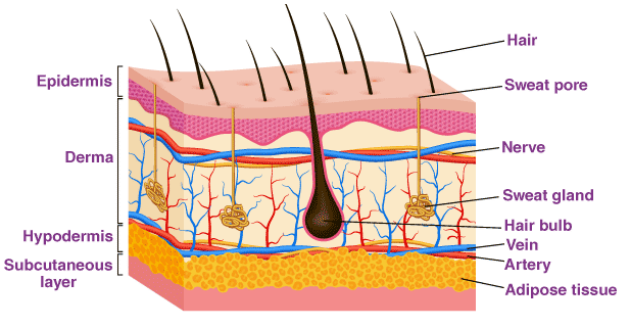

Fig.1. Bacterial skin infections.

In recent years, herbal medicine has gained substantial attention in pharmaceutical and biomedical research because of its natural origin, biocompatibility, lower toxicity, economic affordability, and broad-spectrum therapeutic properties [7]. Medicinal plants contain numerous bioactive phytoconstituents such as flavonoids, alkaloids, tannins, terpenoids, glycosides, phenolics, and essential oils that possess potent antibacterial, anti-inflammatory, antioxidant, wound-healing, and antifungal activities. Herbal extracts obtained from plants such as neem (Azadirachta indica), turmeric (Curcuma longa), aloe vera (Aloe barbadensis), tulsi (Ocimum sanctum), tea tree (Melaleuca alternifolia), and calendula (Calendula officinalis) have demonstrated remarkable efficacy against various pathogenic bacteria [8]. Due to these therapeutic advantages, herbal formulations are increasingly being explored as alternative or complementary treatments for topical bacterial infections [9].

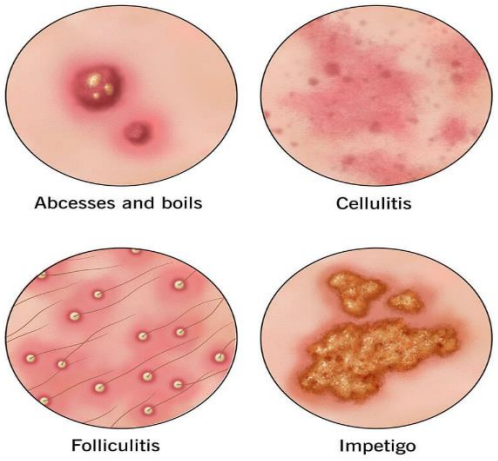

Fig.2. Bacterial Skin Infections.

Despite the significant medicinal potential of herbal compounds, their therapeutic effectiveness is often restricted by several pharmaceutical limitations such as poor aqueous solubility, low skin permeability, instability under environmental conditions, rapid degradation, uncontrolled release, and short residence time at the site of application [10,4]. These drawbacks reduce the bioavailability and antimicrobial efficacy of herbal agents when applied directly to the skin. To overcome these challenges, advanced drug delivery technologies have been developed to improve stability, controlled release behavior, and targeted delivery of herbal bioactive compounds [11]. Among these technologies, microsphere-based drug delivery systems have emerged as a promising approach for enhancing topical therapeutic performance [12,5].

Common Bacteria Causing Skin Infections

Skin infections are primarily caused by pathogenic bacteria that invade the skin and underlying tissues when the natural protective barrier of the skin is disrupted. These microorganisms can enter through cuts, wounds, burns, surgical incisions, insect bites, hair follicles, or damaged skin surfaces. Once inside the skin tissues, bacteria multiply rapidly and trigger inflammatory responses leading to redness, swelling, pain, pus formation, and tissue damage [13]. Several bacterial species are responsible for superficial as well as deep skin infections, among which *Staphylococcus aureus*, *Streptococcus pyogenes*, *Pseudomonas aeruginosa*, and *Escherichia coli* are the most commonly reported pathogens [14].

Staphylococcus aureus

Staphylococcus aureus is one of the most prevalent and clinically significant bacteria responsible for skin and soft tissue infections. It is a gram-positive, spherical bacterium commonly found on the skin and nasal passages of

healthy individuals. Although it normally exists as part of the natural microbial flora, it becomes pathogenic when it enters damaged skin tissues. *S. aureus* causes various skin infections such as boils, abscesses, impetigo, folliculitis, cellulitis, infected wounds, and surgical site infections [15]. The bacterium produces toxins and enzymes that destroy tissues and help the organism spread rapidly within the body [16].

One of the major concerns associated with *S. aureus* is the emergence of Methicillin-Resistant *Staphylococcus aureus* (MRSA), a multidrug-resistant strain that is highly difficult to treat using conventional antibiotics. MRSA infections are increasingly common in hospitals and communities and are associated with prolonged treatment duration and increased mortality risk [17].

Streptococcus pyogenes

Streptococcus pyogenes, also known as Group A Streptococcus (GAS), is another gram-positive bacterium responsible for several skin and soft tissue infections. It commonly causes conditions such as cellulitis, erysipelas, impetigo, and necrotizing fasciitis. This bacterium spreads rapidly through direct contact and can penetrate deeper skin layers causing severe inflammation and tissue destruction [18].

Streptococcus pyogenes produces several virulence factors including streptolysins, exotoxins, and enzymes that enable tissue invasion and immune evasion. In severe cases, untreated infections may lead to complications such as rheumatic fever, septicemia, and kidney inflammation. Due to its aggressive nature, early diagnosis and effective treatment are essential for controlling infections caused by this bacterium [19].

Pseudomonas aeruginosa

Pseudomonas aeruginosa is a gram-negative opportunistic bacterium commonly associated with burn wound infections, diabetic ulcers, surgical wounds, and chronic skin infections. It thrives in moist environments such as hospitals, medical equipment, water sources, and contaminated surfaces [20]. This pathogen is particularly dangerous for immunocompromised individuals and hospitalized patients.

The bacterium possesses remarkable resistance to antibiotics due to its strong biofilm-forming ability and adaptive resistance mechanisms. *P. aeruginosa* infections are characterized by greenish pus formation, foul odor, delayed wound healing, and severe tissue damage. Because of its resistance to multiple antibiotics, infections caused by this bacterium are difficult to treat and require advanced therapeutic approaches [21].

Antibiotic Resistance and Multidrug-Resistant Bacteria

Antibiotic resistance has emerged as one of the most serious global public health threats of the modern era. It occurs when bacteria develop the ability to survive and grow even in the presence of antibiotics that were previously effective against them [27]. Over the past few decades, the widespread and inappropriate use of antibiotics in human medicine, veterinary practices, agriculture, and animal husbandry has accelerated the development of resistant bacterial strains [28, 9, 7, 6, 3]. As a result, many bacterial infections that were once easily treatable have become increasingly difficult to control, leading to prolonged illness, higher medical costs, treatment failure, and increased mortality rates [6].

Bacteria possess remarkable adaptability and can rapidly evolve resistance through genetic mutations or by acquiring resistance genes from other microorganisms. These resistance mechanisms allow bacteria to neutralize antibiotics, alter drug targets, reduce drug penetration, or actively expel antimicrobial agents from their cells. Some bacteria produce enzymes such as beta-lactamases that destroy antibiotics before they can exert their therapeutic action [7]. Others modify their cellular structures, making antibiotics unable to bind effectively. Such adaptations significantly reduce the clinical effectiveness of conventional antibacterial therapy [8].

Table 01 Market-available Topical Antibacterial Formulation

Active ingredient / combination	Typical strength	Dosage form	Main use
Clindamycin phosphate	1% w/w	Gel	Acne; bacterial skin conditions
Clindamycin + Benzoyl peroxide	1% + 2.5–5%	Gel	Acne
Clindamycin + Adapalene	1% + 0.1%	Gel	Acne
Clindamycin + Nicotinamide	1% + 4%	Gel	Acne
Fusidic acid	2% w/w	Gel/ cream/ ointment	Bacterial skin infections
Mupirocin	2% w/w	Usually ointment	Impetigo and localized bacterial infections

Benzoyl peroxide	2.5–5%	Gel	Acne; antibacterial activity
Nadifloxacin	1%	Cream/gel	Acne/bacterial skin infections

Need for Advanced Topical Drug Delivery Systems

Topical drug delivery systems have become an important approach for the treatment of various skin disorders, including bacterial infections, fungal diseases, burns, wounds, inflammation, and dermatological conditions. In topical therapy, drugs are directly applied to the skin surface to achieve localized therapeutic action at the site of infection or injury. Conventional topical formulations such as creams, ointments, lotions, and gels are widely used because they are easy to apply, non-invasive, and capable of reducing systemic side effects [29]. However, despite these advantages, traditional topical drug delivery systems suffer from several pharmaceutical and therapeutic limitations that reduce their overall effectiveness. These challenges have created a strong need for the development of advanced topical drug delivery systems capable of improving drug stability, penetration, retention, and controlled release [30, 9].

One of the major limitations of conventional topical formulations is poor drug penetration through the skin barrier [31]. The skin, particularly the outermost layer known as the stratum corneum, acts as a highly protective barrier that restricts the entry of therapeutic agents into deeper skin tissues. Many drugs, especially herbal bioactive compounds, possess poor solubility and limited permeability, which reduce their absorption and therapeutic effectiveness when applied topically. As a result, only a small fraction of the applied drug reaches the target site, leading to inadequate antimicrobial activity and delayed healing [10].

Problem Identification

Bacterial skin infections have become a major healthcare concern due to the increasing prevalence of antibiotic-resistant microorganisms and the limitations associated with conventional topical antibiotic therapies [32, 33]. Traditional formulations such as creams and ointments often suffer from poor skin penetration, rapid drug release, low retention time, instability of active compounds, and frequent dosing requirements, resulting in reduced therapeutic effectiveness and patient compliance [7, 8]. Moreover, prolonged use of synthetic antibiotics can cause adverse side effects and contribute to antimicrobial resistance. Herbal medicines possess significant antibacterial and wound-healing properties; however, their direct topical application is limited by poor stability and inadequate bioavailability [34, 35]. Therefore, there is a critical need to develop an advanced herbal microsphere-based topical gel system capable of providing controlled drug release, enhanced skin retention, improved antibacterial activity, and safer treatment for bacterial skin infections [9, 10].

Research Significance

The present research on "Design, Formulation, and Evaluation of Herbal Microsphere-Based Topical Gel for Treating Bacterial Infections" is highly significant in the field of pharmaceutical and biomedical sciences because it focuses on developing a safer, more effective, and advanced topical drug delivery system for managing bacterial skin infections [36, 37]. The study addresses the growing global challenge of antibiotic resistance and the limitations of conventional topical therapies such as poor drug penetration, rapid drug release, frequent application, and adverse side effects [38, 39, 40]. By incorporating herbal bioactive compounds into microsphere-based gel systems, the research aims to enhance drug stability, controlled release behavior, skin retention, and localized therapeutic action [1-5].

Research Motivation

The motivation behind this research arises from the increasing prevalence of bacterial skin infections and the growing problem of antibiotic resistance associated with conventional antimicrobial therapies. Traditional topical formulations often show limited effectiveness due to poor skin penetration, rapid drug release, low retention time, and undesirable side effects. Herbal medicines possess natural antibacterial, anti-inflammatory, and wound-healing properties, but their direct application is limited by poor stability and low bioavailability. Therefore, the development of a herbal microsphere-based topical gel is motivated by the need to create a safer, controlled-release, and more effective drug delivery system that can enhance therapeutic efficacy, improve patient compliance, and reduce the dependency on synthetic antibiotics for treating bacterial infections.

Conclusion

Herbal microsphere-based topical gels provide a promising approach for the localized management of bacterial skin infections by combining the therapeutic properties of herbal bioactive compounds with the advantages of microsphere-based controlled drug delivery. Microspheres can improve drug stability, enhance retention at the application site, and provide sustained release, while the topical gel offers convenient application and improved patient compliance. Proper selection of herbal agents, polymers, microsphere preparation methods, and formulation conditions is essential for achieving desirable antibacterial activity and physicochemical properties. Overall, this delivery system has significant potential as a safer and effective alternative or complementary approach to conventional topical antibacterial formulations.

Future Scope

Future research should focus on identifying and standardizing potent herbal antibacterial compounds and developing optimized microsphere systems with improved drug loading, stability, and controlled-release characteristics. Advanced formulation techniques such as nanotechnology, bioadhesive polymers, and stimulus-responsive delivery systems may further enhance therapeutic performance. More extensive in vitro, ex vivo, in vivo, toxicity, stability, and clinical studies are required to establish safety, efficacy, mechanism of action, and long-term therapeutic benefits. Scale-up studies and regulatory standardization could also support the translation of herbal microsphere-based topical gels from laboratory research to commercial pharmaceutical applications.

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