

# FORMULATION AND EVALUATION OF BAEL LEAVES LOADED MICROEMULSION FOR THE TREATMENT OF ACNE VULGARIS

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## ABSTRACT:

Acne vulgaris is a chronic inflammatory disorder of the pilosebaceous unit that affects adolescents and young adults and often persists into adulthood. Conventional topical therapies are associated with limitations such as poor skin penetration, irritation, and low patient compliance. Herbal-based nanocarriers have emerged as promising alternatives to overcome these drawbacks. *Aegle marmelos* (Bael) leaves possess well-documented antibacterial, anti-inflammatory, and antioxidant activities, making them suitable candidates for anti-acne formulations. Microemulsion-based delivery systems provide thermodynamic stability, enhanced drug solubilization, and improved dermal penetration. This review focuses on the formulation and evaluation aspects of bael leaves loaded microemulsion systems for the management of acne vulgaris. The article summarizes the pathophysiology of acne, pharmacological potential of *Aegle marmelos* leaves, principles of microemulsion systems, formulation components, preparation methods, characterization parameters, and evaluation techniques. Emphasis is given to stability, safety, and therapeutic efficacy of herbal microemulsions as novel topical drug delivery systems for acne treatment.

**Keywords:** Acne vulgaris, *Aegle marmelos*, Bael leaves, Microemulsion, Herbal drug delivery, Topical formulation

## 1. INTRODUCTION:

Acne vulgaris is one of the most prevalent dermatological disorders worldwide, characterized by comedones, papules, pustules, nodules, and in severe cases, scarring. It primarily affects areas rich in sebaceous glands such as the face, chest, and back. The condition has a significant psychological and social impact, leading to reduced self-esteem and quality of life. Although several synthetic topical and systemic therapies are available, their long-term use is often associated with adverse effects including skin irritation, dryness, erythema, and antimicrobial resistance. Hence, there is growing interest in herbal-based formulations that are safer, effective, and better tolerated. Microemulsion drug delivery systems have gained considerable attention due to their unique physicochemical properties such as transparency, low viscosity, and enhanced permeation through the stratum corneum. Incorporation of herbal extracts into microemulsions offers synergistic benefits by combining the therapeutic efficacy of plant-based actives with the advanced delivery potential of nanocarriers. Bael leaves (*Aegle marmelos*) are traditionally used in Indian medicine for treating skin disorders and infections, supporting their application in anti-acne formulations.

## ACNE VULGARIS: PATHOPHYSIOLOGY AND TREATMENT LIMITATIONS:

Acne vulgaris is a common chronic inflammatory disorder of the pilosebaceous unit, predominantly affecting adolescents and young adults, although it may persist into adulthood. The disease arises from a complex interplay of multiple pathogenic factors, including excessive sebum production (seborrhea), abnormal follicular keratinization, colonization of hair follicles by acne-causing microorganisms, and subsequent inflammatory responses. Hormonal stimulation, particularly androgens, increases the size and activity of sebaceous glands, leading to overproduction of sebum. This lipid-rich environment promotes follicular blockage and supports microbial proliferation, which in turn triggers the release of inflammatory mediators and formation of acne lesions such as comedones, papules, pustules, and nodules.

Conventional acne therapies primarily aim to target one or more of these pathogenic mechanisms. Topical retinoids normalize follicular keratinization, benzoyl peroxide exerts antimicrobial and keratolytic effects, and topical or systemic antibiotics reduce microbial load and inflammation. Although these agents are clinically effective, their long-term use is often associated with significant limitations, including skin irritation, erythema, dryness, peeling, and reduced patient compliance. The widespread use of antibiotics has also contributed to the emergence of antimicrobial resistance, which compromises treatment outcomes and raises safety concerns.

Another major challenge in acne therapy is the inadequate penetration of conventional formulations into the pilosebaceous units, where the disease originates. Many active agents exhibit poor solubility, instability, or limited permeability across the stratum corneum, resulting in suboptimal therapeutic concentrations at the target site. These drawbacks highlight the need for alternative treatment strategies that can provide targeted delivery, improved skin penetration, enhanced efficacy, and better tolerability. Advanced topical delivery systems, particularly those incorporating herbal bioactives and nanocarrier technologies, offer a promising approach to overcoming these limitations in acne management.

### HERBAL APPROACH IN ACNE MANAGEMENT:

Herbal medicines have a long history of use in the treatment of various skin disorders, including acne vulgaris, owing to their wide range of therapeutic activities and favorable safety profiles. Traditional systems of medicine such as Ayurveda, Siddha, and Unani emphasize the use of plant-based remedies for maintaining skin health and treating inflammatory conditions. Herbal drugs are generally well tolerated and are associated with fewer adverse effects when compared to conventional synthetic agents, making them suitable for long-term management of chronic skin diseases like acne.

Plant-derived bioactive compounds possess diverse pharmacological properties that directly address the underlying pathogenic mechanisms of acne. Many medicinal plants exhibit significant antibacterial activity against acne-causing microorganisms, thereby reducing microbial colonization within the pilosebaceous unit. In addition, anti-inflammatory phytoconstituents help suppress the release of pro-inflammatory mediators, leading to a reduction in redness, swelling, and pain associated with acne lesions. Antioxidant compounds further contribute by neutralizing reactive oxygen species and minimizing oxidative stress, which plays a crucial role in acne progression and tissue damage. The wound-healing and skin-regenerative properties of herbal actives also promote faster resolution of lesions and reduce the risk of scarring.

A key advantage of herbal therapies over synthetic drugs is their multitargeted mode of action. Herbal actives act synergistically on multiple pathways involved in acne pathogenesis, including sebum regulation, microbial inhibition, inflammation control, and tissue repair. This holistic approach reduces the likelihood of drug resistance and minimizes adverse reactions commonly observed with prolonged use of synthetic antimicrobials and retinoids. Furthermore, the growing consumer preference for natural, sustainable, and eco-friendly products has significantly increased interest in herbal topical formulations. As a result, extensive research is being directed toward the development of scientifically validated, standardized, and effective herbal-based delivery systems for acne management.

### *Aegle marmelos* (Bael): Botanical, Macroscopical and Microscopical Profile

*Aegle marmelos* (family Rutaceae) is a medium-sized deciduous tree widely distributed throughout India, Sri Lanka, and Southeast Asia. It is well known in traditional medicinal systems for its therapeutic applications, particularly in skin, gastrointestinal, and inflammatory disorders. Among various plant parts, the leaves are most commonly used for topical and internal medicinal preparations due to their rich phytochemical content.

#### Macroscopical Characteristics

The leaves of *Aegle marmelos* are alternate, trifoliate, and aromatic when crushed. Each leaf consists of three leaflets arising from a common petiole. The leaflets are ovate to elliptic, measuring approximately 4–10 cm in length, with an entire or slightly crenate margin. The apex is acute to acuminate, while the base is symmetrical or slightly tapering. The upper surface of the leaf is dark green, smooth, and glossy, whereas the lower surface appears lighter green and slightly pubescent. The venation is reticulate, characteristic of dicotyledonous plants. The leaves emit a characteristic pleasant odor due to the presence of volatile oils, which is indicative of their medicinal value.

#### Microscopical Characteristics

Microscopical examination of the bael leaf reveals diagnostic features useful for pharmacognostic identification. A transverse section of the leaf shows a dorsiventral structure, typical of dicot leaves. The upper epidermis consists of a single layer of compactly arranged rectangular cells covered with a thin cuticle, while the lower epidermis contains numerous stomata, predominantly of the paracytic type.

Below the upper epidermis, the palisade parenchyma is composed of one to two layers of elongated, tightly packed cells rich in chloroplasts, facilitating photosynthesis. The spongy parenchyma, located beneath the palisade layer, consists of loosely arranged cells with large intercellular spaces, aiding gaseous exchange. Oil glands and secretory cavities, a characteristic feature of the Rutaceae family, are commonly observed in the mesophyll region and are responsible for the presence of essential oils.

The midrib region shows a collateral vascular bundle, with xylem oriented towards the upper side and phloem towards the lower side, surrounded by parenchymatous tissue. Calcium oxalate crystals and fibers may also be present, contributing to the diagnostic microscopical profile of the leaf.

The combined macroscopical and microscopical features of *Aegle marmelos* leaves serve as important parameters for authentication, quality control, and standardization of herbal raw materials used in pharmaceutical formulations, including topical anti-acne preparations.

## PHARMACOLOGICAL ACTIVITIES OF BAEL LEAVES:

### Antibacterial activity:

Bael leaf extracts exhibit notable antibacterial activity against acne-causing microorganisms, particularly those involved in follicular infections. The phytochemicals present in the leaves disrupt microbial cell walls, inhibit bacterial enzyme systems, and reduce microbial proliferation within the pilosebaceous unit. By lowering the bacterial load on the skin, bael leaves help prevent the formation and progression of inflammatory acne lesions.

### Anti-inflammatory activity:

Inflammation plays a central role in the development of acne lesions, leading to redness, swelling, and pain. Bael leaves contain anti-inflammatory compounds that suppress the production and release of pro-inflammatory mediators such as cytokines and prostaglandins. This action helps in reducing erythema, edema, and irritation associated with acne, thereby improving lesion appearance and patient comfort.

### Antioxidant activity:

Oxidative stress contributes significantly to acne pathogenesis by damaging skin cells and enhancing inflammatory responses. The antioxidant constituents of bael leaves effectively scavenge free radicals and reactive oxygen species, protecting skin tissues from oxidative damage. This antioxidant effect not only limits acne severity but also supports overall skin health and prevents post-inflammatory skin damage.

### Wound healing and skin regeneration:

Bael leaf extracts are known to promote wound healing by enhancing cell proliferation, collagen synthesis, and tissue repair. In acne management, this property aids in faster healing of lesions and reduces the risk of scarring and pigmentation. Improved skin regeneration further contributes to restoration of normal skin texture and integrity following acne resolution.

## Microemulsion Drug Delivery Systems

Microemulsions are thermodynamically stable, isotropic dispersions of oil, water, surfactant, and co-surfactant with droplet sizes typically ranging from 10 to 100 nm. They differ from conventional emulsions by their spontaneous formation and long-term stability.

### Advantages of Microemulsions for Topical Delivery

- ✓ Enhanced solubility of hydrophilic and lipophilic drugs
- ✓ Improved skin penetration and bioavailability
- ✓ Reduced irritation due to lower surfactant concentration at the skin surface
- ✓ Ease of preparation and scalability
- ✓ Transparent and cosmetically acceptable formulations

### Components of Bael Leaves Loaded Microemulsion

The selection of appropriate components is a critical step in the development of bael leaves loaded microemulsion systems, as each component directly influences formulation stability, drug solubilization, skin permeation, and therapeutic efficacy. In the context of a herbal anti-acne microemulsion, the components are chosen to ensure compatibility with bael leaf extract, safety for topical application, and enhanced delivery to the pilosebaceous unit.

## OIL PHASE:

The oil phase plays a vital role in solubilizing the lipophilic phytoconstituents present in bael leaf extract, such as essential oils and non-polar flavonoids. It also significantly affects drug release characteristics and skin permeation behavior of the formulation. Natural oils like sesame oil are commonly preferred in herbal microemulsions due to their excellent biocompatibility, skin-friendly nature, and intrinsic therapeutic properties. Sesame oil additionally exhibits emollient, antioxidant, and mild antimicrobial effects, which complement the anti-acne activity of bael leaves. The choice of oil phase therefore contributes not only to formulation stability but also to enhanced penetration of active constituents into deeper skin layers.

### Surfactant and Co-surfactant:

Surfactants are essential for reducing interfacial tension between the oil and aqueous phases, thereby facilitating the spontaneous formation of a stable microemulsion. In topical herbal formulations, non-ionic surfactants are preferred because of their low

toxicity, minimal skin irritation, and good compatibility with plant extracts. Co-surfactants are added to increase the flexibility and fluidity of the interfacial film, enabling the formation of nanosized droplets. Together, the surfactant and co-surfactant system enhances the solubilization of bael leaf extract, improves formulation stability, and promotes efficient penetration of active compounds through the stratum corneum.

### **Aqueous Phase:**

The aqueous phase usually consists of purified water and serves as the continuous phase in oil-in-water microemulsion systems intended for topical use. It may also contain hydrophilic constituents of the bael leaf extract, contributing to the overall therapeutic effect. The aqueous phase helps maintain appropriate viscosity, spreadability, and skin feel of the formulation, which are important for patient compliance. Additionally, it supports hydration of the stratum corneum, thereby facilitating enhanced penetration of the encapsulated herbal actives and improving the overall efficacy of the anti-acne microemulsion.

Overall, the careful selection and optimization of the oil phase, surfactant–co-surfactant system, and aqueous phase are essential for developing an effective, stable, and patient-friendly bael leaves loaded microemulsion for acne management.

### **METHOD OF PREPARATION OF BAEL LEAVES MICROEMULSION:**

The preparation of bael leaves loaded microemulsion involves a systematic and stepwise approach to ensure optimal incorporation of the herbal extract and formation of a stable, efficient delivery system. Initially, bael leaves are subjected to an appropriate extraction process using suitable solvents to obtain a concentrated extract rich in bioactive phytoconstituents. The extract is then filtered, concentrated, and stored under controlled conditions to preserve its therapeutic activity.

Following extraction, comprehensive solubility studies are carried out to identify suitable formulation components. The solubility of the bael leaf extract is evaluated in various oils, surfactants, and co-surfactants to select components that provide maximum solubilization of the active constituents. This step is crucial, as adequate solubilization directly influences drug loading, stability, and release characteristics of the microemulsion. Based on these studies, biocompatible oils, non-ionic surfactants, and suitable co-surfactants are selected to ensure safety and effectiveness for topical application.

Pseudoternary phase diagrams are then constructed using the chosen oil, surfactant–co-surfactant mixture, and aqueous phase. These diagrams help identify the concentration ranges over which clear, isotropic, and thermodynamically stable microemulsions are formed. The microemulsion region obtained from the phase diagram guides the selection of optimal component ratios and ensures reproducibility of the formulation.

The optimized microemulsion is prepared by gradually mixing the oil phase containing the bael leaf extract with the surfactant and co-surfactant mixture, followed by slow addition of the aqueous phase under constant stirring. Continuous stirring facilitates uniform dispersion of components and promotes spontaneous formation of nanosized droplets. The process is continued until a clear, transparent, and homogeneous system is obtained, indicating successful microemulsion formation. The prepared formulation is then allowed to equilibrate and subjected to further evaluation to confirm its stability, physicochemical properties, and suitability for topical anti-acne application.

### **EVALUATION AND CHARACTERIZATION OF MICROEMULSION:**

Comprehensive evaluation and characterization of bael leaves loaded microemulsion are essential to ensure formulation quality, stability, safety, and therapeutic effectiveness for topical acne treatment. Each parameter provides critical information regarding the physicochemical properties and performance of the microemulsion system.

#### **PHYSICAL APPEARANCE AND CLARITY:**

The prepared microemulsion is visually examined for transparency, color, and homogeneity. A clear or transparent appearance indicates the formation of a true microemulsion with uniform nanosized droplets, while absence of phase separation or turbidity confirms physical stability. Color uniformity also reflects proper incorporation of the bael leaf extract within the formulation.

#### **pH Determination**

The pH of the microemulsion is measured using a calibrated pH meter to ensure compatibility with skin physiology. A pH range close to that of normal skin is desirable to minimize the risk of irritation, dryness, or disruption of the skin barrier. Maintaining an appropriate pH is particularly important for herbal formulations intended for prolonged topical use.

## Droplet Size and Distribution

Droplet size and size distribution are determined using particle size analysis techniques to confirm nanoscale dimensions. Smaller and uniformly distributed droplets provide a larger surface area, which enhances skin penetration and improves bioavailability of the bael leaf phytoconstituents. A narrow size distribution also indicates formulation uniformity and stability.

## Viscosity and Rheological Behavior

Viscosity measurements are performed to evaluate the flow characteristics and spreadability of the microemulsion. Suitable viscosity ensures ease of application, uniform spreading on the skin surface, and better patient acceptability. Rheological behavior also influences drug release and residence time of the formulation at the site of application.

## Stability Studies

Stability studies are conducted to assess the thermodynamic stability of the microemulsion system. Centrifugation tests help detect any tendency toward phase separation, while storage stability studies under different temperature conditions evaluate long-term physical and chemical stability. A stable formulation retains its clarity, homogeneity, and therapeutic properties over time.

## In vitro Antimicrobial and Anti-acne Evaluation

The antimicrobial activity of the bael leaves loaded microemulsion is evaluated against acne-causing microorganisms to confirm its antibacterial efficacy. Additionally, *in vitro* anti-acne and anti-inflammatory studies assess the formulation's ability to reduce inflammatory responses associated with acne. These evaluations collectively demonstrate the therapeutic potential of the microemulsion system for effective acne management.

## CONCLUSION:

The formulation of bael leaves loaded microemulsion offers an effective, stable, and patient-friendly approach for the topical treatment of acne vulgaris. The synergistic combination of herbal therapeutics and microemulsion technology enhances skin penetration, efficacy, and safety. This review highlights the potential of *Aegle marmelos* based microemulsions as a novel herbal nanocarrier system for acne therapy.

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