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Herbal Nanoemulsions for Topical Management of Acne: A Detailed Review

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ABSTRACT:
Acne vulgaris is a prevalent inflammatory skin disorder affecting millions worldwide, particularly adolescents, and often results in both physical and psychological complications. Its pathogenesis involves excessive sebum production, follicular hyperkeratinization, microbial colonization by *Cutibacterium acnes*, and inflammation, influenced by genetic, hormonal, dietary, and environmental factors. Conventional therapies—including topical retinoids, antibiotics, and systemic agents—are effective but limited by adverse effects, antibiotic resistance, and systemic toxicity. Herbal remedies, with their antimicrobial, anti-inflammatory, antioxidant, and sebum-regulating properties, have emerged as safer alternatives; however, their therapeutic efficacy is constrained by poor solubility, instability, and inadequate skin penetration. Nanoemulsion-based delivery systems overcome these limitations by enhancing solubility, stability, bioavailability, and skin permeation, while enabling controlled release and reducing irritation. Prepared by low- or high-energy methods, nanoemulsions are characterized by droplet size, zeta potential, viscosity, pH, stability, antibacterial activity, and skin compatibility. Integrating herbal medicine with nanoemulsion technology represents a promising, safe, and effective strategy for topical acne management, combining traditional knowledge with modern drug delivery innovations.

INTRODUCTION:

Acne vulgaris, commonly known as acne, is one of the most common skin problems affecting millions of people around the world. Acne vulgaris is an inflammatory skin condition that can occur at any age, but it is most common during the teenage years. About 85% of teenage girls and 95% of teenage boys experience acne, and around 20% of them develop moderate to severe acne. It can cause discomfort, low self-confidence, anxiety, depression, and long-term skin damage in young people. [1]

The development of acne is linked to several factors working together—extra sebum (oil) production, blockage of hair follicles due to excess keratin, growth of *Propionibacterium acnes* (now called *Cutibacterium acnes*), and inflammation. The main goals of acne treatment are to prevent scarring, control current acne lesions, shorten the duration of the condition, and reduce emotional and physical problems. While planning treatment, a must consider the patient's overall health, severity of acne, hormone history, and personal preferences, improving physical appearance is also an important goal. [2]

Acne can be treated using topical or systemic therapies, topical treatments are easy to use because the patient can apply them directly to the affected area. However, the stratum corneum, the outermost layer of the skin, acts as a strong barrier and prevents many drugs from entering the deeper layers. This low penetration often leads to poor treatment results, because of this, topical therapy alone is sometimes not enough for moderate or severe acne, and

systemic therapy may be added.[3]

Traditional acne treatments like antibiotics, retinoids, and hormonal therapies can be effective, but they often cause side effects such as skin dryness, irritation, and long-term issues like antibiotic resistance. These challenges show that there is a strong need for new, safer, and more effective treatment approaches for acne. [4]

Herbal medicine, used for centuries in traditional healing systems, is now gaining attention as a promising option for acne management. Many plant extracts show strong anti-inflammatory, antimicrobial, antioxidant, and oil-controlling effects. However, most herbal extracts face challenges such as poor solubility, low stability, and limited absorption into the skin. [5]

Modern nanotechnology, especially the development of nanoemulsions, can overcome these issues. Nanoemulsions improve the solubility, stability, and bioavailability of herbal compounds, allowing them to penetrate the skin more effectively. This makes nanoemulsions an innovative and powerful approach for enhancing the acne-fighting potential of herbal ingredients. [6]

The Pathogenesis of Acne Vulgaris:

The word acne comes from the Greek word "ákme" which refers to small bumps on the skin like pustules and papules. Most people with acne start with mild to moderate symptoms. In some cases, it may gradually become **severe**. For many individuals, acne reduces with age and often goes away on its own. But some people may continue to have acne even in their 30s, 40s, or later. [7]

Acne mainly affects the face and upper neck, but it can also appear on the chest, back, and shoulders. In addition to physical symptoms, acne also affects a person's mental health including low self-esteem, anxiety, depression, and in severe cases, even suicidal thought. [8]

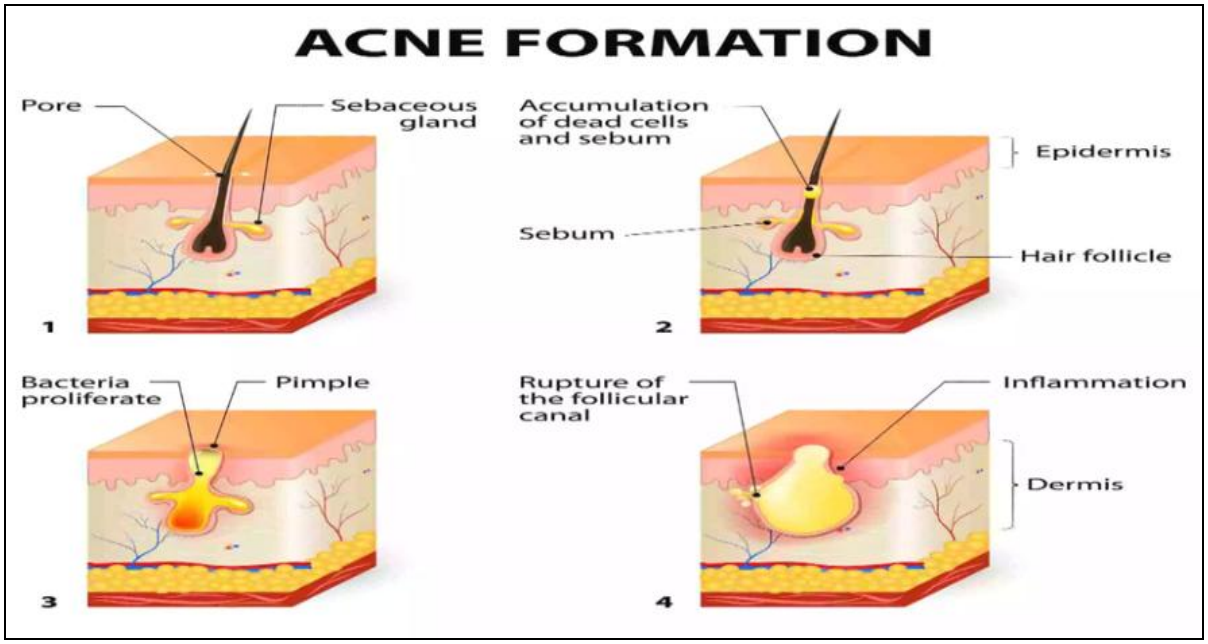

Figure 1: The Process of Acne formation on the skin

A) Major factors causing acne:

1. **Excessive sebum production:** Sebum hypersecretion plays a crucial role in acne formation by promoting comedone development and creating favourable conditions for *Propionibacterium acnes* (*P. acnes*) colonization. Excess sebum contributes to follicular blockage and supports bacterial proliferation, leading to inflammation and acne lesion development. [9]

2. **Follicular hyper keratinization:** Obstruction of the pilosebaceous canal leads to the enlargement of acne lesions. This blockage results from the excessive growth of keratinized cells within the duct, which restricts the normal outflow of sebum. Alterations in sebaceous lipid composition can further induce hyperproliferation of corneocytes. Additionally, comedone formation may be associated with a local deficiency of linoleic acid within the pilosebaceous duct. [10]
3. **Abnormal bacterial function:** Acne-prone skin is frequently colonized by *Staphylococcus epidermidis* and *Propionibacterium acnes*, with *P. acnes* promoting inflammation through the activation of chemotactic mediators and comedone disruption. [11]

B) Factors that contribute to acne development:

1. **Hormonal Influences:** Acne is strongly influenced by hormonal changes, particularly increased androgen levels during puberty, hormonal imbalances associated with polycystic ovarian syndrome (PCOS), menstrual cycle variations, and the use of exogenous hormones or anabolic steroids, all of which enhance sebaceous gland activity. [12]
2. **Stress:** Stress-induced elevation of cortisol contributes to acne exacerbation by increasing inflammation and sebum secretion. [2]
3. **Diet:** Emerging evidence suggests a correlation between acne and dietary patterns, including high-glycaemic index foods, dairy products, whey protein supplementation, and diets rich in saturated fats. These factors stimulate insulin-like growth factor-1 (IGF-1) signaling, promoting sebum production and follicular keratinocyte proliferation. [13]
4. **Genetics:** A strong hereditary predisposition exists in acne, with multiple genes involved in the regulation of sebaceous activity, inflammation, and follicular keratinization. [3]
5. **Medications:** Several medications, including corticosteroids, lithium, isoniazid, phenytoin, and high-dose vitamin B12, are known to induce or aggravate acne lesions. [14]

C) Types of acne lesions:

Acne lesions are classified into non-inflammatory and inflammatory types.

I. Non-inflammatory Lesions:

1. Open comedones (blackheads): Occur when follicular plugs are exposed to air, leading to oxidation of melanin and darkening of the lesion. [7]
2. Closed comedones (whiteheads): Formed when hair follicles are fully obstructed by accumulated keratin and sebum. [13]

II. Inflammatory Lesions:

1. Cysts: Deep, fluid-filled sacs with pus that often lead to scarring. [11]
2. Nodules: Large, painful, deep-seated lesions caused by extensive follicular destruction and dermal inflammation. [15]
3. Pustules: Inflamed papules containing visible pus due to accumulation of neutrophils. [8]
4. Papules: Small, red, and tender bumps resulting from localized inflammation. [11]

Treatment of acne:

Effective acne management should focus not only on safe medical treatment but also on reducing psychological stress through emotional and social support. [5]

The main goals of acne treatment are:

- To control and treat existing acne lesions
- To prevent new blemishes as much as possible
- To shorten the duration of the disease and minimize complications

When planning a treatment regimen, several factors must be considered, including the patient's medical condition, severity of acne lesions, hormonal status, and patient preference for oral or topical therapy. [9]

Topical therapy is primarily used for the management of mild to moderate acne, whereas systemic therapy is mainly

employed in severe cases, often in combination with topical agents. Commonly used topical treatments (Table 1) include retinoids, antibiotics (doxycycline, erythromycin, minocycline), isotretinoin, and hormonal therapy are used in combination with topical agents for the treatment of severe acne. Although conventional topical therapies act locally at the site of application, they may cause skin irritation; this drawback can be minimized by using lower drug concentrations in formulations. [16]

Compared to systemic therapy, topical treatment has fewer side effects. Oral retinoids like isotretinoin may cause adverse effects such as nosebleeds, dry lips (cheilitis), dry skin, inflammation, temporary worsening of lesions, photosensitivity, and increased blood lipid levels. In contrast, topical retinoids mainly cause mild irritation and tolerability issues, but long-term use of systemic antibiotics in any route may lead to antibiotic resistance, whereas plant based topical herbal treatment present a relatively lower risk, safe and long-term effect with less side effects. [17]

Also C. acnes is a normal part of the skin microbiome, but when it grows excessively or becomes imbalanced, it can cause inflammation and lead to acne. Treatments that target C. acnes, such as antibiotics and topical medications, may cause side effects like skin irritation, antibiotic resistance, and disturbance of the normal skin microbiota. Disruption of the skin microbiome can increase the risk of secondary infections or worsen existing skin problems. [18]

Table 1. Some of the topical anti-acne drugs

Drug	Mechanism of action	Drawbacks	Ref
Topical retinoids: (Isotretinoin, Adapalene, Tretinoin, Metretinide, Tazarotene)	They act on microcomedones, the early precursor lesions of acne. also exhibit anti inflammatory properties.	High pigmentation, scaling, Burning sensation, teratogenicity & systemic toxicity.	[19]
Topical antibiotics: (Erythromycin, Azelaic acid, Nadifloxacin, Clarithromycin)	It acts on abnormal follicular epithelial overgrowth, decreases follicular blockage and micro comedone formation. It inhibits the growth of *P. acnes* and reduces inflammation.	Peeling, itching, dryness, bacterial resistance, swollen, itching, redness on skin.	[20]
New agents: (Benzoyl peroxide, Salicylic acid, Tretinoin, Clindamycin)	This are the most preferred in the treatment of acne. Reducing both inflammatory and non-inflammatory acne lesions. It helps prevent and reduce the development of *P. acnes* resistance.	Skin irritation, initially show skin burning and dry, Hives and rashes on the skin.	[4]

Therefore, effective acne management should focus on maintaining a balance between controlling C. acnes and preserving the overall skin microbiome to reduce side effects and improve treatment outcomes. [21]

The increasing preference for natural products over synthetic options in the treatment of acne vulgaris because they are both effective and safer. Studies show that natural plant extracts can work better than synthetic antibiotics like erythromycin in treating mild to moderate acne. This is important because acne-causing bacteria (*C. acnes*) are becoming resistant to many antibiotics, which reduces the success of traditional treatments. Many plants naturally have antimicrobial, antioxidant and many more properties, making them good alternatives to synthetic drugs without adding to the problem of antibiotic resistance. In addition, natural products usually cause fewer side effects than synthetic medicines, which may lead to less skin irritation, allergic reactions, or long-term health problems. [22]

Rationale for Herbal Remedies:

Herbs have been used to care for the skin for a very long time. Long before modern dermatology existed, people treated skin problems using leaves, roots, and plant pastes. In India, Ayurveda played a major role in skin care. [23] It viewed skin diseases as signs of internal imbalance, such as excess *pitta* (body heat). Ancient texts like the *Charaka Samhita* describe the use of turmeric for its cooling and anti-inflammatory effects, while neem was commonly used to treat infections and wounds. Similarly, Unani medicine used herbal oils and plant-based balms for persistent skin problems and Siddha medicine in South India relied on aloe vera to heal and soothe the skin. These treatments were not random; they were developed through centuries of observation and experience and are still used today. [24]

This use of herbs for skin care was not limited to India. Around the world, traditional communities used local plants

to treat skin conditions. For example, Indigenous Australians applied calendula leaves to cuts, wounds, and acne, a practice that later became popular worldwide. In Europe, witch hazel was traditionally used to tighten the skin and reduce inflammation long before it became a commercial product. Today, modern science is helping us understand why these plants work. Researchers now identifed active compounds such as eugenol in Basil and glabridin in Licorice Root, and these are being used in modern creams, gels, and face masks. [25]

Since 2020, interest in herbal treatments for acne has increased greatly, the COVID-19 pandemic encouraged people to look for safer, natural, and sustainable health options. In India, government support through AYUSH and initiatives like Make in India has boosted research on herbal products such as neem extracts and polyherbal creams.[26] Globally, the rise of clean beauty products that are natural, vegan, and eco-friendly has increased demand for plant-based skin treatments.[27] Clinical studies are now comparing herbal products (Table 2) with common acne treatments like azelaic and clizdamycin. Many patients prefer herbal options because they are gentler on the skin and reduce concerns about antibiotic resistance. [28]

Table 2. Herbs used to treat acne vulgaris

Name of plant	Part used	Active constituents	Medicinal uses	Ref
Achillea millefolium L.	Flowering tops	An Alkamide: N-(21- hydroxy-21-(piperidin1-yl) henicosa-17, 19- diyl-1-yl) acetamid	Burn, acute eczema	[29]
Aegle marmelos (L.) (Bael)	Leaves Seeds	Achyranthine, achyranthes, betaine, ecdysterone, hentriacontane, oleanolic acid glycosides, saponins A, B, C, D	Anti-inflammatory & anti-bacterial property	[30]
Berberis aquifolium	Root	Jatrorrhizine, Berberine and Protoberberine	Chronic skin rashes (pustule)	[31]
Caesalpinia sappan L	Heartwood	Brazilin, Protosappanin A, Protosappanin C, Protosappanin D, Protosappanin E	Potential antiacne agent	[32]
Citrus hystrix (kaffir lime)	Essential oils	Linalool, linoleic acid, d-limonene, and Seychellean	An alternative AV treatment. (Usually applied directly to the skin.)	[33]
Lens culinaris Medik (Lentil)	Seed	Minerals, polyphenol, proteins, essential amino acids, fibres.	Topically used for skin disorders and burns	[34]
Serenoa repens (Saw palmetto)	Berries	Flavonoids, fatty acids, sterols	Oil control and hormonal acne and orally more effective	[35]
Cannabis sativus	seeds	Linoleic acid, Alpha-linolenic acid, Oleic acid	relieve pain in itchy skin.	[31]
Simmondsia chinensis	leaves seeds	wax esters, few free fatty acids, sterols, and vitamin	Anti-Acne and Antipsoriasis Activities	[36]
Matricaria chamomilla L	Leaves Flower heads	Bisabolol oxide A, camazu lene, o-cimene, α-farnesene, spathuleno	Antiseptic, Anti-inflammatory	[37]

One major strength of herbal medicine is its ability to adapt to modern technology. In India, traditional herbal remedies are now developed using advanced delivery systems like turmeric nanoemulsions and neem-based serums, which help improve their effectiveness and shelf life. Worldwide, tea tree oil has moved from traditional use to being widely accepted in acne treatments, this change is supported by scientific research. [38] Many studies have examined how herbal ingredients work and why they may be safer than strong chemical treatments. [39] Indian brands such as Patanjali and Himalaya support their products with clinical studies. Today, laboratory testing, clinical trials, and AI-based analysis are used to scientifically validate herbal medicines, making them valuable supportive treatments for acne. [40]

Importance of Nanoemulsion in Delivery of Herbal Drugs:

Herbal ingredients do not work on the skin by themselves they need a way to be delivered. In India, many people still use traditional methods, such as applying honey mixed with aloe, these methods are simple and popular, but modern science has improved the way herbs are used on the skin. [41]

Today, creams and gels are the most common forms. Products like Medimix neem face wash and Ayur aloe vera gel

are good examples, also Indian companies are also developing patented herbal blends. For example, Patanjali's Saundarya cream combines aloe vera and turmeric, and small studies have shown about 30% improvement in acne. [24]

In recent years, natural bioactive compounds and phytopharmaceuticals have attracted significant global interest because of their therapeutic potential, but their use in medicines is limited because they dissolve poorly, penetrate tissues weakly, and have low bioavailability, as a result, natural bioactives are less effective in treating various health conditions. [42]

These limitations can be overcome by formulating herbal drugs into nanoemulsions, nanoemulsions are considered an effective drug delivery system because they show smooth and fluid behaviour and interact well with skin cells. They have very small droplet size, which improves skin penetration and drug permeability. Nanoemulsions also protect the drug and can evenly deliver volatile, irritating, and high-molecular-weight drugs, due to their fluid nature and the presence of emulsifiers at the interface, nanoemulsions easily associate with skin cells. In addition, the surface charge of nanoemulsions enhances their interaction with the skin, leading to improved drug efficacy. [43]

Advantages of Nanoemulsions in Topical Delivery:

1. Controlled Drug Release:

Nanoemulsions can be designed to release drugs in a controlled or sustained manner. By modifying the oil phase or adjusting the type and number of surfactants, the release rate of the drug can be fine-tuned. This sustained release maintains effective drug levels over a longer duration, reduces the frequency of application, improves patient adherence, and minimizes side effects caused by abrupt drug spikes. This makes nanoemulsions particularly useful for chronic dermatological conditions such as acne or psoriasis. [6]

2. Improved Skin Penetration:

Nanoemulsions enhance the delivery of drugs through the skin due to their extremely small droplet size, typically ranging from 20 to 200 nanometers. These tiny droplets can closely interact with the skin surface and penetrate the stratum corneum more efficiently, which is the main barrier to topical absorption. Their high surface area also increases the concentration gradient, promoting better diffusion into the skin. Additionally, the surfactants and co-surfactants present can temporarily alter the lipid structure of the stratum corneum, further facilitating drug penetration into deeper skin layers or for systemic transdermal delivery. [44]

3. Enhanced Drug Solubility:

Nanoemulsions greatly improve the solubility of poorly water-soluble (lipophilic) drugs. Many topical active pharmaceutical ingredients (APIs) have limited water solubility, which reduces their absorption and therapeutic effect. In nanoemulsions, the oil phase acts as a solubilizing reservoir, allowing lipophilic drugs to remain dissolved even at higher concentrations. This improved solubilization increases the drug's thermodynamic activity, making it easier for the drug to move from the formulation into the skin. As a result, nanoemulsions enhance local bioavailability and provide more effective treatment at the target site. [45]

4. Non-irritant and Cosmetically Acceptable:

For regular use, topical products must be effective and comfortable to apply. Nanoemulsions meet these needs very well. They spread easily on the skin, absorb quickly, and do not leave a greasy or sticky feel. This provides a smooth and pleasant user experience, which is important for both cosmetic and dermatological products. In addition, nanoemulsions often use non-ionic and skin-friendly surfactants, which lowers the risk of irritation and allergic reactions, making them suitable for sensitive skin. Their clear or slightly transparent appearance also adds to their cosmetic appeal. [46]

Formulation and Development of Herbal Nanoemulsion:

A nanoemulsion usually contains oil, a surfactant, a co-surfactant, and water. These ingredients must be carefully selected to maximize the effectiveness of the product, before making a nanoemulsion, careful selection of ingredients, correct concentrations, proper order of addition, suitable preparation method are essential to obtain a stable and effective product.

- **Oil Phase**:

The oil phase is a key component of nanoemulsions because it solubilizes lipophilic anti-acne drugs, making these systems effective carriers. Most anti-acne drugs are oil-soluble, and the fatty acid chain length of the oil influences stability and viscosity, with short-chain oils forming low-viscosity nanoemulsions and long-chain oils providing greater stability. While drug solubility is important when selecting an oil, some oils also enhance therapeutic effects; for example, tea tree and eucalyptus oils can act both as active anti-acne agents. [47]

- **Aqueous Phase:**

The aqueous phase forms the continuous phase in oil-in-water nanoemulsions and plays an important role in dispersing surfactants and stabilizing oil droplets. It is usually composed of purified water, such as distilled or deionized water. In some formulations, aqueous solutions containing salts, electrolytes, or buffer systems like phosphate-buffered saline are used to improve stability and maintain suitable conditions for the formulation. [48]

- **Surfactant:**

Surfactants are amphiphilic molecules with a hydrophobic part that binds to oil and a hydrophilic part that interacts with water. They are classified as anionic, cationic, or non-ionic, with non-ionic surfactants being preferred due to lower toxicity**.** Common examples include Tween, Labrasol, and Cremophor. Choosing the appropriate surfactant is essential for nanoemulsion stability, and the HLB value guides the selection of a surfactant compatible with the chosen oil. [48]

- **Co-surfactant:**

Co-surfactants support surfactants by further reducing interfacial tension, making it easier to form fine droplets and achieve stable nanoemulsions. They also enhance the solubilizing capacity of surfactants. Common co-surfactants include short-chain alcohols like ethanol, isopropyl alcohol, or butanol, which lower viscosity and help produce smaller droplet sizes. [49]

- **Stabilizers:**

Stabilizers improve the long-term stability of nanoemulsions by preventing droplet coalescence, flocculation, or phase separation. They can increase viscosity or strengthen the interface around droplets. Viscosity enhancers like xanthan gum and carbomers improve texture and stability, while antioxidants such as vitamin E protect the oil phase from oxidation. [43]

Methods of Preparation of Nanoemulsion:

Low-Energy Methods: Low-energy emulsification uses natural changes in the system, like composition or temperature, to lower interfacial tension and create tiny droplets. These methods work due to thermodynamic or kinetic effects rather than mechanical force (Table 4).

Table 3. Low-Energy method of various emulsification process

Emulsification process	Mechanism of emulsification	Advantages	Disadvantages	Application	Ref
Phase Inversion Temperature	It uses non-ionic surfactants, such as polyoxyethylene-based types, whose solubility changes with temperature. At a specific point called the PIT (Phase Inversion Temperature), the surfactant dissolves equally well in water and oil, leading to phase inversion and smaller droplet formation.	No high-pressure equipment is needed and very small droplets (around 100 nm) can be formed.	This method is not suitable for drugs sensitive to heat and needs accurate temperature control.	Cosmetics, food emulsions, pharmaceutical emulsions.	[50]
Spontaneous Emulsification	Nanoemulsions form spontaneously when an organic phase (oil, surfactant, and co-solvent) is mixed into water, creating turbulence at the interface and forming droplets.	This method is simple, uses little energy, and works well for poorly soluble drugs.	This method works only with certain surfactants and oils and may need organic solvents.	Self-emulsifying drug delivery systems (SEDDS), lipid-based formulations.	[51]

Emulsion Phase Inversion Composition	Altering the composition, particularly the water-to-oil ratio, can switch the emulsion from water-in-oil (W/O) to oil-in-water (O/W). This inversion creates strong shear at the interface, producing small droplets.	No heating is required, making it suitable for temperature-sensitive drugs, and simple stirring is enough.	This method is sensitive to ingredient ratios and may not be consistent if the conditions are not carefully controlled."	Topical and oral nanoemulsion formulations.	[52]

High-Energy Methods: High-energy emulsification is known as a top-down approach because it begins with bigger droplets and applies high mechanical energy to divide them into nano-scale droplets, forming a nanoemulsion. This method is chosen when accurate droplet size control, good long-term stability, and large-scale production are needed (Table 4).

Table 4. High-Energy method of various emulsification process

Emulsification process	Mechanism of emulsification	Advantages	Disadvantages	Application	Ref
Microfluidization	In this method, a pre-emulsion is forced through tiny microchannels under very high pressure (up to 30,000 psi). The fluid streams hit each other at high speed, creating strong shear forces that break the droplets into nano-sized particles.	This method produces emulsions with a uniform droplet size, offers good reproducibilityand can be easily scaled up for large-scale production.	Regular cleaning is required to prevent contamination and the equipment is expensive, needs high maintenance.	Injectable emulsions, protein and vaccine delivery, cosmetics.	[51]
High-Pressure Homogenization	A pre-emulsion is pushed through a narrow valve or small opening under very high pressure (500–1500 bar). The strong shear, turbulence, and cavitation forces then break the oil droplets into much smaller sizes.	suitable for both oil-in-water (O/W) and water-in-oil (W/O) emulsions and This method produces very small and uniform droplets, can be scaled up for industrial use.	This method produces heat, which may damage heat-sensitive drugs, and it also requires a high initial investment.	Pharmaceuticals, cosmetics, food emulsions, vaccines.	[53]
Ultrasonication	High-frequency sound waves (about 20–40 kHz) produce alternating high- and low-pressure cycles in the liquid. This forms tiny cavitation bubbles that collapse strongly, generating shock waves that break the oil droplets into smaller sizes.	This method is effective for heat-sensitive drugs and is simple to use at the laboratory scale.	It carries a risk of metal contamination from the probe tip and not suitable for large-scale production.	Lab-scale formulation of nanoemulsions for drug delivery and cosmetics.	[54]

Characterization of Nanoemulsion:

1. **Droplet Size Analysis:** Droplet size is measured by dynamic light scattering (DLS). nanoemulsions usually have droplet sizes in the range of 20 to 200 nm. [55]

2. **Polydispersity:** The polydispersity index is measured to assess the uniformity of droplet size distribution in the nanoemulsion. A lower PDI value indicates a more uniform and stable system. [55]

3. **Zeta Potential:** Zeta potential shows surface charge of droplets and helps predict the stability of nanoemulsions. A high zeta potential value (±30 mV) suggests good stability. [56]

4. **pH:** The pH of a nanoemulsion should be close to the skin's natural pH (~5.5) to avoid irritation or allergic reactions. Formulations with unsuitable pH can damage the skin barrier, so pH adjustment using buffers or mild acids/bases is necessary for safe and long-term dermatological use. [57]

5. **Viscosity measurements:** The viscosity of nanoemulsions is measured using a Brookfield rotary viscometer at

different shear rates. Samples are equilibrated and tested at 37 ± 0.2 °C using a thermostatic water bath. [58]

6. **Refractive Index and Transparency:** Transparency and refractive index indicate the physical stability of nanoemulsions. High clarity and a refractive index close to water or skin suggest fine droplet dispersion, while changes in refractive index over time indicate instability. Clear or slightly opalescent appearance is preferred for cosmetic and dermatological products. [58]

7. **Stability Studies:**

- Physical Stability: It refers to the ability of a nanoemulsion to resist phase separation, droplet coalescence, flocculation, and Ostwald ripening.
- Thermal and Centrifugation Tests: Performed to check nanoemulsion stability. Heating tests show if droplets stay intact at different temperatures, and centrifugation checks if they resist separation.
- Shelf-life: Tested at different temperature for an extended period to monitor any changes in droplet size, phase separation, or chemical composition. This ensures the formulation remains effective and safe during its shelf life. [59]

8. **Antibacterial Activity against acnes:** Evaluates how effectively the nanoemulsion inhibits or kills the bacterium. By measuring MIC (lowest concentration preventing bacterial growth) and MBC (lowest concentration killing bacteria), researchers can determine if the formulation is effective against acne-causing bacteria. This ensures the nanoemulsion can reduce bacterial load on the skin, helping to control and treat acne. [59]

9. **Skin Permeation Studies:** These studies measure how well the drug in the nanoemulsion penetrates the skin. Using excised skin in Franz diffusion cells, this helps optimize the formulation by providing important information about the drug's penetration, absorption rate, and distribution across different skin layers. [60]

Future Directions:

1. Market Growth & Segment Expansion:

The nanoemulsion market is expected to increase from approximately USD 8–8.2 billion in 2024 to around USD 17–20 billion by 2030–2035, growing at an annual rate of about 6–7% (CAGR). This growth is driven by rising applications in pharmaceuticals, cosmetics, food and beverages, nutraceuticals, agriculture, industrial coatings, and emerging areas such as antimicrobial and CBD-based products. Among these sectors, pharmaceuticals and cosmetics dominate the market, together accounting for nearly 90% of total demand, with pharmaceuticals contributing 60–70% and cosmetics 25–30%. [61]

2. Novel Bioactive Discovery:

Future research should focus on the identification of new plant species and natural compounds with anti-acne activity, along with a better understanding of their mechanisms of action at the molecular and genetic levels. There is also a need to develop standardized formulations with improved bioavailability to enhance therapeutic effectiveness. Additionally, exploring synergistic interactions among active compounds in herbal formulations may lead to more effective anti-acne treatments. [38]

3. Personalized Herbal Medicine:

A holistic dermaceuticophyte approach combining personalized herbal therapy, diet control, and lifestyle modification may offer effective acne prevention. Future research should emphasize identifying genetic or phenotypic markers that influence individual responses, developing customized herbal formulations based on acne etiology, and integrating traditional medicine with modern pharmacogenomics to enhance therapeutic outcomes. [50]

4. Technological & Sustainable Innovation:

Advanced formulation techniques such as high-pressure homogenization, microfluidization, low-energy self-emulsification, and Pickering emulsions stabilized with nanocellulose are becoming more popular because they offer better control over formulation properties, lower environmental impact, and reduced production costs. At the same time, there is a growing shift toward natural, biodegradable, and plant-based surfactants and oils, in response to

increasing consumer awareness and stricter regulatory requirements for environmentally friendly products. [38]

5. Integration with Conventional Medicine:

Future research should focus on identifying the best ways to integrate herbal therapies with conventional healthcare. This includes developing evidence-based guidelines for combining herbal and mainstream treatments, training healthcare professionals in the safe and effective use of herbal medicines, and establishing clear treatment policies that define patient selection and monitoring methods. In addition, careful evaluation of potential herb–drug interactions and contraindications are essential to ensure patient safety.[62]

CONCLUSION:

Acne vulgaris is a multifactorial inflammatory skin disorder that significantly affects both physical appearance and psychosocial well-being. Conventional therapies such as retinoids, antibiotics, and hormonal agents remain effective but are limited by adverse effects, microbiome disruption, and rising antibiotic resistance. Herbal remedies, with their antimicrobial, anti-inflammatory, antioxidant, and sebum-regulating properties, offer a safer alternative; however, their therapeutic potential is often constrained by poor solubility, instability, and inadequate skin penetration.

Nanoemulsion-based delivery systems address these limitations by enhancing solubility, stability, and follicular penetration of herbal actives. Their small droplet size enables efficient passage through the stratum corneum and targeted delivery to hair follicles—the primary site of acne pathogenesis—while controlled release and favorable skin compatibility improve patient adherence.

The integration of herbal medicine with nanotechnology thus represents a promising, safe, and effective strategy for acne management. Continued research into novel plant-derived bioactives, personalized formulations, and sustainable technologies will further strengthen this approach and facilitate its incorporation into mainstream acne therapy.

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