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Acne and Emerging Nanotechnological Therapies: A Comprehensive Overview

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ABSTRACT:
Acne vulgaris is a multifactorial chronic inflammatory disorder of the pilosebaceous unit, commonly affecting adolescents and young adults. Its pathogenesis involves increased sebum production, follicular hyperkeratinization, Cutibacterium acnes colonization, and immune-mediated inflammation. Conventional therapeutic approaches such as topical retinoids, antibiotics, and hormonal therapies, though effective, are often associated with adverse effects, antibiotic resistance, and poor patient compliance. To overcome these limitations, nanotechnology has emerged as a revolutionary platform offering targeted, controlled, and sustained drug delivery with improved therapeutic outcomes. This review comprehensively explores the underlying pathophysiology of acne and highlights recent advancements in nanotechnological interventions, including lipid-based nanoparticles, liposomes, etc. These nanocarriers exhibit enhanced skin permeation, stability, and bioavailability while minimizing systemic exposure and irritation. In addition, the review discusses the current challenges, regulatory perspectives, and future potential of nanotechnology-driven therapeutics in dermatology. This integrated overview aims to provide a deeper insight into acne management and the translational promise of nanomedicine.

1. Introduction

Acne is one of the most common dermatological disorders, affecting individuals across all age groups, though it is especially prevalent among adolescents and young adults [1]. Lesions typically appear on the face, neck, chest, and upper back, causing both physical and psychological discomfort. Acne exists in several forms, including neonatal acne, infantile acne, occupational acne, acne vulgaris, severe nodular acne, acute-onset acne, friction-induced acne, acne excoriée, chemically-induced acne, and drug-related acne [2]. Among these, acne vulgaris is the most widespread, constituting the majority of clinical cases. It presents with diverse types of lesions categorized into non-inflammatory (e.g., blackheads and whiteheads) and inflammatory (e.g., papules, pustules, nodules, and cysts). The pathogenesis of acne is multifactorial, involving sebaceous gland hyperactivity, abnormal keratinization, proliferation of Cutibacterium acnes, and inflammatory responses [3]. These factors are modulated by genetic predispositions, hormonal imbalances, diet, and environmental conditions, which together complicate treatment outcomes. Therapeutic interventions include topical retinoids, benzoyl peroxide, systemic antibiotics, hormonal agents, and in severe cases, isotretinoin. However, treatment responses vary widely due to individual differences in skin biology and the complex etiology of the disease [4]. In recent years, research has begun to focus on emerging therapeutic avenues, particularly the role of nanotechnology in acne management. With the advent of nanoscience in the late 20th century, the fields of medicine and pharmaceuticals have witnessed a paradigm shift [5]. Nanotechnology refers to the design, manipulation, and application of materials on a nanoscale (1–100 nm)—a scale at which materials exhibit unique physical, chemical, and biological properties [6]. The incorporation of nanoparticles and nanocarriers into drug delivery systems has led to the development of nanopharmaceuticals that offer numerous advantages over conventional therapies [7]. These include enhanced

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bioavailability, target-specific delivery, controlled release, and reduced systemic toxicity. Nanocarriers such as liposomes, dendrimers, micelles, carbon nanotubes, and polymeric nanoparticles have been explored for delivering anti-acne agents directly to the pilosebaceous unit, thereby improving therapeutic efficacy while minimizing side effects. Furthermore, nanotechnology has enabled dual-purpose systems that serve both diagnostic and therapeutic functions—a concept known as theranostics [8]. This integration allows for real-time monitoring of drug response and optimization of treatment regimens. Notable FDA-approved nanomedicine examples such as Doxil, Abraxane, Genexol-PM, and Feraheme demonstrate the vast potential of these systems in clinical settings, highlighting their benefits in terms of stability, targeting, and efficacy [9]. This comprehensive review aims to elucidate the biological basis of acne, evaluate current therapeutic strategies, and delve into emerging nanotechnological interventions that hold promise in transforming acne management. By exploring the interface between dermatology and nanomedicine, this work underscores the importance of personalized, targeted, and efficient treatment approaches in modern skin care [10].

2. Pathophysiology of Acne

Acne can be triggered or intensified by a wide range of factors, including inherited traits, environmental conditions (such as heat, air pollutants, humidity levels, ultraviolet radiation, and exposure to substances like mineral oils or halogenated chemicals), dietary habits, hormonal imbalances, psychological stress, tobacco use, and the use of pore-clogging medications like male hormones, halogen compounds, and corticosteroids [11]. Microbial presence and certain skincare or cosmetic products can further aggravate the condition. Acne vulgaris often results in physical discomfort, emotional distress, and visible disfigurement, which may leave lasting scars. Beyond the physical effects, affected individuals frequently experience feelings of nervousness and self-consciousness, which can contribute to a depressive mental state [12].

3. Genetic Factors

Acne is a multifactorial skin condition shaped by various internal and external contributors. One of the most significant internal factors is genetics. A strong hereditary component is often observed, as individuals with a familial history of acne are more likely to develop the condition themselves [13]. Genetic makeup affects numerous processes that lead to acne formation, such as oil gland activity, the way skin cells shed inside hair follicles, and how the immune system reacts to bacterial presence—especially that of Cutibacterium acnes. Certain inherited traits, like variations in androgen receptor genes, can heighten oil production in the skin, making it more prone to breakouts [14].

4. Environmental Factors

External elements also play a pivotal role in the development and progression of acne. Dietary choices, weather conditions, air pollution, and daily habits can all influence the skin's health. For instance, diets high in sugar and dairy have been linked to more severe acne, likely due to their effect on hormones that stimulate oil production and inflammation [15]. Warm, humid environments can cause skin cells to swell and clog pores, fostering a favorable setting for bacterial growth. Airborne pollutants such as nitrogen dioxide and sulfur-based gases can add oxidative stress to the skin, worsening acne symptoms. Furthermore, emotional stress has been identified as a trigger, primarily because it affects hormone levels that, in turn, increase sebum production [16].

5. Hormonal Influences

Hormonal fluctuations are deeply entwined with acne pathogenesis, particularly through their impact on sebaceous (oil-producing) glands. Male sex hormones, or androgens, are central to this process—they promote the growth of sebaceous cells, increase fat storage within them, and encourage excessive skin thickening within hair follicles [17]. These changes collectively result in heightened oil secretion and more severe acne outbreaks. Two distinct but related conditions often observed in acne-prone individuals are excessive oiliness and changes in the quality of sebum, both of which create a favorable environment for bacterial growth and inflammation [18].

Hormones exert their influence by activating key biological pathways. For instance, androgens boost lipid production by activating the mTOR pathway

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and its downstream effectors, which enhance fat synthesis. These hormones also suppress the Wnt/β-catenin pathway, promoting genes like c-MYC that encourage the maturation of sebaceous cells. Insulin-like growth factor 1 (IGF-1) is another critical hormone in acne formation; it modifies how specific genes are expressed and boosts oil gland activity by regulating proteins involved in lipid production and androgen signaling [19]. Beyond these localized effects, hormonal disorders throughout the body can be at the root of adult-onset acne. Symptoms like irregular menstrual cycles, unwanted body hair, thinning scalp hair, and sudden or persistent breakouts can signal underlying hormonal imbalances [20]. These may stem from conditions such as obesity, metabolic disturbances, underactive thyroid glands, or hormonal syndromes like polycystic ovary syndrome. A comprehensive hormonal assessment—especially during specific times in the menstrual cycle—can help identify abnormalities that may be contributing to acne [21].

6. Microbiome

The community of microorganisms living on our skin, known as the skin microbiome, plays an important role in keeping the skin balanced and healthy [22]. This includes bacteria like C. acnes and Staphylococcus species, as well as fungi. While an overgrowth of C. acnes is associated with acne, it's actually the specific strains and their diversity that determine whether they trigger breakouts. Some types of C. acnes provoke strong immune responses and inflammation, while others support a more peaceful skin environment by encouraging anti-inflammatory signals [23]. When this microbial harmony is disrupted—a state known as dysbiosis—the risk of acne increases. Harmful bacteria can activate immune pathways that lead to inflammation and impaired skin barrier function [24]. C. acnes, in particular, interacts with immune cells by releasing damaging enzymes and reactive molecules, triggering inflammatory pathways and increasing oil production. This causes a cascade of reactions, including skin cell buildup and inflammation, which worsens acne [25]. Emerging evidence also highlights a link between the gut microbiome and skin health. The intestinal ecosystem, rich in various microbes, plays a role in immunity, nutrient absorption, and protection against harmful invaders [26]. This microbial environment differs from person to person based on diet, medications, and lifestyle. Individuals with acne often show less diverse gut flora and a skewed balance of certain microbial groups—features commonly associated with Western-style diets [27].

The gut and skin communicate through systemic pathways, meaning that changes in gut microbes and their by-products can influence skin health through the bloodstream [28]. These interactions can affect how skin cells grow and function, particularly via hormonal and inflammatory pathways like mTOR signaling. Some beneficial gut microbes produce anti-inflammatory compounds, while others may worsen inflammation, illustrating the complexity of the gut-skin connection [29].

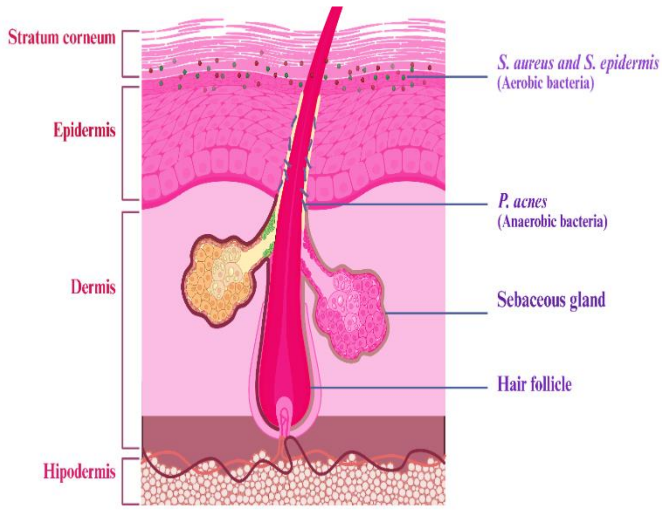

Figure 1: Schematic representation of skin architecture highlighting microbial involvement in acne pathogenesis

7. Inflammation

Inflammation is a hallmark of acne and arises from both the body's initial immune response (Figure 2) and longer-term immune memory. C. acnes is central to this process, as it activates sensors on skin cells that detect microbial invaders [30]. These sensors then prompt immune cells to release inflammatory messengers like interleukins, which are found in abundance in acne-affected skin. The bacteria also activate deeper immune responses involving protein complexes inside immune cells, which further amplify inflammation through cytokine release [31]. The involvement of adaptive immunity is evident

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early in acne development. Even in its initial stages, immune cells like helper T cells gather around hair follicles, showing that inflammation starts before visible changes in the skin appear. The immune system's reaction is not only swift but also specific; it includes memory cells and specialized white blood cells that respond strongly to C. acnes. These cells release inflammatory substances that perpetuate redness, swelling, and discomfort [32]. Furthermore, C. acnes can stimulate cellular pathways that lead to the production of enzymes, inflammatory molecules, and tissue-degrading proteins. These substances contribute to the destruction of skin structures, leading to deeper inflammation and scarring. Over time, chronic inflammation results in long-lasting changes, such as the formation of atrophic scars filled with plasma and memory immune cells [33]. Hormones also fuel this inflammatory process. IGF-1, for example, increases the production of inflammatory molecules in skin oil glands, and this effect can be toned down by certain inhibitors. Androgens, which boost IGF-1 levels, promote the activity of white blood cells and enzymes that break down tissue structures, worsening inflammation. White blood cells, particularly neutrophils, contribute by releasing reactive compounds like hydrogen peroxide, creating a feedback loop that intensifies skin irritation and damage [34].

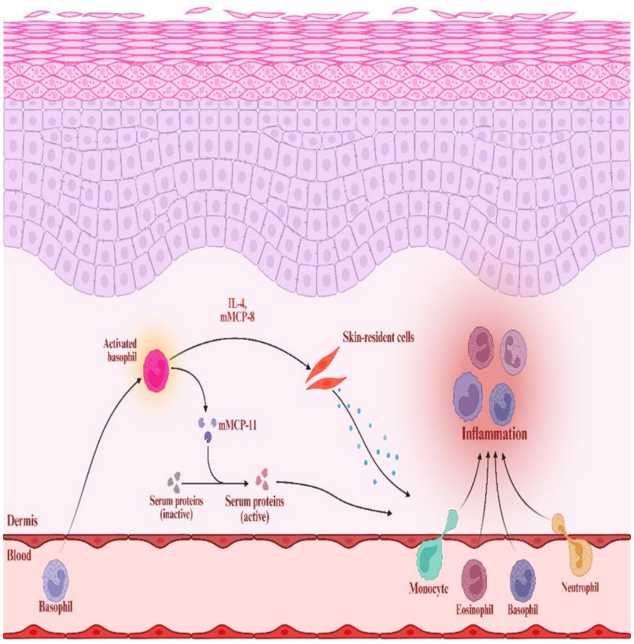

Figure 2: illustration depicts the immune-mediated inflammatory pathway in the skin, initiated by basophil activation in the dermis. Activated basophils release IL-4, mMCP-8, and mMCP-11, leading to activation of serum proteins and stimulation of skin-resident cells. These events trigger the recruitment of immune cells including monocytes, eosinophils, basophils, and neutrophils, culminating in localized inflammation.

8. Types of Acne lesions

Acne is categorized into multiple variants, such as acne conglobata, rosacea-related acne, acne fulminans, cosmetic-induced acne, acne excoriée (also known as picker's acne), drug-induced acne, chloracne, and mechanical acne. However, acne vulgaris remains the most widespread type, representing approximately 99% of all acne conditions [35]. This form of acne is characterized by two primary types of lesions: non-inflammatory and inflammatory. Non-inflammatory lesions include open and closed comedones, while inflammatory one's manifest as papules, pustules, nodules, and cysts. Comedones are classified into two forms: closed comedones, commonly referred to as whiteheads, and open comedones, known as blackheads [36]. Blackheads are mild, non-inflammatory blemishes that develop when excess sebum and dead skin obstruct hair follicles. These lesions are termed open comedones because the blockage is exposed to air, leading to oxidation and a dark coloration, typically black or brown. They frequently appear on areas like the face, arms, chest, neck, back, and shoulders [37]. Whiteheads are small, non-inflammatory bumps formed when oil, bacteria, and skin debris clog hair follicle openings. They are called closed comedones because the surface remains sealed, giving them a white or flesh-colored appearance. Whiteheads are most common in the T-zone, which includes the forehead, nose, and chin, but may occur elsewhere on the body [38]. Papules arise as part of the skin's inflammatory response to bacterial invasion, hormonal fluctuations, and overproduction of oil. They are red, tender bumps smaller than 5 mm without visible pus, and represent a transitional phase between non-inflammatory and inflammatory acne [39]. Pustules are inflamed lesions containing a central core of pus. These red bumps, often topped with a yellow or white head, are caused by clogged pores filled with oil and skin cells. Pustules can appear across various body areas, including the face, chest, back, shoulders, armpits, hairline, and groin [40]. Nodules represent a more serious form of acne involving deeper layers of the skin. These firm, painful lumps occur when bacteria, oil, and dead skin become trapped and cause significant inflammation. Unlike typical pimples, nodules are larger (exceeding 5–10 mm), do not contain pus, and often persist for extended periods. They are commonly found around the chin and jawline [41]. Cysts, or cystic acne, are the most severe type of inflammatory acne, forming deep under the skin when pores are blocked by oil, debris, and bacteria. These painful, fluid-filled swellings are often red or white and may lead to permanent scarring. Cystic acne can develop on the face, neck, chest, back, shoulders, arms, and other areas, and individuals affected usually present with both inflammatory and non-inflammatory lesions [42].

9. Treatment Strategies

Current treatment strategies for acne aim to target the multiple factors involved in its development, such as abnormal skin cell shedding, excess oil production, bacterial growth, and inflammation [43]. Topical treatments are fundamental in managing acne due to their direct effect on the skin, limited systemic side effects, and ease of use. Retinoids, a class of vitamin A derivatives, work by binding to specific receptors in skin cells, promoting cell turnover, reducing oil secretion, and decreasing inflammation [44]. These are categorized into generations, with newer ones designed to be more effective and less irritating. Tretinoin was the first retinoid approved for acne and helps normalize skin shedding while controlling sebum. Adapalene and tazarotene, later retinoids, selectively target certain receptors and are effective with fewer side effects, though tazarotene can cause more irritation [45]. The most recent retinoid, trifarotene, specifically targets receptors in the skin and has shown promising results in reducing acne lesions but may still cause some irritation. Side effects of retinoids often include dryness, redness, and increased sensitivity to sunlight, which can be managed by starting with lower doses, using moisturizers, and applying sunscreen. These agents are generally avoided during pregnancy, with safer alternatives like azelaic acid or clindamycin recommended [46]. Combining retinoids with other treatments such as benzoyl peroxide or antibiotics often enhances results but may increase irritation initially. Benzoyl peroxide is a widely used antimicrobial agent that kills acne-causing bacteria and helps prevent antibiotic resistance, though it can cause dryness and redness and may bleach fabrics. Topical antibiotics like clindamycin, erythromycin, and minocycline reduce inflammation and bacteria but should not be used alone due to resistance concerns; combining them with benzoyl peroxide reduces this risk [47]. Other topical options include azelaic acid, which treats acne and post-inflammatory pigmentation with anti-inflammatory and antimicrobial effects and is safe for sensitive skin and pregnancy. Salicylic acid serves as a mild exfoliant and anti-inflammatory agent, useful for mild acne or those intolerant to stronger treatments, though it can cause irritation and sometimes worsen inflammation temporarily. Dapsone gel offers antimicrobial and anti-inflammatory benefits and is a useful alternative for certain patients, including those with sensitive skin or specific contraindications, and generally has minimal side effects. However, combining dapsone with benzoyl peroxide should be avoided due to temporary skin discoloration. Overall, topical acne treatments work best when tailored to individual skin types and combined thoughtfully to balance effectiveness and tolerability [48]. Clascoterone (Winlevi®) is the first FDA-approved topical antiandrogen treatment for acne, suitable for all genders, and represents a significant advancement in acne therapy since isotretinoin's introduction in 1982. Although it is not yet approved in the EU, clascoterone offers both anti-inflammatory and antiandrogenic benefits, making it effective for treating acne in men and women alike. It works by blocking the binding of dihydrotestosterone (DHT) to androgen receptors in the skin's sebaceous glands, thereby reducing sebum production and lowering inflammation caused by pro-inflammatory cytokines [49]. Once absorbed, clascoterone is quickly converted into an inactive form, minimizing the risk of systemic side effects. Clinical trials involving over a thousand patients with moderate to severe acne showed that 1% clascoterone cream significantly decreased both inflammatory and non-inflammatory acne lesions, with treatment success rates notably higher than placebo. The cream was well tolerated, with mild local side effects such as redness and dryness occurring at similar frequencies to placebo, and no serious systemic adverse effects were reported [50]. Although rare cases of asymptomatic adrenal suppression were noted with high doses, these effects resolved after stopping treatment. While systemic hormonal treatments like oral contraceptives or spironolactone also modulate hormones, they carry more systemic risks, distinguishing clascoterone as a safer topical alternative. Further studies are needed to define its optimal use fully, but clascoterone's unique mode of action and good safety profile make it a promising addition to acne treatment options, especially in combination with other therapies [51]. Hyaluronic acid, a key structural component of the extracellular matrix, plays an essential role in skin health. It binds to receptors found in sebaceous glands and has demonstrated the ability to suppress lipid formation and decrease sebum levels in a dose-responsive manner, suggesting its value in acne therapy [52]. Cannabidiol (CBD) is gaining attention for its interaction with the skin's natural endocannabinoid system, a regulatory mechanism for maintaining cutaneous balance. Its anti-inflammatory properties and capacity to inhibit lipid synthesis, reduce sebocyte activity, and modulate cellular signaling pathways position it as a viable option for managing acne-related inflammation and oil production. In severe and resistant acne cases, biologic agents have been explored, particularly those targeting inflammatory pathways such as tumor necrosis factor and interleukins. These therapies have shown potential in controlling intense inflammatory forms of acne and related conditions by modulating specific immune responses. However, not all biologics have proven effective in clinical settings, emphasizing the need for further research and optimization [53]. The skin and gut microbiome are also emerging as crucial elements in acne development. Studies involving the transfer of healthy skin microorganisms to acne-prone individuals indicate the feasibility of modulating the microbiome as a therapeutic strategy. Enhancing the skin's natural bacterial balance through the use of topical or oral probiotics may suppress harmful bacterial strains, stimulate the body's production of beneficial antimicrobial agents, and reduce inflammatory signaling [54]. Probiotic-based treatments, whether applied topically or taken orally, have been associated with improvements in acne symptoms. These benefits include reduced lesion size, less redness, and decreased numbers of acne-causing bacteria. Additionally, probiotics have been shown to modulate key immune markers, indicating their role in reducing systemic inflammation. Vaccine development targeting acne-related bacterial toxins and virulence factors has shown promise in animal models, though human data are still lacking. Another innovative approach involves the use of bacteriophages—viruses that specifically attack bacteria—to selectively reduce acne-causing microbes while preserving the overall skin microbiome. While preclinical data are encouraging, clinical confirmation remains necessary [55]. Synthetic antimicrobial peptides have emerged as another innovative strategy. These molecules exhibit both antimicrobial and immunomodulatory properties and have demonstrated effectiveness against antibiotic-resistant acne bacteria in experimental studies [56]. Given the central role of signaling pathways like Akt/mTOR in acne pathophysiology, there is growing interest in targeting these molecular routes to reduce sebum output [57]. Both synthetic drugs and naturally derived compounds—such as plant-based polyphenols—have shown the capacity to interfere with these pathways. They help regulate sebaceous gland activity and reduce the clinical severity of acne. For example, certain plant-derived substances have demonstrated considerable efficacy in decreasing lipid production and improving skin condition when applied topically [58].

10. Emerging Nanotechnological Therapies

Modern nanopharmaceutical design is evolving with innovative approaches [59], along with environmentally friendly (green) design strategies (Figure 3).

11. Nanosuspension Technology

Nanosuspension technology is a promising nanotech strategy to boost the pharmaceutical effectiveness of drugs and plant extracts by improving their solubility and oral absorption. One common technique is nanoprecipitation [60], where the plant extract is first dissolved in an organic solvent (like ethanol) and filtered. This solution is then slowly introduced into a water phase containing a stabilizing agent such as a surfactant or polymer, under continuous stirring. This process yields stable nanosuspensions with small particle sizes and narrow size distribution. Such formulations have demonstrated physical stability, safety, and enhanced biological activity [61].

12. Nano-Encapsulation

Nanocapsules have gained recognition as excellent carriers for delivering pharmaceuticals, nutraceuticals,

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and bioactive compounds [62]. Characterized by a core–shell structure with sizes typically between 10 and 1000 nanometers, nanocapsules offer controlled drug release, improved stability, and targeted delivery capabilities. Various materials and fabrication methods are employed to create these carriers, expanding their potential for medical and other applications [63].

13. Materials for Nanocapsule Preparation

Nanocapsules can be made from diverse materials, each with unique benefits. Commonly used substances include polymers, lipids, and inorganic nanoparticles. They facilitate drug delivery through multiple administration routes, reduce toxicity, and enhance stability. Due to their small size, nanocapsules can actively target cells and tissues [64]. These often have an oily core ideal for housing fat-soluble drugs, surrounded by a polymer shell that regulates drug release. Biocompatible and biodegradable polymers like PLGA, PLA, and chitosan are frequently used. These polymers can be synthesized using various methods such as emulsion polymerization or self-assembly, enabling precise control over particle characteristics and drug loading [65]. The polymer shell is critical for protecting the drug and influencing the release pattern and distribution within the body. Natural polymers, particularly polysaccharides like chitosan and alginate, are favored for their compatibility, gelation ability, and adhesive properties. Chitosan, with its positive charge, can interact effectively with negatively charged microbial surfaces, enhancing therapeutic effects. Combinations of polymers, such as chitosan and dextran sulfate, provide stable nanocapsules with tunable release behaviors. Protein-based shells, such as those made from albumin, offer additional benefits like biodegradability and reduced immune response, and can be designed to self-assemble into hollow nanostructures suitable for drug delivery [66]. Synthetic materials like aliphatic polyesters, including PLA, PLGA, and PCL, are widely researched due to their biocompatibility and ability to degrade within the body. PCL, in particular, has a longer degradation time making it suitable for sustained release applications and is often more cost-effective [67]. Lipid nanocarriers, including liposomes, solid lipid nanoparticles, and nanostructured lipid carriers, are valued for their high drug loading capacity and controlled release profiles. They are typically composed of phospholipids, triglycerides, and cholesterol, and prepared by various techniques such as solvent evaporation and microemulsion [68]. Inorganic Nanocapsules: Nanoparticles made from materials like mesoporous silica, gold, or magnetic particles offer multifunctional capabilities including targeted delivery, controlled release, and imaging. These are synthesized through controlled chemical processes to achieve desired size and surface properties [69]. Vegetable oils such as soybean and palm oils, along with fatty acids and medium-chain triglycerides, serve as excellent oily cores in nanocapsules due to their safety and ability to dissolve fat-soluble drugs, while sometimes offering therapeutic effects themselves [70]. For example, copaiba oil used as a core material enhances the solubility of certain hydrophobic anti-cancer drugs and contributes anti-inflammatory benefits. Other essential oils like turmeric and lemongrass provide antibacterial and antioxidant properties when used in nanocapsules [71]. Nanocapsules can also incorporate aqueous cores to carry hydrophilic drugs, such as gemcitabine hydrochloride and doxorubicin, enhancing their delivery and efficacy against cancer cells. Encapsulation protects sensitive molecules like nucleotides and proteins from degradation and improves their cellular uptake [72].

Hollow-core nanocapsules are created by using a removable solid template, enabling controlled drug release and improved biocompatibility. Common template materials include calcium carbonate, silica, and polystyrene, which can be dissolved or removed under mild conditions to preserve the nanocapsule shell [73].

14. Lipid-Based Nanoparticles

The advancement of sophisticated lipid-based nanoparticles (LNPs) has become essential in tackling complex biomedical challenges and overcoming physiological obstacles, especially in cancer nanomedicine. Since the first cancer nanomedicine received regulatory approval in the mid-1990s, there has been remarkable progress in designing intelligent nanomedicines [74]. These designs enhance therapeutic efficacy by modifying both the external surfaces and internal structure of LNPs to improve drug delivery within tumors while avoiding rapid breakdown and clearance in the body [75]. Recent innovations focus on creating hybrid nanoparticles that combine lipid and polymer components, enabling simultaneous delivery of multiple drugs, improved tumor targeting, and combined therapeutic and diagnostic functions (theranostics). Multifunctional nanoparticle platforms aim to combat drug-resistant cancer cells and break through biological barriers that limit the effectiveness of anticancer agents [76]. In medical imaging, LNPs have garnered significant attention due to their ability to enhance various imaging modalities such as MRI, ultrasound, CT, PET, and SPECT. Each imaging technique requires specific contrast agents to improve diagnostic clarity. Lipid-based nanoparticles, including solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), and liposomes, serve as effective contrast agents because of their unique physicochemical properties [77]. In breast cancer treatment, where conventional methods such as surgery, chemotherapy, and radiation have limited success due to metastasis and chemotherapy resistance, lipid-based nanocarriers have emerged as promising drug delivery systems [78]. These nanocarriers, including nanoemulsions, SLNs, NLCs, and liposomes, demonstrate the ability to inhibit cancer cell proliferation, reduce the likelihood of tumor recurrence, and minimize metastasis following chemotherapy. Despite advances in breast cancer management, systemic toxicity and multidrug resistance remain significant hurdles that nanocarriers may help overcome by enhancing drug specificity and reducing side effects [79].

15. Liposomes

Liposomes are widely regarded as one of the most effective and versatile nanocarriers for delivering pharmaceutical agents. These small vesicles consist of one or more lipid bilayers that can encapsulate hydrophilic, lipophilic, and amphiphilic compounds, making them highly adaptable for medical applications. Their natural lipid composition renders them biocompatible and safer than many synthetic carriers such as dendrimers or carbon nanotubes [80]. Liposomes can be composed of lipids with varying chain lengths and saturation levels, tailored to match the properties of the encapsulated drug, including its stability at specific temperatures. Nanoliposomes—liposomes under 100 nm in diameter—are particularly valuable due to their nanoscale size, which influences their biodistribution and cellular uptake [81]. Traditional liposome preparation methods often involve organic solvents, which can be challenging to remove completely and may pose risks to the final product's stability and safety. To address this, alternative solvent-free techniques have been developed, such as using glycerol to aid lipid dispersion, facilitating the formation of anionic liposomes suitable for delivering sensitive molecules like siRNA [82]. Despite their advantages, liposomes face limitations such as limited stability, batch variability, difficulties in sterilization, and relatively low drug loading capacity. To enhance their stability and prolong drug release, liposomes can be coated with biopolymers like chitosan, forming "chitosomes" which show improved robustness and are particularly useful for transdermal drug delivery [83]. Recent developments include surface modifications to liposomes to evade immune system recognition and prolong circulation time. For example, coating liposomes with DNA and forming a protein corona can reduce uptake by immune cells more effectively than traditional PEGylation. These strategies improve the bioavailability and therapeutic performance of liposomal formulations [84]. Beyond traditional liposomes, diverse variants such as ufasomes, phytosomes, terpesomes, bilosomes, and aspasomes have been designed, each with unique compositions and coatings tailored for specific therapeutic purposes. PEGylation or combinations of PEG with other polymers extend circulation time and reduce clearance [85]. An exciting area of research involves biomimetic liposomes coated with natural cell membranes from sources such as red blood cells, leukocytes, platelets, stem cells, or even cancer cells. These biomimetic nanocarriers enhance drug bioactivity, immune evasion, and targeting, while protecting the encapsulated drugs from degradation. Hybrid cell membrane-coated liposomes combine membranes from different cell types to further boost targeting and therapeutic efficacy. For example, liposomes cloaked with both red blood cell and cancer cell membranes, surface-modified with targeting peptides such as the RGD tripeptide, have shown increased tumor localization and therapeutic effectiveness without damaging healthy tissues [86].

16. Metal-Based Nanoparticles

Metal-based nanoparticles (MNPs), including metal oxide nanoparticles (MONPs), quantum dots, and metal-organic frameworks, have diverse applications in drug delivery and medical diagnosis due to their unique physical and chemical properties. Magnetic

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nanoparticles such as iron, nickel, and cobalt are particularly notable for their responsiveness to magnetic fields, high chemical stability, catalytic activity, and antimicrobial properties [87]. Iron oxide nanoparticles are extensively studied for diagnostic imaging, chemotherapy delivery, hyperthermia, photodynamic therapy, and gene delivery. Magnetic nanocomposites, including magnetoplasmonic hybrids, are being engineered for multimodal imaging and targeted photothermal cancer therapy. For example, Au-MnO heterostructured nanoparticles have been developed for imaging-guided photothermal treatment, aiming to reduce chemotherapy side effects and improve contrast agent safety [88]. Advances in magnetic hydroxyapatite nanoparticles encapsulating photosensitizers and silk fibroin protein enable combined imaging and photodynamic therapy, showing promising results in inducing cancer cell apoptosis upon laser activation [89]. Surface modifications of magnetic nanoparticles with ligands enable targeted drug delivery to specific tissues such as the gastrointestinal tract, enhancing treatment precision and minimizing off-target effects. Magnetic nanoparticles have been functionalized with chemotherapy drugs like 5-fluorouracil, irinotecan, and oxaliplatin for colon cancer therapy [90]. Platinum nanoparticles stabilized with poly(acrylic acid) act as efficient antioxidants by scavenging reactive oxygen species (ROS), which are implicated in aging and oxidative stress-related diseases. These “nanozymes” mimic natural enzymes such as superoxide dismutase and catalase, offering potential in mitigating oxidative damage [91]. Other metal nanoparticles such as selenium nanoparticles (SeNPs) exhibit antioxidant properties that promote wound healing and serve as nutritional supplements with reduced toxicity. Silver nanoparticles (AgNPs), well-known for their antimicrobial and anti-inflammatory properties, are used extensively in pharmaceutical and environmental applications [92]. While many metal oxide nanoparticles like zinc oxide (ZnO), iron oxide, and titanium dioxide (TiO_2) have been approved for medical uses such as wound dressings and imaging agents, concerns remain about their long-term safety due to possible accumulation in organs and cytotoxic effects [93]. In response to concerns over hazardous chemical synthesis methods, there has been a shift toward green, biological synthesis approaches for metal and metal oxide nanoparticles. These environmentally friendly techniques utilize microorganisms, fungi, and plant extracts to produce nanoparticles that are biocompatible and cost-effective, reducing toxic residues [94]. The increasing prevalence of antibiotic-resistant microbes and healthcare cost pressures have stimulated research into nano-sized antiseptics, which potentially offer broad-spectrum antimicrobial activity with a lower likelihood of inducing resistance [95].

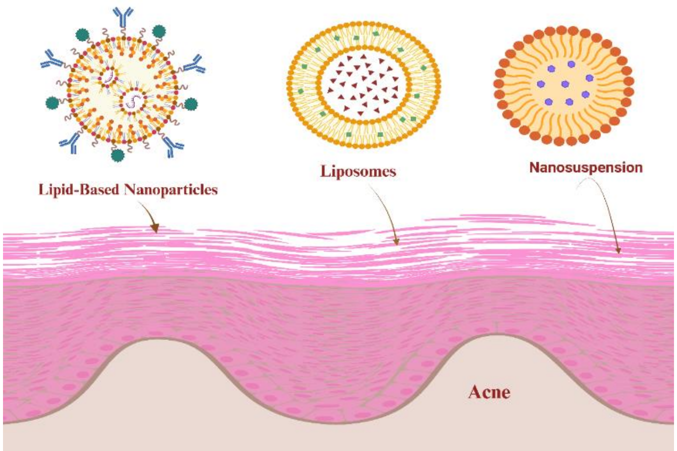

Figure 3: Emerging nanotechnological approaches for targeted acne treatment

Future Prospective

The future of acne management is poised to be transformed by the rapid progress in nanotechnology, with an emphasis on precision, personalization, and multifunctionality. Emerging trends suggest a shift toward personalized nanomedicine, where patient-specific factors such as skin microbiome composition, genetic profile, and hormonal status guide the design of nanoformulations [96]. This individualized approach holds the potential to enhance treatment efficacy while minimizing adverse effects. In parallel, smart nanocarriers that respond to internal (e.g., pH, enzymes) or external (e.g., temperature, light) stimuli are gaining attention for their ability to release therapeutic agents precisely at the site of inflammation or infection. These systems not only improve drug bioavailability but also reduce systemic exposure and toxicity. Multifunctional nanoplatforms that integrate anti-inflammatory, antibacterial, antioxidant, and sebum-regulating activities are expected to become standard, offering a comprehensive strategy to tackle the multifactorial nature of acne. Additionally, advances in materials science will facilitate the development of biodegradable and eco-friendly nanoparticles, addressing growing concerns over the environmental impact of synthetic nanomaterials. The use of lipid-based systems, dendrimers, solid lipid nanoparticles, and nanomicelles will be refined to improve stability, skin adhesion, and follicular targeting [97]. Clinical translation will be accelerated by high-throughput screening, artificial intelligence, and machine learning, which can predict optimal formulations and patient responses. However, the regulatory landscape will need to evolve alongside these innovations, ensuring that safety, efficacy, and ethical standards are rigorously upheld. Future therapies may also incorporate digital technologies such as wearable patches and mobile health applications, allowing real-time monitoring of acne progression and automated delivery of therapeutic agents. Together, these advances herald a new era in acne treatment—one that is highly targeted, sustainable, and deeply aligned with the principles of precision medicine [98-100].

Conclusion

Acne remains a prevalent and complex dermatological condition requiring innovative and effective treatment modalities beyond conventional therapies. Emerging nanotechnological approaches offer a paradigm shift in acne management by enabling targeted drug delivery, minimizing side effects, and enhancing treatment efficacy. Nanocarriers such as liposomes, lipid-based nanoparticles, and nanosuspensions have demonstrated considerable potential in preclinical and clinical studies due to their ability to penetrate the skin barrier and deliver therapeutic agents precisely at the site of inflammation. While challenges such as large-scale manufacturing, regulatory approval, and long-term safety remain, the integration of nanotechnology into acne therapy represents a promising frontier. Continued interdisciplinary research and clinical validation are imperative to translate these nanosystems from bench to bedside, ultimately revolutionizing the treatment landscape for acne and related skin disorders.

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Data availability

All data obtained during this study are included in this manuscript.

Ethics approval and consent to participate

Not applicable.

Consent for publication

The work described has not been submitted elsewhere for publication, in whole or in part, and all authors participated in the work and have agreed to the content of the manuscript.

Competing interests

The authors declare that they have no known competing financial interests or personal relationships that could influence the work reported in this study.

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