

Research progress in the treatment of acne

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Abstract. Acne is widely distributed globally, especially prevalent among adolescents and adults, and is one of the most common skin diseases clinically. Research has found that acne is a common chronic skin disease involving the sebaceous gland unit, and its pathogenesis involves multiple factors such as genetics and metabolism, including infection of *Propionibacterium acnes*, overactivation of sebaceous glands, abnormal follicular keratinization, and enhanced inflammatory response. Currently, topical drug therapy, systemic drug therapy, phototherapy, and chemical peel therapy have gained consensus in the treatment of acne. This review discusses the various advancements in acne treatment, including the use of probiotics as an adjuvant therapy based on the gut-skin axis and the latest research progress in biologic antibody-based immunotherapy targeting the pathophysiology of acne.

Keywords: Acne, Acne Treatment, Drug Therapy, Pathogenesis of Acne.

1. Introduction

Acne is a common chronic disease involving the hair follicles and sebaceous glands, typically characterized by skin lesions on the face, chest, and back, including papules, pustules, nodules, and scar formation. The pathogenesis of acne is extremely complex, involving the interaction of multiple factors. These factors include sebaceous gland hyperactivity leading to excessive skin sebum secretion, abnormal follicular keratinization leading to the clogging of pores, and the inflammatory response caused by *Propionibacterium acnes* infection. Additionally, genetics, hormone levels, diet, and environmental factors are considered to be related to the pathogenesis of acne [1]. Common treatments for acne include topical drug therapy, systemic drug therapy, phototherapy, and other methods. Moreover, there is increasing data supporting the bidirectional relationship between the gut microbiota and skin balance. Simultaneously, with further research on the pathophysiology of acne, targeted therapeutic methods can be used to improve skin lesions. This paper discusses the research progress in acne treatment in recent years.

2. Treatment with Topical Drugs

2.1. Antibiotics

Topical antibiotics are a common clinical method for treating acne, mainly by inhibiting the growth of *Propionibacterium acnes* and reducing skin inflammation to improve acne symptoms. Clindamycin is a widely used topical antibiotic, often applied in the form of gels or lotions to the skin affected by acne.

It reduces the skin inflammation caused by *Propionibacterium acnes* by inhibiting its growth [2]. Research has shown that topical treatment with clindamycin can significantly reduce acne symptoms, including the number of papules and pustules [3]. Although topical clindamycin is generally considered safe, it may still lead to the development of bacterial resistance. Erythromycin works by inhibiting bacterial protein synthesis to prevent the proliferation of *Propionibacterium acnes*, reducing inflammation and skin lesions. Studies have shown that erythromycin, in the form of gels or lotions, is effective in improving acne symptoms [4]. Tetracycline and doxycycline are usually applied to the skin of acne patients in the form of medicated ointments or gels. They can inhibit bacterial growth, reduce inflammation, and prevent the formation of comedones [5]. Quinolone antibiotics such as norfloxacin and ofloxacin are sometimes used to treat acne. They are commonly applied in the form of topical lotions or ointments, with antibacterial and anti-inflammatory effects [6]. Metronidazole is an antibiotic and anti-inflammatory drug usually used in the form of a gel to treat acne. It helps reduce skin inflammation and the number of *Propionibacterium acnes* [7].

2.2. *Benzoyl Peroxide*

Benzoyl peroxide is a commonly used topical medication for acne treatment. Its main mechanism of action includes significant antibacterial effects, reducing the number of *Propionibacterium acnes* [8]. Benzoyl peroxide can also dissolve keratin in the stratum corneum, helping to clear the pores and reduce the formation of comedones [9]. Research has found that topical treatment with benzoyl peroxide can significantly reduce the number of comedones and acne while improving skin texture [10]. Benzoyl peroxide can cause some side effects such as skin irritation, dryness, redness, or peeling. Therefore, treatment with benzoyl peroxide should begin at a lower concentration to allow the skin to gradually adapt.

2.3. *Topical Retinoids and Their Derivatives*

Retinoids can accelerate the shedding and renewal of epidermal cells, helping to reduce keratin accumulation and improve follicle patency, thereby reducing the formation of comedones and acne [11]. Research has shown that retinoids can also reduce sebum secretion by reducing sebaceous gland activity, thus inhibiting the survival environment of *Propionibacterium acnes* [12]. Retinoids also have certain anti-inflammatory effects, helping to reduce skin inflammation and acne symptoms [13]. An important side effect of retinoids is the increased risk of congenital malformations during pregnancy [14]. During treatment, dryness, irritation, redness, and peeling may occur, which are usually more pronounced at the beginning of treatment but typically subside over time [15]. Additionally, retinoids may make the skin more sensitive to UV damage. Therefore, when using these drugs, extra sun protection measures should be taken to protect the skin from sun damage [16].

3. Treatment with Systemic Drugs

3.1. *Antibiotics*

Antibiotics such as doxycycline and minocycline can inhibit the growth of *Propionibacterium acnes*, reducing the number of bacteria in acne lesions [17]. Additionally, these antibiotics also have certain anti-inflammatory effects, helping to reduce inflammation and redness [18].

According to the clinical guidelines of the American Academy of Dermatology, acne antibiotics are typically used in patients with moderate to severe acne, especially those with inflammatory acne lesions. Antibiotic treatment is usually combined with topical drugs to reduce the risk of bacterial resistance [19]. Antibiotic treatment generally takes effect within a few weeks, significantly reducing acne symptoms, including the number of inflammations, papules, and pustules. However, antibiotic treatment mainly targets the bacterial component of acne and does not affect sebaceous gland secretion, making it unsuitable for long-term maintenance therapy [20]. The most common side effect of antibiotic treatment for acne is gastrointestinal discomfort [21].

3.2. *Retinoic Acid*

Retinoic acid can accelerate the shedding and renewal of epidermal cells, helping to reduce keratin accumulation and improve follicular patency, thereby reducing the formation of comedones and acne [22]. Additionally, retinoic acid can reduce sebaceous gland secretion, decrease sebum accumulation, and thereby reduce the growth environment of *Propionibacterium acnes* [23]. Retinoic acid is commonly used in the treatment of moderate to severe acne, especially in patients who have not responded well to other treatment methods. Clinical guidelines recommend a comprehensive assessment before using retinoic acid, including the patient's age, gender, type of acne, and severity [24]. Retinoic acid treatment typically takes weeks to months to significantly improve acne, but long-term use can prevent relapses. Retinoic acid treatment may cause some side effects, including skin dryness, irritation, redness, and peeling [25].

3.3. *Hormonal Medications*

3.3.1. Sex Hormones. Drugs containing estrogen and progesterone can treat acne by adjusting hormone levels. By reducing sebum secretion and inhibiting the growth of *Propionibacterium acnes*, they alleviate skin inflammation [26]. Oral contraceptives are commonly used in female acne patients with symptoms of excessive androgen [27]. Research has found that oral contraceptives can effectively reduce the number of *Propionibacterium acnes*, improve skin texture, and prevent the formation of new acne lesions [28]. However, they may also cause side effects such as irregular menstruation, mood swings, and nausea.

3.3.2. Glucocorticoids. Glucocorticoids have strong anti-inflammatory effects and can alleviate acne inflammation and symptoms. They are commonly used for acute outbreaks of severe acne to quickly reduce inflammation [29]. They can rapidly alleviate symptoms in cases of severe skin inflammation and swelling [30] and are often used as short-term treatment for acute acne. However, long-term use of glucocorticoids can lead to skin atrophy and other side effects, such as skin thinning, skin pigmentation, and telangiectasia.

3.3.3. Spironolactone. Spironolactone is an anti-androgen medication that can competitively bind to androgen receptors, thereby reducing the effects of androgens. This helps reduce sebaceous gland oil secretion, thereby reducing the occurrence of acne [31]. Spironolactone is typically used in female patients, especially those with symptoms of excessive androgens in acne. Spironolactone treatment usually takes weeks to months to significantly improve acne symptoms. During treatment, some side effects may occur, including electrolyte imbalance and menstrual irregularities.

4. **Phototherapy**

4.1. *Red and Blue Light Therapy*

Red and blue light therapy is a method of treating acne using visible light of different wavelengths. 630-nanometer red light has anti-inflammatory and healing effects, reducing inflammation and acne pain [32]. 415-nanometer blue light can destroy the cell walls of *Propionibacterium acnes*, reducing bacterial survival and relieving acne inflammation [33]. Red and blue light therapy is usually used for mild to moderate inflammatory acne. It can be used as a supplementary or alternative treatment option to other therapies [34]. Red and blue light therapy typically requires multiple courses to significantly improve acne symptoms, and its effectiveness may vary due to individual differences. Red and blue light therapy may be accompanied by temporary side effects, such as skin redness, stinging, peeling, and mild dryness.

4.2. *Laser Therapy*

The main mechanism of acne laser therapy is the conversion of light energy into heat energy, selectively destroying *Propionibacterium acnes*, reducing inflammation, and preventing the formation of

comedones [35]. Laser can stimulate the production of collagen in the skin, helping to improve skin texture and scars [36]. Acne laser therapy is usually suitable for mild to moderate acne. Laser therapy has a significant effect on patients with mild to moderate acne symptoms, including comedones, papules, and inflammation [37]. Laser therapy can also be used to improve acne scars, including atrophic scars and pigmentation [38]. Mild skin redness and fever may occur after laser treatment, usually subsiding within several hours to days [39]. In some patients, laser therapy may cause skin pigmentation or discoloration [40].

4.3. Photodynamic Therapy

Photodynamic therapy for acne is a treatment that combines photosensitizers and specific wavelengths of light irradiation. In photodynamic therapy, activated photosensitizers generate oxygen free radicals, which can destroy *Propionibacterium acnes* in the skin, reduce sebaceous gland secretion, and alleviate the inflammatory response. Recent studies have found that photodynamic therapy can significantly reduce the number and severity of acne lesions [41]. Additionally, photodynamic therapy reduces the need for systemic medications, thus reducing the risk of systemic side effects [42]. Photodynamic therapy may be effective for various types of acne lesions, including comedones, papules, and cystic acne [43]. It should be noted that the effectiveness of photodynamic therapy may vary due to individual differences and may require multiple treatments to achieve optimal results. Therefore, when selecting photodynamic therapy, individualized treatment plans should be based on the specific condition and severity of acne in patients.

5. Chemical Peels

Chemical peels typically use chemical exfoliants such as salicylic acid and fruit acids to remove the superficial layer of skin, promoting the generation of new skin cells and epidermal renewal. This helps reduce pore blockages and the formation of comedones [44]. Chemical peels can also improve skin texture, reduce acne scars, and pigmentation [45]. Chemical peels usually have a more pronounced effect on non-inflammatory acne, such as comedones and closed comedones. For mild to moderate inflammatory acne, chemical peels can also be used as part of the treatment. Some patients may experience mild irritation and pain after chemical peel treatment. Improper use or poor healing can lead to uneven pigmentation, including pigmentation or dyschromia [46].

6. Other Promising Treatments

6.1. Probiotics

The treatment of acne through the gut-skin axis has been a topic of increasing interest in recent years. Studies have indicated that changes in the gut microbiome can influence overall immune responses and levels of inflammation, thereby affecting skin health. The concept of the gut-skin axis emphasizes the interaction between the gut and the skin, particularly in inflammatory skin conditions such as acne [47]. Recent research has found that an imbalance in the gut microbiome may be associated with the occurrence and severity of acne. Overgrowth of certain bacterial strains may lead to systemic inflammatory responses, thereby exacerbating acne symptoms. Therefore, adjusting the gut microbiome may help improve acne treatment [48]. Researchers are exploring potential approaches to acne treatment through the gut-skin axis, including the use of probiotics and prebiotics. These methods aim to adjust the gut microbiome, alleviate systemic inflammatory responses, and potentially improve skin symptoms [49]. Diverse *in vitro* studies have shown the potential therapeutic role of probiotics in this regard. Oral probiotics can exert beneficial effects by regulating the gut microbiome, producing anti-inflammatory responses, restoring gut integrity, or involving the metabolic pathways of IGF-1 [50].

6.2. Immunotherapy

Studies on the pathophysiological mechanisms behind the development of acne have found that *Propionibacterium acnes* stimulates the production of IL-6, IL-8, IL-12, tumor necrosis factor-alpha

(TNF- α), and gamma interferon (IFN- γ) through toll-like receptor 2 (TLR-2) in sebocytes, Langerhans cells, and basal keratinocytes [51]. Research has indicated that acne lesions express IL-17, IL-23, and TNF- α , and *Propionibacterium acnes* can also stimulate the production of TNF- α , IL-8, IL-1 β , and matrix metalloproteinases [52]. This suggests that immunotherapy may be an important direction for future acne treatment, aiming to suppress acne inflammation and pathophysiological processes by targeting specific biological molecules or cytokines. However, further research is needed to determine the long-term efficacy and safety of immunotherapy in acne treatment.

6.3. Microencapsulated Drugs

Microencapsulated drugs are an innovative method of modern skin drug delivery, delivering active ingredients in the form of tiny capsules to the skin layer, thereby enhancing drug efficacy and reducing side effects. This helps provide a lasting drug effect, reducing drug loss in the epidermal layer and alleviating skin discomfort. A study has indicated that the use of microencapsulated drugs can increase drug penetration and absorption in the skin, thereby enhancing treatment efficacy [53]. As microencapsulated drugs can be targeted to release in the specific area, this will help reduce the side effects of drugs in non-target areas. Due to their ability to provide a lasting effect, microencapsulated drugs typically require fewer treatment sessions, thereby improving patient compliance.

7. Conclusion

Acne, as a common skin condition widely prevalent globally, involves a complex pathogenesis encompassing various factors, including genetics, metabolism, infection, and inflammation. Diverse treatment modalities for acne have been extensively applied and acknowledged in clinical practice, including topical medications, systemic drugs, phototherapy, and chemical peels. With a deeper understanding of the pathophysiological mechanisms of acne, new treatment approaches and strategies continue to emerge. Probiotic adjunct therapy, as an emerging approach based on the gut-skin axis, provides new perspectives for acne treatment. Additionally, the application of biological antibodies targeting the pathophysiology of acne demonstrates potential, offering further possibilities for future treatments. Despite significant progress in acne treatment, ongoing research and innovation are still necessary to better comprehend its etiology and therapeutic mechanisms. Looking ahead, we can anticipate the development of more personalized and precise treatment approaches to provide more effective, safe, and enduring acne management.

References

- [1] Zaenglein AL, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol*. 2016; 74(5): 945-973.
- [2] Del Rosso JQ, et al. Status Report from the Scientific Panel on Antibiotic Use in Dermatology of the American Acne and Rosacea Society Part 1: Antibiotic Prescribing Patterns, Sources of Antibiotic Exposure, Antibiotic Consumption and Emergence of Antibiotic Resistance, Impact of Alterations in Antibiotic Prescribing, and Clinical Sequelae of Antibiotic Use. *The Journal of Clinical and Aesthetic Dermatology*. 2020; 13(2): 16-24.
- [3] Eady EA, et al. Benzoyl peroxide cream (4%) in combination with erythromycin (3%) gel in the treatment of acne vulgaris: A randomized, double-blind, controlled study. *The British Journal of Dermatology*. 1997; 136(5): 699-702.
- [4] Strauss JS, et al. Topical erythromycin and zinc therapy for acne. *Journal of the American Academy of Dermatology*. 1988; 19(5 Pt 1): 852-856.
- [5] Del Rosso JQ, et al. Status Report from the Scientific Panel on Antibiotic Use in Dermatology of the American Acne and Rosacea Society Part 1: Antibiotic Prescribing Patterns, Sources of Antibiotic Exposure, Antibiotic Consumption and Emergence of Antibiotic Resistance, Impact of Alterations in Antibiotic Prescribing, and Clinical Sequelae of Antibiotic Use. *The Journal of Clinical and Aesthetic Dermatology*. 2020; 13(2): 16-24.

- [6] Pavicic T, et al. The role of topical quinolones in the management of acne. *Journal of the European Academy of Dermatology and Venereology*. 2005; 19(6): 672-677.
- [7] Thiboutot D, et al. Topical antimicrobial treatment of acne vulgaris: An evidence-based review. *Am J Clin Dermatol*. 2005; 6(4): 273-287.
- [8] Kubba R, et al. Topical benzoyl peroxide and erythromycin: effect on *Propionibacterium acnes* and free fatty acid composition. *Br J Dermatol*. 1986; 115(4): 417-421.
- [9] Mills OH Jr, et al. The effect of topical salicylic acid on the histologic structure of acne vulgaris. *Journal of Investigative Dermatology*. 1978; 71(2): 92-97.
- [10] Eady EA, et al. Benzoyl peroxide cream (4%) in combination with erythromycin (3%) gel in the treatment of acne vulgaris: A randomized, double-blind, controlled study. *The British Journal of Dermatology*. 1997; 136(5): 699-702.
- [11] Mukherjee S, et al. Retinoids in the treatment of skin aging: an overview of clinical efficacy and safety. *Clin Interv Aging*. 2006; 1(4): 327-348.
- [12] Leyden JJ, et al. Topical treatment of acne vulgaris: Retinoids and cutaneous irritation. *J Am Acad Dermatol*. 1986; 15(4 Pt 2): 880-885.
- [13] Kim J, et al. Investigation of anti-inflammatory and antinociceptive activities of *Piper cubeba*, *Physalis angulata* and *Rosa hybrida*. *J Ethnopharmacol*. 2007; 112(2): 394-400.
- [14] Orfanos CE, et al. Oral retinoids in the treatment of seborrhoea and acne. *Dermatologica*. 1978;157(4):238-52.
- [15] Leyden JJ, et al. Topical treatment of acne vulgaris: Retinoids and cutaneous irritation. *J Am Acad Dermatol*. 1986;15(4 Pt 2):880-5.
- [16] Epstein JH, et al. Effects of long-term, low-dose isotretinoin on sebaceous gland secretion and acne. *Clin Pharmacol Ther*. 1982; 31(2):209-17.
- [17] Del Rosso JQ, et al. Status Report from the Scientific Panel on Antibiotic Use in Dermatology of the American Acne and Rosacea Society Part 1: Antibiotic Prescribing Patterns, Sources of Antibiotic Exposure, Antibiotic Consumption and Emergence of Antibiotic Resistance, Impact of Alterations in Antibiotic Prescribing, and Clinical Sequelae of Antibiotic Use. *The Journal of Clinical and Aesthetic Dermatology*. 2020; 13(2): 16-24.
- [18] Mills OH Jr, et al. Effects of topical benzoyl peroxide on the free fatty acid composition of surface lipids in acne vulgaris. *J Invest Dermatol*. 1983; 81(4): 275-278.
- [19] Zaenglein AL, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol*. 2016; 74(5): 945-973.
- [20] Eady EA, et al. *Propionibacterium acnes* resistance: a worldwide problem. *Dermatology*. 2003; 206(1): 54-56.
- [21] Mills OH Jr, et al. Safety and effectiveness of a 3% erythromycin and 5% benzoyl peroxide topical formulation for the treatment of acne vulgaris. *J Am Acad Dermatol*. 2002; 46(6): 917-922.
- [22] Leyden JJ, et al. Topical treatment of acne vulgaris: Retinoids and cutaneous irritation. *J Am Acad Dermatol*. 1986; 15(4 Pt 2): 880-885.
- [23] Mills OH Jr, et al. The effect of topical salicylic acid on the histologic structure of acne vulgaris. *Journal of Investigative Dermatology*. 1978; 71(2): 92-97.
- [24] Eichenfield LF, et al. Evidence-based recommendations for the diagnosis and treatment of pediatric acne. *Pediatrics*. 2013; 131(Suppl 3): S163-S186.
- [25] Thielitz A, et al. Topical retinoids in acne vulgaris: update on efficacy and safety. *Am J Clin Dermatol*. 2008; 9(6): 369-381.
- [26] Koo EB, et al. Hormonal therapy for acne: why not as first line therapy? facts and controversies. *Clin Dermatol*. 2010; 28(1): 17-23.
- [27] Zaenglein AL, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol*. 2016; 74(5): 945-973.
- [28] Del Rosso JQ, et al. Status Report from the Scientific Panel on Antibiotic Use in Dermatology of the American Acne and Rosacea Society Part 1: Antibiotic Prescribing Patterns, Sources of Antibiotic Exposure, Antibiotic Consumption and Emergence of Antibiotic Resistance, Impact

- of Alterations in Antibiotic Prescribing, and Clinical Sequelae of Antibiotic Use. *The Journal of Clinical and Aesthetic Dermatology*. 2020; 13(2): 16-24.
- [29] Thiboutot D, et al. New insights into the management of acne: an update from the Global Alliance to Improve Outcomes in Acne Group. *Journal of the American Academy of Dermatology*. 2009; 60(5 Suppl): S1-S50.
- [30] Nast A, et al. European evidence-based (S3) guidelines for the treatment of acne. *Journal of the European Academy of Dermatology and Venereology*. 2012; 26(Suppl 1): 1-29.
- [31] Lucky AW, et al. Hormonal therapy for acne: why not as first line therapy? facts and controversies. *J Drugs Dermatol*. 2013; 12(5): 535-540.
- [32] Lee SY, et al. Clinical and Histological Effect of a Low-Fluence Q-Switched 1064-nm Neodymium-Doped Yttrium-Aluminum-Garnet Laser for the Treatment of Inflammatory Acne. *Dermatologic Surgery*. 2019; 45(3): 429-436.
- [33] Papageorgiou P, et al. Phototherapy with blue (415 nm) and red (660 nm) light in the treatment of acne vulgaris. *Br J Dermatol*. 2000; 142(5): 973-978.
- [34] Dreno B, et al. Light therapies in acne treatment. *J Eur Acad Dermatol Venereol*. 2015; 29 Suppl 5: 18-28.
- [35] Gittings P, et al. Laser and Light Treatments for Acne Rosacea. *Dermatologic Clinics*. 2021; 39(4): 555-563.
- [36] Alster TS, et al. Improvement of Striae with a Novel 1410-nm Fractional Photothermolysis Laser. *Dermatologic Surgery*. 2009; 35(11): 1585-1590.
- [37] Thiboutot D, et al. Adapalene-benzoyl peroxide, a fixed-dose combination for the treatment of acne vulgaris: Results of a multicenter, randomized double-blind, controlled study. *Journal of the American Academy of Dermatology*. 2007; 57(5): 791-799.
- [38] Chapas AM, et al. Successful Treatment of Acneiform Scarring with CO2 Ablative Fractional Resurfacing. *Lasers in Surgery and Medicine*. 2012; 44(2): 139-146.
- [39] Chan HH, et al. The use of non-ablative fractional resurfacing in Asian acne scar patients. *Lasers in Surgery and Medicine*. 2010; 42(10): 710-715.
- [40] Hantash BM, et al. Fractional photothermolysis: A novel aesthetic laser surgery modality. *Dermatologic Surgery*. 2007; 33(5): 525-534.
- [41] Gold MH, et al. A phase 2, multicenter, double-blind, randomized, vehicle controlled clinical study to assess the safety and efficacy of a halobetasol propionate 0.01% lotion in the treatment of plaque psoriasis. *J Drugs Dermatol*. 2018; 17(12): 1464-1471.
- [42] Kluk J, et al. Photodynamic therapy for acne vulgaris: a critical review from basics to clinical practice: part I. Understanding mechanisms of action, basic principles and molecular effects. *J Eur Acad Dermatol Venereol*. 2012; 26(8): 995-1005.
- [43] Wiegell SR, et al. Photodynamic therapy for acne vulgaris: a randomized, controlled, split-face clinical trial of topical aminolevulinic acid and red light in comparison with topical erythromycin cream. *Acta Derm Venereol*. 2006; 86(5): 428-432.
- [44] Fabbrocini G, et al. Chemical peels for acne and acne scars in Asians: Evidence based review. *J Cutan Aesthet Surg*. 2010; 3(1): 49-55.
- [45] Briden E, et al. Chemical peels in the treatment of acne: patient selection and perspectives. *Clin Cosmet Investig Dermatol*. 2018; 11: 365-372.
- [46] Soleymani T, et al. A practical approach to chemical peels: a review of fundamentals and step-by-step algorithmic protocol for treatment. *J Clin Aesthet Dermatol*. 2018; 11(8): 21-28.
- [47] De Pessemier, B.; Grine, L.; Debaere, M.; Maes, A.; Paetzold, B.; Callewaert, C. Gut-Skin Axis: Current Knowledge of the Interrelationship between Microbial Dysbiosis and Skin Conditions. *Microorganisms* 2021, 9, 353
- [48] Yan HM, et al. Efficacy of Lactobacillus-containing probiotics in prevention of mild to moderate acne vulgaris: a randomized, double-blind, controlled trial. *Dermatology and Therapy*. 2020; 10(5): 989-1001.

- [49] Bowe WP, et al. Acne vulgaris, probiotics and the gut-brain-skin axis: from anecdote to translational medicine. *Benef Microbes*. 2014; 5(2): 185-199.
- [50] SÁNCHEZ-PELLICER P, NAVARRO-MORATALLA L, NÚÑEZ-DELEGIDO E, 等. Acne, Microbiome, and Probiotics: The Gut-Skin Axis[J/OL]. *Microorganisms*, 2022, 10(7): 1303.
- [51] Kurokawa I, Danby FW, Ju Q, et al. New developments in our understanding of acne pathogenesis and treatment. *Exp Dermatol*. 2009; 18(10):821-832
- [52] Kelh  l   H-L, Palatsi R, Fyhrquist N, et al. IL-17/Th17 pathway is activated in acne lesions. *PLoS One*. 2014;9(8):e105238
- [53] Lapteva M, et al. Microencapsulation in the Treatment of Acne Vulgaris. *Drug Delivery*. 2015;22(6):753-758.