What is new acne?

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Abstract

Acne vulgaris is a multifactorial skin disease, and its pathogenesis includes increased sebum production (hyperseborrhea), hyperkeratosis, proliferation of Cutibacterium acnes (C. acnes) and inflammation. In particular, sebum overproduction is a major concurrent event in the development of acne lesions because sebum serves as a nutrient source for C. acnes, activating toll-like receptors TLR2 and TLR4, leading to the release of proinflammatory cytokines/chemokines such as interleukin-1α (IL-1α), IL-6, IL-8, tumour necrosis factor-α (TNF-α), and adhesion molecule like intercellular adhesion molecule-1. It can also promote hyperkeratinisation, resulting from abnormal keratinisation of infundibular epithelium. Therefore, developing novel cosmetic active for acne, by targeting a diverse range of pathological factors is of particular importance. Pronounced properties of Rhodomyrtus tomentosa through the molecules of interest it contains suggest a path towards developing a novel anti-acne agent. This is the method that Greentech used.

Acne vulgaris is an inflammatory and multifactorial skin disease[1] affecting more than 85% of adolescents and often continuing into adulthood.[2] The majority of epidemiologic studies of acne have focused on adolescents. Those who have studied adult acne reported a higher prevalence of acne among male patients before the age of 16 years, but a higher prevalence among female patients after the age of 23 years. The overall prevalence of acne does decline with age in both sexes, but it is clear that a significant number of individuals experience either a worsening of acne symptoms or fail to experience improvement after the teenaged years.

Moreover, although most epidemiological data in Western countries concern Caucasian skin types, acne is also a significant problem for Asian skin. In fact, in one large intercontinental epidemiological study among women, the prevalence of clinical acne was reported to be similar between geographical zones, 24% in Caucasian, 30% in Asian and 23% in continental Indian women. However, acne type was found to vary between skin subtypes. Asian women were reported to have a higher prevalence of infammatory acne than comedonal acne (20% vs 10%), compared to Caucasian women, for whom comedonal acne was more prevalent (14%) than infammatory acne (10%).[3]

Acne is influenced by the biochemical relationship between them and the pilosebaceous unit. Inflammatory cytokines, chemokines, active oxygen, and zinc are known to be associated with the development of acne. Further, steroid metabolism is known as one of the important factors related to sebum secretion and comedone formation in acne. Other factors including air pollution, aggressive skin care products, medication, mechanical, family factors and, more recently, lifestyle and stress have been suggested as having an impact on acne.[4]

In fact, in recent years, an increasing number of studies indicate a link between skin problems and exposure to airborne pollutants, such as particulate matter (PM), volatile organic compounds, ozone, nitrogen dioxide and sulfur dioxide. As a recent example, NO_2 exposure has been linked to pigment spot formation on cheeks in both Caucasian and Asian women. Yet, few data are available today concerning the prevalence or exacerbation of acne symptoms and pollution exposure.

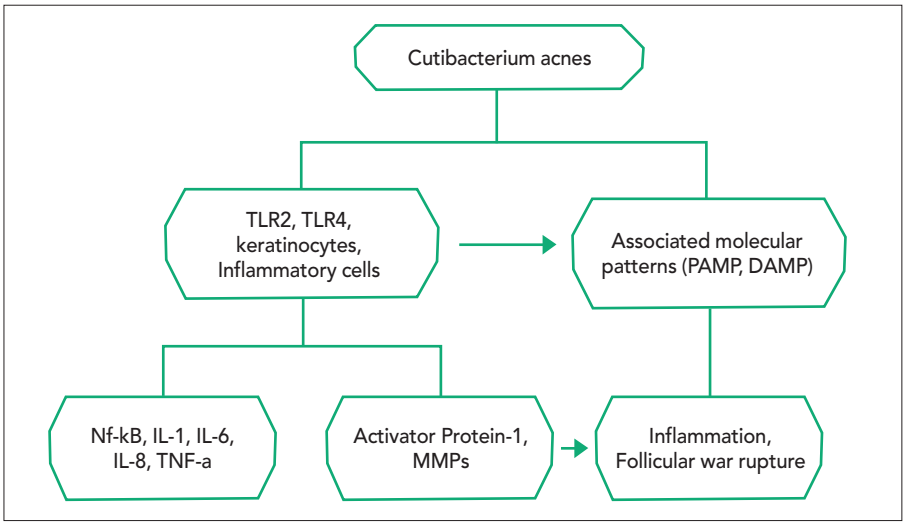

Figure 1: Role of *Cutibacterium acnes* in acne vulgaris (from Bath *et al.* 10)

Moreover, even if for many years nutrition was believed to cause or worsen acne, it has become a dermatological doctrine over recent decades that there is no direct association between diet and acne.[5] Cordain et al. were the first to question this belief, by studying acne-free populations having no hyperglycaemic carbohydrate and no dairy product intake.[6] The authors have shed some new light on this issue through their hypothesis that acne is a typical disease of Western civilisation and thus associated with what we eat. Indeed, ecological studies suggest that the incidence of acne is low in non-Western societies and increases with the adoption of a Western diet, characterised by a high intake of dairy products, hyperglycaemic food and free fatty acids.[7] Thus, modern lifestyle nutrition, obesity and eating disorders also are factors that play a role in the physiopathology of acne. Recent research has focused on the interaction between insulin/insulin growth factor-1 (IGF-1) signalling and the stimulation of sebocyte proliferation and differentiation. Indeed, Growth factors may play an important role in both lipogenesis and inflammation, IGF-1 and insulin having a direct effect on TLRs and innate immunity that is completely independent of *C. acnes* signals.

Concerning the pathophysiology, acne is accepted to have a multifactorial etiology, based on three main observations: increased sebum production (under hormonal stimulation), abnormal keratinisation of the pilosebaceous duct, and it is becoming increasingly evident that acne is driven by an inflammatory reaction to *C. acnes*. Recent research has shed some new light on the involvement of the sebaceous gland, as well as

on the pro-inflammatory activity of the cutaneous microbiome. During puberty, alteration of the sebaceous lipid profile, called dysseborrhoea, stress, irritation, cosmetics and potential dietary factors lead to inflammation and formation of different types of acne lesions. Dysbiosis, the process leading to a disturbed skin barrier and disequilibrium of the cutaneous microbiome, resulting in the proliferation of *C. acnes* strains, is another important process that triggers acne. *C. acnes* releases many enzymes such as proteinases, lipases, hyaluronidases and chemotactic factors that are integral in the inflammatory cascade. It directs immune reactions by modulation of the T helper 1/T helper 2 response and induction of monocyte-derived dendritic cell maturation. *C. acnes* stimulates the host innate immune response by activating toll-like receptors and recognising pathogen-associated molecular patterns (PAMPs).

C. acnes also stimulates inflammasome formation, which are large complexes formed when PAMPs are sensed by DAMP (damage associated molecular patterns) from the host leading to the activation of caspase-1, IL-1β, IL-8 and matrix metalloproteinases (MMPs) resulting in the hyperkeratinisation of the pilosebaceous unit (Fig 1). Rebalancing the natural microbiome of the skin by restoring the natural skin barrier, limiting the proliferation of *C. acnes* on the skin by using topical antibacterials which do not cause resistance and regulating quantity and quality of sebum will be the main acne treatment challenges in the future.[8]

A skin care product dedicated to acne may provide a protective barrier from pollution, restore microbiome balance to prevent over abundant bacteria (including *C. acnes*) colonisation and control disease severity and post-inflammatory pigmentation. Pathophysiology of acne involves three factors, hyperseborrhoea and dysseborrhea, abnormal follicular keratinization and *C. acnes* proliferation in the pilosebaceous unit. Thus, acne requires complete action on all identified targets to achieve the balance of healthy and clear skin. Based on its ethnopharmacology and pharmacognosy knowledges, Greentech Research has focused on *Rhodomyrtus tomentosa* (RT), all parts of this plant (leaves, roots, buds and fruits) being used in traditional Vietnamese, Chinese and Malaysian medicine for long time. Ellagitannins, stilbenes, anthocyanins, flavonols and phenolic acids are the phenolic compounds identified in the fruit. Among them, piceatannol, a stilbene, has biological activities, including antioxidant, anti-inflammatory, anti-microbial properties, and is photoprotective candidate for UV-induced skin damage.[9] RT also contains acylphloroglucinols with rhodomyrtone as the main compound. Rhodomyrtone showed strong antibacterial activity against a wide range of Gram-positive pathogenic bacteria, as well as anti-biofilm property against staphylococci causing severe infections. More specifically rhodomyrtone inhibits *C. acnes* proliferation.[10] In order to highlight multifunctional properties of Acnilys® as anti-acne active ingredient, we developed different cellular models and an *in vivo* study and proved Acnilys efficacy on prevention of hyperseborrhea, limitation of *C. acnes* proliferation and its deleterious effects, and on reduction of inflammation induced by dysseborrhea. Moreover, our active promotes moisturisation and radiance.

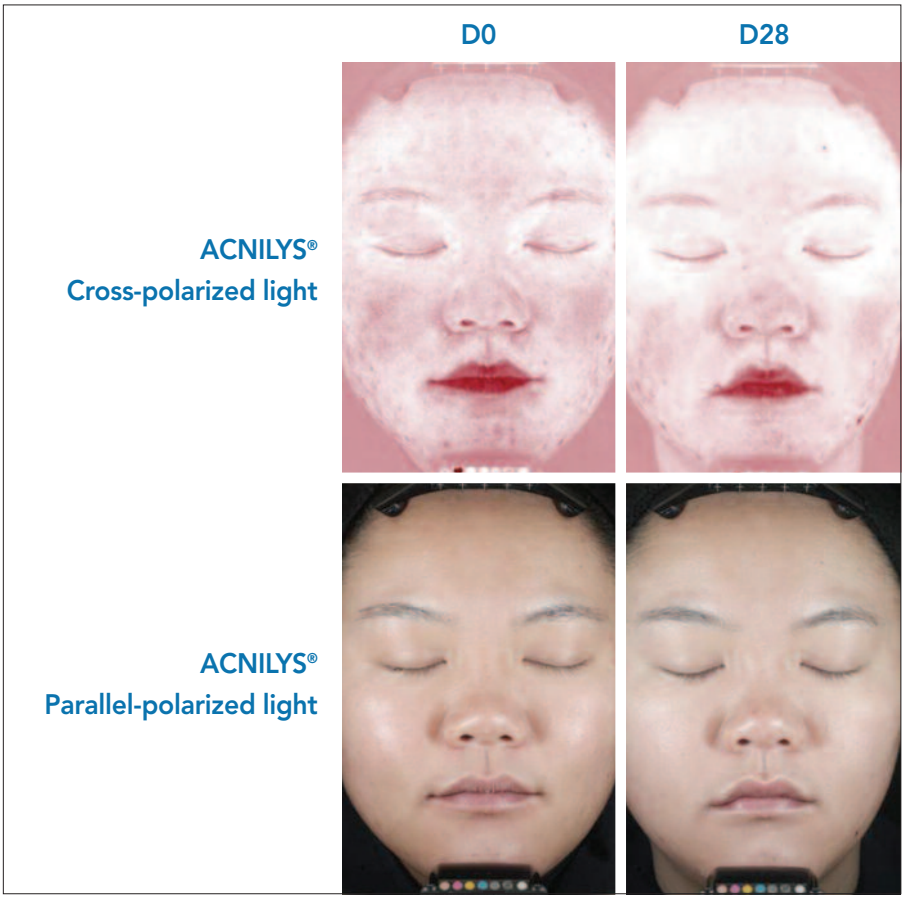

Figure 2: Illustrations of volunteer at D0 and D28.

As shown in Figure 2, cross-polarised light highlights the anti-redness and anti-inflammatory lesions action of Acnilys, the skin is less red and has fewer spots. Parallel-polarised light highlights the anti- sebum action of Acnilys after 28 days of treatment, the skin is less oily, less shiny. To summarise, Acnilys is a multifunctional active, which balances oily, acne-prone and blemish skins.

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