Impure Skin: (Not) a Problem for Mature Skin?
Combating impure skin

■ Impure skin: More than a cosmetic problem

Without doubt impure skin and acne are among the most emotional topics in the cosmetics industry. Those who are afflicted with it are often exposed to severe suffering. It is a major challenge for cosmetic producers to offer efficient cosmetic solutions for this problem. Over decades, cosmetic producers have primarily been devoted to the young target group that suffers from acne during puberty (acne vulgaris). However, acne can occur in almost all age groups. Newborns (acne neonatorum) and small infants (acne infantum), for example, may also be affected by acne. Acne tarda represents a very special area in cosmetics and especially women in menopause may suffer from it. This type of acne in adults is milder than that in adolescents. Nevertheless, it may present a large psychological burden for those concerned, because they had hoped to have overcome such problems after puberty.

A growing number of cosmetic producers is dedicated to this potential group of customers. The reasons for this are obvious: Menopausal acne concerns female consumers who are familiar with applying anti-aging and skin care products and are willing to spend more money for it. The rather moderate form of acne tarda allows producers to offer and market milder products which have a long-term, physiological effect. In contrast to products for adolescents it is easier to create more comprehensive series targeted at this group. Besides inhibiting the formation of dihydrotestosterone, products may refer to other approaches connected with impure skin, including antibacterial, antioxidative or moisturizing effects. In addition, it is possible to incorporate active ingredients which allow anti-aging claims. Many manufacturers have done this for a long time, especially on the U.S. market. The doctor brand »Murad®« advertises an »anti-aging acne« series, Patricia Wexler M. D. offers an »anti-aging cleanser«, »Skin Refinish« (M2) is said to fight skin impurities on the one hand and wrinkles on the other, and Jan Marini Skin Research™ promises to relieve the skin problems of adults which include acne tarda. The renowned US brand proactiv® solution strives to develop the European market for products treating impure skin. The proactiv® brand addresses idols of the younger target group such as US celebrities Justin Bieber and Julianne Hough. Interestingly, celebrities who are older than thirty including Jennifer Love Hewitt and Vanessa Williams are featured in advertisements of proactiv®. In Europe, Susan Sideropoulos (born 1980) and Regina Halmich (born 1976) are featured. German producer Beiersdorf now addresses women who long after puberty still have to fight impure skin with its »Pure Effect« Nivea series.

Abstract

In the past, manufacturers used to tailor cosmetic solutions targeting impure skin and acne mainly to the needs of a young consumer group. However, acne can occur during almost all stages of life, including during menopause. Meanwhile, many cosmetic manufacturers have identified women suffering from so-called menopausal acne as potential customers. Their high purchasing power and their familiarity with the application and price ranges of anti-aging or skin care products offer ample scope for the design of elaborate products. In this article, BASF experts Torsten Clarius, Nabil Abdul-Malak, Corinne Reyermier, Isabelle Bonnet and Boris Vogelgesang introduce innovative cosmetic active ingredient options for the formulation of skin care products that meet the various needs of this particular group of consumers. In the course of this, they analyze the hormonal causes for impure skin in women during menopause and, on the basis of test results, demonstrate in great detail the performance of the cosmetic active ingredients presented.
■ Causes for impure skin and acne

The sebaceous gland discharges into the hair follicle, an elongated invagination on the epidermis, at the end lower of which hair is formed in the hair root. Sebocytes, specific cells in the sebaceous gland, produce sebum, which is pressed in a holocrine secretion into the duct when cells burst and are then pushed onto the skin through the follicle’s exit (Fig. 1) (1). There, sebum spreads in dependence of the skin’s humidity and environmental conditions. The sebum which is produced in the sebaceous glands contains various glycerides, wax ester, cholesterol, free fatty acids and squalene, etc (2).

If too much sebum is produced, conglomerates and comedones may be formed which block the duct. An increase in horny cells (hyperkeratosis) may additionally inhibit the outward flow so that subsequently open and closed comedones are formed. The micromilieu in the comedones and the sebum presents ideal conditions for microorganisms. Propionibacteria release lipases which split fats and release fatty acids which, on the other hand, trigger inflammatory reactions. Chemotactically effective substances such as cytokine IL-1α and reactive oxygen species (ROS) also play a major role in these inflammatory processes.

Generally, acne may occur in all areas of the skin which have many sebaceous glands. For the most part these unfortunately are the areas which are usually not covered by clothing. Thus, the forehead, nose, cheeks, and chin (»t zone«) as well as back, upper arms, legs and scalp may be concerned (3).

Milder forms of acne, including comedonal acne, are suitable for cosmetic treatment. In more serious cases, where, depending on the degree of skin changes and their state of inflammation, papules, pustules and knots are distinguished, cosmetic products may accompany a dermatological therapy. The causes of impure skin are of both extrinsic and intrinsic nature. Environmental factors or bacterial settlement may play a role. Patients who take steroid-containing drugs may be confronted with overly oily skin. Unsuitable cosmetic products can also cause comedones (4,5). Allergies and a hornification disorder of the hair follicle as well as a genetic disposition towards an increased production of sebum are among the intrinsic causes. Nevertheless, it is undisputed that the decisive factor is of hormonal nature (6). Testosterone is metabolized by the 5α-reductase enzyme into a biologically even more effective dihydrotestosterone (DHT), which unfolds its efficacy via the androgenous receptor. DHT has a 50-fold higher affinity to the androgenous re-

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**Fig. 1** Schematic representation of sebum production through activation of the DHT receptor

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**Fig. 2** Measurement of type 1α-reductase gene expression in normal human keratinocytes cultured in monoclayers
Combating impure skin at its peak prior to and during the first months of birth and then drastically decreases, and increases again at the age of eight (8). The hydrophobic character of the sebum certainly increases the impermeability of the skin towards exterior influences. A decreased sebum production is, however, not a physiologic reaction to short-term exogenic circumstances, as the sebum reaches the skin surface only ten days after the synthesis (9).

The role of hormones

In women, the climacteric period starts at approximately the age of 35 and may vary individually. Slowly but steadily, the hormonal balance and the hormone production of the ovaries are reduced until menopause starts between the ages of 40 to 55. The proportion of male hormones (andro gens) is increased in relation to the female hormones; resulting in a relative hyperandrogeny, where the adrenal androgens have no counterparts. As early as at the beginning of the hormonal fluctuations skin changes may appear; as a rule, they appear at the age of 50 when the estrogen levels are significantly reduced. Hair loss may be a consequence; the skin becomes oilier whereas its dryness increases simultaneously. Scientists assume that a major cause for increasing acne in women throughout the past few years is the increasing burden on women by work and the family. Chronic stress leads to a certain level of stress hormones in the body. They have a slight rest androgenic effect and attack the sebaceous glands at the same receptor.

Ways to fight impure skin

By using keratolytic or astringent substances, many cosmetic ingredients which fight impure skin avoid the actual cause of acne. This lies in the hormone-regulated, increased sebum production. The major role here is assumed by DHT which is synthesized in the sebaceous glands by catalysis of the membrane-attached 5α-reductase (10). Another factor is that 5α-reductase occurs in two isoforms and that only 5α-reductase type 1 is responsible for the sebum formation, whereas 5α-reductase type 2 plays a role in hair loss (11). Therefore, the inhibition of 5α-reductase type 1 is the most promising approach to reducing the excess sebum production. However, only few specific inhibitors are known including zinc derivatives which are frequently incorporated in cosmetics. Their efficacy in terms of impure skin seems to be attributable to their anti-inflammatory properties.

Identification of active ingredients via qRT-PCR

Our target was to identify a highly specific inhibitor of 5α-reductase type 1. Therefore, 100 potential candidates for active ingredients were tested on human keratinocyte cultures with the aid of qRT-PCR. The reference substance zinc gluconate reduced the expression of 5α-reductase type 1 gene by 58 % when compared to the untreated control culture (Fig. 2).
The test substance with the best result was N-methylglycine. Mat-XS™ Clinical is a solution of the amino acid N-methylglycine (Fig. 3), which was first identified by German chemist Justus von Liebig as «Sarkosine». N-methylglycine which has a sweet taste occurs as an intermediate step in the choline and glycine metabolisms.

**Ex vivo study**

To prove the postulated effect mechanism, a study was conducted on human skin biopsies where the actual transformation of testosterone into dihydrotestosterone was determined. Here, zinc gluconate also served as reference substance. In the presence of 2% Mat-XS™ Clinical in the culture medium, 36% less DHT was formed (Fig. 4).
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**In vivo studies**

In humans squalene exclusively occurs as a component of sebum. In this way, it may serve as a benchmark for the synthesis activity of sebocytes. Therefore, the squalene content of sebum was measured with Sebutape™ after a 4-week application period in 25 test persons in vivo. In this study, 2 % Mat-XS™ Clinical decreased the squalene content in sebum by 19 % (Fig. 5).

**Multicenter study in Thailand and France**

In order to prove the expected effects of Mat-XS™ Clinical in vivo, a multicenter study was conducted in Bangkok and Bordeaux including a total of 90 test persons with oily skin. The test products, light O/W emulsions, contained either 1 % zinc gluconate or 2 % Mat-XS™ Clinical and were applied twice daily throughout four weeks. The results were evaluated dermatologically and with the aid of digital photos. In addition, the test persons were asked to state their perception in a questionnaire. Almost all test persons (96 %) of the French trial panel confirmed that their skin had a matter appearance (Fig. 6). The same percentage of the panel stated that their skin became oilier more slowly (Fig. 7). 88 % stated a more regular complexion (Fig. 8). The pore size decreased by 20.5 % (Fig. 9). The results obtained from the trial panel with Caucasian skin were comparable with those obtained from the Asian panel and confirm that Mat-XS™ Clinical is an excellent active ingredient for combatting impure skin.

**Inhibition of DHT formation and further suitable approaches**

The oppression of the transformation of testosterone into dihydrotestosterone is the decisive approach to combat skin impurities before and after menopause. However, it becomes possible to develop series of skin care and conditioning products in a more comprehensive way. Mild
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Fig. 9 Clinical evaluation of pore size Caucasian volunteers after 28 days of treatment. Illustrative pictures taken under polarized light.

Fig. 10 Changes in mean improvement of pore density and volume for responding volunteers after 28 days of treatment with 0.4 or 3% Beta-Hydroxyde™ ACSD

Fig. 11 Image analysis of replicas illustrating the best improvement in pore volume and density, before and after 28 days of treatment with Beta-Hydroxyde ACSD™

*, ** significant difference vs. T0; p<0.01 and p<0.001 respectively; Tukey’s test
significant improvement in the skin’s appearance and a decrease in red spots (Fig. 12).

**Summary**

Combating impure skin is a topic which reaches a large number of consumers and which is by no means restricted to adolescent consumers. Thus, women before and during menopause present a target group for the industry who are not only interesting from a cosmetic point of view but also because of their purchasing power. The multitude of causes and accompanying features allow the formulation of care series with a wide spectrum. An extensive range of specific active ingredients which have been tested on large panels is available to support the efficacy of formulations and which help to create products for specific purposes.

**References**

(1) Role of hormones in pilosebaceous unit development, Deplewski D, Rosenfeld RL, Endocrine Reviews, 2000, 21: 363-392.


Fig. 12 Clinical evaluation of the occupation rate of red blotches and their color intensity; digital photos for illustration after 28 days of treatment with Betapur™ 2%