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Treating large pores

Chios mastic to improve oily skin, large pores and acne

KEYWORDS: Impure skin, pores, acne, Chios mastic, sebum, 5α-reductase, skin care.

ABSTRACT

Mastic is the resin harvested from the Pistacia lentiscus trees from the Greek island of Chios. It has been used as a precious natural remedy against various ailments since ancient times. The water-insoluble oleoresin was made available for skin care application by using special extraction techniques. In this form, mastic inhibits the sebum production enhancing enzyme 5α-reductase type I and blocked IL-1α effects in vitro. In clinical studies with volunteers suffering from oily skin, enlarged pores and acne signs it was shown that mastic visibly reduces pore size, shininess and the number of blemishes, which makes mastic an ideal active to treat impure skin.

INTRODUCTION

It is a common misconception that oily and impure skin is a problem that mostly teenagers have to face. In fact, many adults still struggle with skin impurities, or even suffer from new-onset problems long after puberty, which can take a toll on their confidence and emotional well-being. One main cause of these impurities is the overproduction of sebum by sebocytes of sebaceous glands situated in the hair follicles, which leads to a general oily appearance of the skin. Furthermore, high sebum production levels are associated with increased pore size. Obstruction of the sebaceous duct due to high sebum levels and hyperkeratinization leads to comedo formation, which can result in a blackhead if the sebum plug is oxidized or a whitehead/microcyst if the whole canal is closed off by skin cells. Such a blockage can trap bacteria inside the duct, which are able to multiply by feeding off the excess sebum. These bacteria can cause inflammation and may lead to pustules and lesions. Greasy skin, comedones and enlarged pores all contribute to an impure appearance of the skin and share excess sebum production as a common cause.

The main regulator of sebum formation in the sebaceous gland is the hormone dihydrotestosterone (DHT), which is formed through the irreversible reduction of testosterone by the enzyme 5α-reductase (1). There are three isoforms of 5α-reductase (type I, II and III), with 5α-reductase type I being the isoform responsible for sebum production and the major isoform expressed in skin cells, especially in the sebocytes of the sebaceous glands (2). DHT binds to the same androgen receptor as testosterone but it possesses an up to ten times higher receptor binding affinity and potency for transcriptional activation of target genes that lead to sebocyte differentiation and sebum production (3). Therefore, preventing DHT generation by inhibiting 5α-reductase type I results in reduced sebum production and clearer skin.

An extract of *Pistacia lentiscus* resin to treat impure skin

Pistacia lentiscus is a tree from the cashew family, growing in dry areas of Mediterranean Europe. Its resin, called mastic, is only harvested from the southern part of the Greek island of Chios. Mastic is an oleoresin, a mix of essential oils and resin, which are in turn mainly composed of monoterpenes and triterpenes, respectively. Particular environmental factors in Chios, such as soil and climate, led to *Pistacia lentiscus var. chia* trees that are able to produce more resin than trees growing elsewhere. For harvesting, the resin is produced in an environmentally friendly way by scratching the surface of the trunk and main branches, which leads to teardrop-shaped secretion of mastic, fittingly called "tears of Chios" in Greece. Once solidified, the resin can be washed and collected (Figure 1). The UNESCO has recognized the tradition and know-how of cultivating mastic in a sustainable way by adding it to their "List of Intangible Cultural Heritage" in 2014. Since ancient times, mastic has been used for a plethora of medical applications such as chewing gum with antiplaque effects, against digestive disorders, bronchitis, snakebite, and skin lesions due to its antiseptic qualities. It was in great demand and therefore worth its weight in gold. In modern times, studies confirmed the antibacterial and anti-inflammatory properties of *Pistacia lentiscus* resin as well as unveiled its antioxidant and anti-cancer capacities (4). The antibacterial and anti-inflammatory properties already indicate its potential for the treatment of oily and impure skin. It is further known that the mastic resin has an astringent effect which is the reason for its use in wound healing (5). This astringent activity may also help to shrink pores.

Figure 1. Dried mastic resin.

MATERIALS AND METHODS

Preparation of mastic extracts

To render the water-insoluble mastic useable for skin care application, it was homogenized in glycerine, alcohol and lecithin. In this manner, mastic was stabilized in liposomes (PoreAway, INCI: Pistacia Lentiscus Gum/Pistacia Lentiscus (Mastic) Gum (and) Lecithin (and) Glycerin (and) Alcohol

(and) Aqua/Water). For an alcohol-free version, the mastic resin was first dissolved in an oil phase and then homogenized into a water phase using hydrogenated lecithin (PoreAway oA, INCI: Pistacia Lentiscus Gum / Pistacia Lentiscus (Mastic) Gum (and) Hydrogenated Lecithin (and) Phenethyl Alcohol (and) Ethylhexylglycerin (and) Caprylic / Capric Triglyceride (and) Aqua / Water).

Analysis of 5α-reductase activity
Cell extracts from HEK293 cells stably expressing 5α-reductase type I were added to the steroid hormone androstenedione. The reduction of androstenedione to androstanediol in presence of different concentrations of mastic liposomes was detected via liquid chromatography followed by mass spectrometry.

Analysis of cytokine release by IL-1α-stimulated keratinocytes
Normal human epidermal keratinocytes (NHEK) were treated or not (control) with the mastic nanoemulsion and pre-incubated for 24 hours. After pre-incubation, the medium was removed and replaced with culture medium containing or not (control) the mastic nanoemulsion and the inflammation inducer IL-1α at 10 ng/ml. The cells were incubated for 48 hours. A control without inducer (non-stimulated control) was performed in parallel. The release of the inflammation mediator CCL20 was quantified by ELISA.

Clinical study to evaluate pore size
To test the effect of mastic on pore size in vivo, a double-blind clinical trial was performed with 20 healthy Caucasian volunteers (average age 43) with enlarged pores on the cheeks, as assessed by a dermatologist. They applied a placebo cream on one side and the same cream containing 2% mastic liposomes on the other side of the face twice daily for 28 days. Silicon imprints of the test areas were taken before as well as after 14 and 28 days of treatment, which were then analyzed by Primos 5.7 high-res (GFMesstechnik GmbH, Teltow, Germany). The changes of pores were evaluated in two different ways: the refinement of pores was approximated by the assessment of the general roughness of skin, which was caused by the dilatation of the pores. Additionally, the total pore area was determined by filtering the datasets to separate point-shaped structures of extreme depth (pores) from the ground structure.

Clinical study to analyze shininess and acne lesions
For this double-blind clinical trial, 44 volunteers (Thai, female, 30 to 52 y) with oily skin and visible comedones on their face were split into two groups and either applied a placebo cream or the same cream containing 2% mastic liposomes twice daily on their face for 28 days. Macrophotographs of the faces were taken before and after treatment to evaluate the anti-comedogenic and mattifying effect. Blackheads and microcysts were counted on four different facial zones (forehead, temples, cheeks, chin) and the shininess of the skin was evaluated by a clinician.

Clinical study to analyze pores, sebum production and moisture
A double-blind clinical trial was performed in Seoul, South Korea with 23 healthy volunteers (Korean, female, 21 to 48 y) with oily skin and enlarged pores on the cheeks. They applied a placebo cream on one side and the same cream containing 2% mastic nanoemulsion on the other side of the face twice daily for 14 days. Skin parameters were measured before as well as after 1 and 2 weeks of treatment. Pore number and size were analyzed using the ANTERA 3D® CS camera system (Miravex Limited, Ireland). Production of sebum was measured with the Sebumeter® SM810 (Courage + Khazaka, Germany) and skin hydration with the Corneometer® CM825 (Courage + Khazaka, Germany).

RESULTS

Inhibition of 5α-reductase type I
To assess a possible direct inhibitory effect of mastic liposomes on 5α-reductase type I, a cell-free assay system was used. As expected, 5α-reductase type I was enzymatically active and catalyzed androstenedione reduction. However, when different amounts of mastic liposomes were added, this inhibited 5α-reductase type I activity in a concentration-dependent manner (Figure 2). Furthermore, the half maximal inhibitory concentration (IC_{50}) was determined in this assay, which represents the concentration that is required for 50% enzymatic activity inhibition in vitro. Mastic liposomes possess an IC_{50} value of 274 µg/ml. For the first time we could demonstrate an inhibition of the enzyme 5α-reductase type I, a well-known etiologic factor for oily skin, by mastic resin.

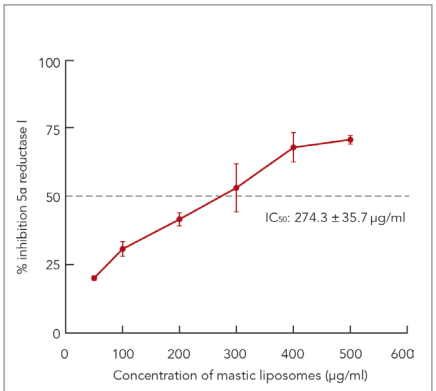

Figure 2. Inhibition of 5α-reductase type I activity by mastic liposomes and determination of the IC_{50} value.

Inhibition of inflammatory reaction
Increased sebum production can lead to the formation of comedones and then to the colonization by *Cutibacterium acnes* which causes an immune response leading to an inflammatory reaction. To assess a possible anti-inflammatory effect of the mastic resin, the mastic nanoemulsion was tested in a cell culture assay with primary human keratinocytes. After stimulation with the inflammation-inducing IL-1α, the treated keratinocytes showed a clear concentration-dependent reduction in the release of the chemokine CCL20 (Figure 3). Inhibition of CCL20 release indicates a direct role of the mastic resin in reducing acne. CCL20 was found to be upregulated after skin barrier disruption and during inflammatory skin conditions but it was also shown to be involved in the inflammatory pathway typical for acne lesions (6, 7).

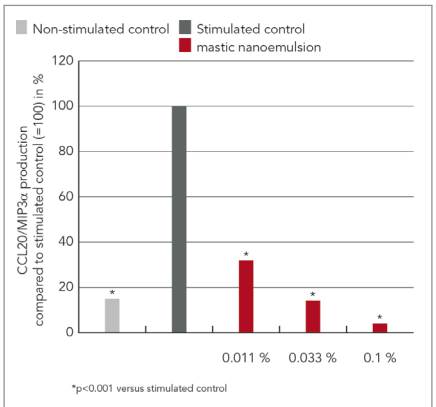

Figure 3. Inhibition of the release of the inflammation mediator CCL20 by the mastic nanoemulsion.

Reduction of pore size, shininess and acne lesions
Since mastic liposomes were able to inhibit 5α-reductase type I, the enzyme responsible for DHT formation, it would suggest

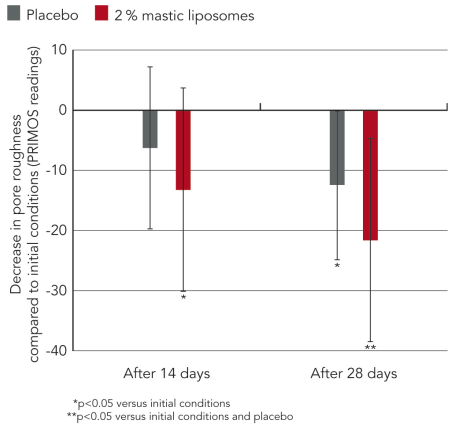

Figure 4. Pore refinement after treatment with placebo cream or a cream containing 2% mastic liposomes. The data represent mean ± standard deviation.

that application of mastic liposomes in vivo would lead to decreased sebum production. A reduction of sebum could in turn decrease the occurrence of comedones and minimize pore size. Treatment of the skin with a cream containing 2% mastic liposomes led to a significant pore refinement. Compared to initial conditions, pore roughness was reduced by more than 8% after 14 days and almost 15% after 28 days (Figure 4). A refining effect was observed in 95% of volunteers. Pore size was significantly reduced by more than 6% compared to initial conditions. A reduction of total pore area was observed in 75% of the volunteers.

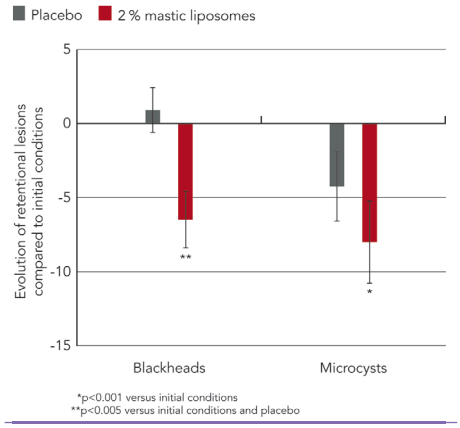

Figure 5. Evaluation of blackhead and microcyst occurrence compared to initial conditions after 28 days of treatment with 2% mastic liposomes. The data represent mean number of lesions ± standard error of the mean.

After having established the pore size reduction effect of mastic, a second double-blind clinical study was carried out to specifically investigate how this resin affects comedo formation and shininess of the skin. A strong decrease of blackheads and microcysts compared to initial conditions was observed for volunteers using mastic liposomes, with a reduction of almost 40% and almost 30%, respectively (Figure 5). Additionally, 32% of the volunteers treated with mastic exhibited a visible reduction in shininess whereas the volunteers treated with the placebo didn't show any visible net reduction in shininess. The mattifying effect of mastic liposomes was also confirmed by self-evaluation of the volunteers, where 95% found their skin less oily and noticed a general improvement of their skin quality. Furthermore, the macrophotographs also revealed a remarkable mattifying and pore refining effect (Figure 6).

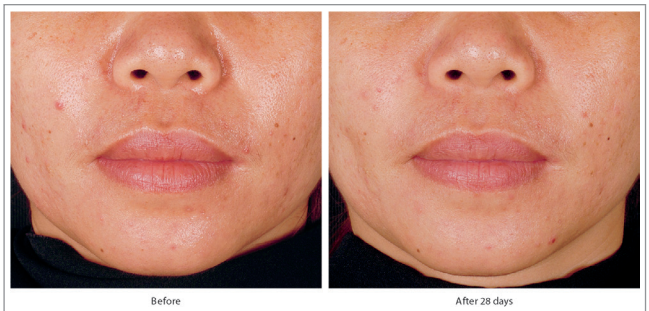

Figure 6. Macrophotograph of a volunteer before and after 28 days treatment with 2% mastic liposomes.

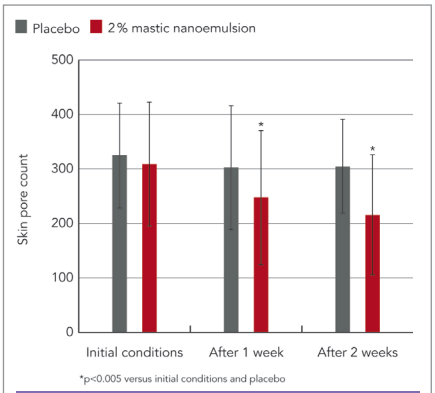

Figure 7. Reduction of pore count after treatment with a cream containing 2% mastic nanoemulsion. The data represent mean ± standard deviation.

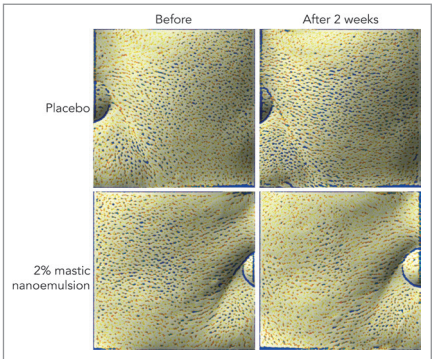

Figure 8. Skin profile images of a volunteer before and after 14 days treatment with 2% mastic nanoemulsion.

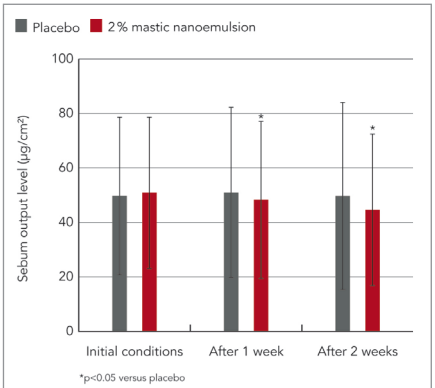

Figure 9. Inhibition of sebum production after treatment with a cream containing 2% mastic nanoemulsion. The data represent mean ± standard deviation.

Decrease in signs of oily skin and nonetheless increase in moisture

With the mastic nanoemulsion a new clinical study on oily Asian skin was performed in Seoul, South Korea. A cream containing 2% mastic nanoemulsion was applied over 2 weeks. Compared to the placebo treatment there was a significant reduction in pore number (Figure 7) and size (result not shown) already after one week treatment with the mastic cream.
A special LED camera was used to analyze skin topography. The images nicely reflect the measured values (Figure 8). Sebum measurements on the cheeks showed a significant placebo-controlled reduction already after one week and more pronounced after two weeks (Figure 9).

Although there was less sebum produced, skin hydration was significantly improved (Figure 10).
The reason for the development of a nanoemulsion version, in addition to the mastic liposomes, was to have an ethanol-free version because ethanol could lead to irritated, dry skin. As the mastic extract is intended to reduce sebum production, a more dry skin could be expected.
But although the nanoemulsion clearly reduced sebum production, it turned out to also improve skin moisture.

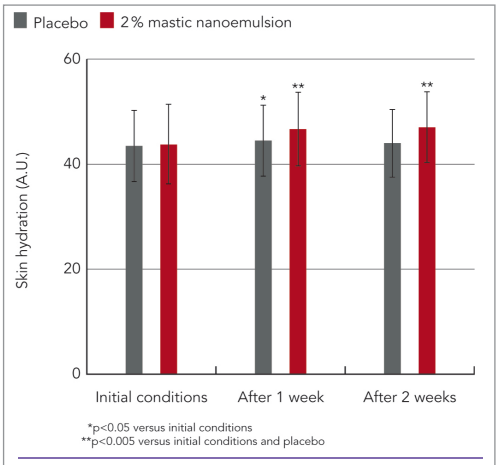

Figure 10. Increase in skin hydration after treatment with a cream containing 2% mastic nanoemulsion. The data represent mean ± standard deviation.

CONCLUSIONS

The resin of the *Pistacia lentiscus* tree, called mastic, possesses various antibacterial, anti-inflammatory and astringent activities, which have been used since ancient times. Extracts of the mastic resin were able to inhibit 5α-reductase type I and to block the inflammatory reaction in acne lesions. Furthermore, clinical studies showed that mastic is able to reduce pore size, shininess, and skin impurities, leading to a visible improvement of overall skin quality. This demonstrates that this new active is efficient in the treatment of blemished, shiny skin and enlarged pores.

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ABOUT THE AUTHOR

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NEWS

TONY O'LENICK: 30 YEARS IN SILTECH, 40 YEARS IN THE PERSONAL CARE SCIENCE

After 30 years of service to **Siltech** and the personal care industry Mr. Tony O'Lenick has decided to retire. He leaves a legacy of having contributed to the expanded use of silicones in various personal care applications. Tony is also responsible for teaching many new personal care formulators how to capitalize on the many benefits of silicones via his numerous educational pursuits, including several publications, volunteer efforts for the SCC and IFSCC and countless speaking engagements.

For the past 20 years Tony served as the President of Siltech LLC, a subsidiary of Siltech Corporation, and the designated distributor for Siltech's products in the US Personal Care market. He has been instrumental in expanding Siltech's customer base among key users of specialty silicones and this is especially impressive given that Tony O'Lenick was Siltech LLC's only employee. We wish him all the best in his retirement and know that he will enjoy more time with his family and eight grandchildren.

NEWS