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Mastic liposome treatment for shiny and impure skin

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 stabilising it in a liposomal preparation. In this form, mastic inhibits the sebum production enhancing enzyme 5α-reductase type I *in vitro*. In clinical studies with volunteers suffering from oily skin and impurities 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.

Figure 1: *Dried mastic resin.*

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,[1] which can take a toll on their confidence and emotional wellbeing. 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.[2] Obstruction of the sebaceous duct due to high sebum levels and hyperkeratinisation leads to comedo formation, which can result in a blackhead if the sebum plug is oxidised 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.

So what causes increased sebum production in the first place? 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.[3] 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.[4] 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.[5] Therefore, preventing DHT generation by inhibiting 5α-reductase type I results in reduced sebum production and clearer skin.

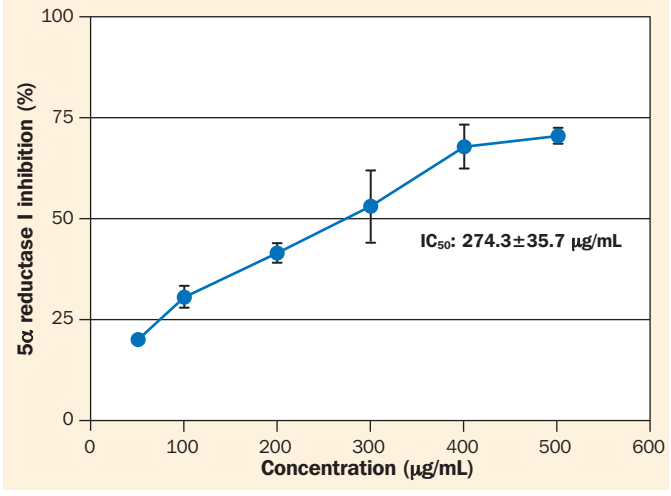

Figure 2: *Inhibition of 5α-reductase type I activity by mastic liposomes and determination of the IC_{50} value.*

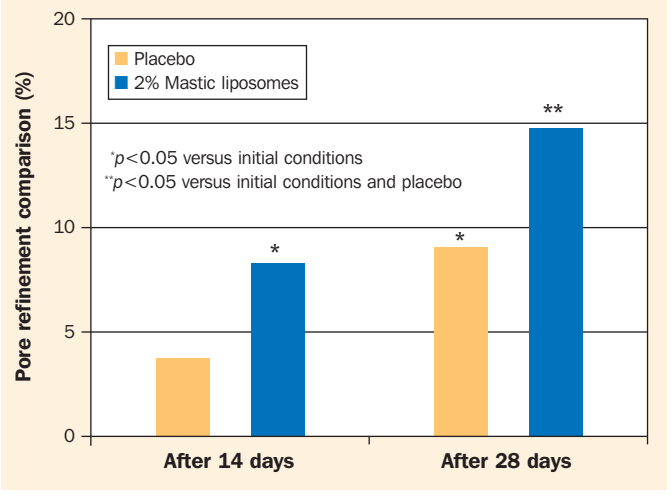

Figure 3: *Pore refinement after treatment with placebo cream or a cream containing 2% mastic liposomes.*

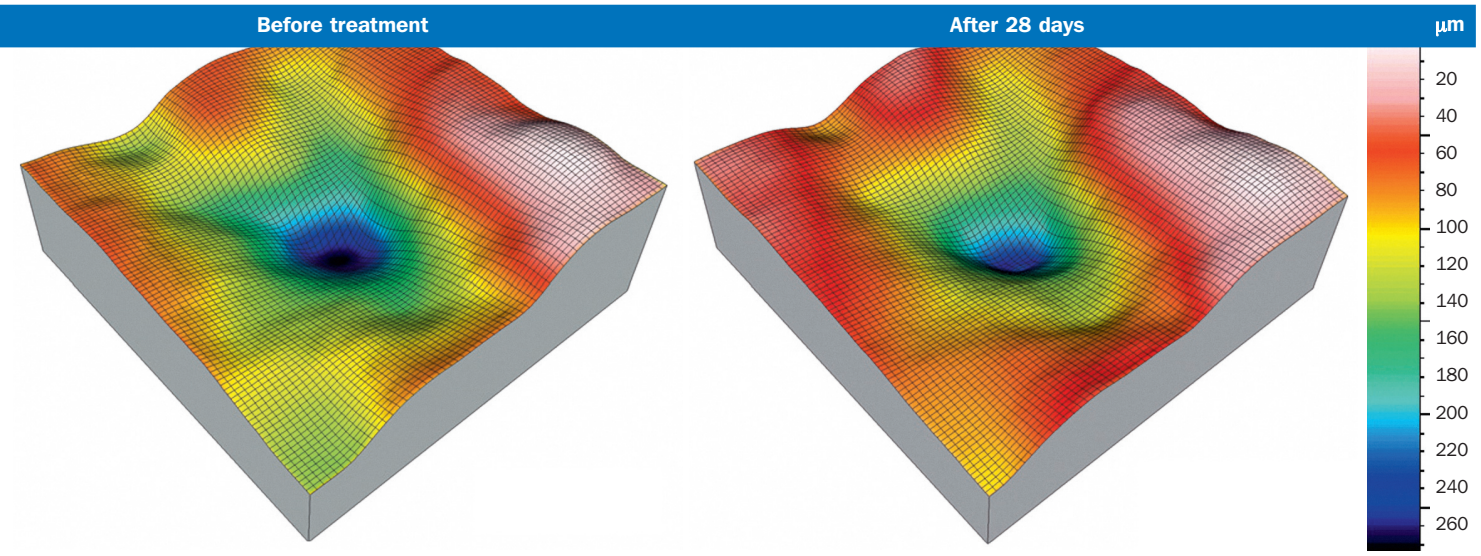

Figure 4: *Reduction of pore size opening after 28 days' treatment with 2% mastic liposomes.*

A new active based on *Pistacia lentiscus* gum 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. 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 (Fig. 1). UNESCO has recognised 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 and for filling dental cavities, 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* gum as well as unveiled its antioxidant and anti-cancer capacities.[6]

Mastic is an oleoresin, a mix of essential oils and resin, which are in turn mainly composed of monoterpenes and triterpenes, respectively. To render the water-insoluble mastic useable for skin care application, it was homogenised in glycerine, alcohol and lecithin. In this manner, mastic was stabilised in liposomes (PoreAway/INCI Name: Pistacia Lentiscus Gum/Pistacia Lentiscus (Mastic) Gum (and) Lecithin (and) Glycerin (and) Alcohol (and) Aqua/Water).

Results and discussion

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. For this, cell extracts from HEK293 cells stably expressing 5α-reductase type I were added to the steroid hormone androstenedione. The reduction of androstenedione to 5α-androstenedione was detected via liquid chromatography followed by mass spectrometry.

As expected, 5α-reductase type I was enzymatically active and catalysed androstenedione reduction. However, when different amounts of mastic liposomes were added, this inhibited 5α-reductase type I activity in a concentration-dependent manner (Fig. 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.

Reduction of pore size

Since mastic liposomes were able to inhibit 5α-reductase type I, the enzyme responsible for DHT formation, it would suggest 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 minimise pore size.

To test the effect of mastic on pore size *in vivo*, a double-blind clinical trial was performed with 20 healthy 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 analysed by Primos 5.7 high-res (GFMesstechnik GmbH, Teltow, Germany). The changes of pores were evaluated in

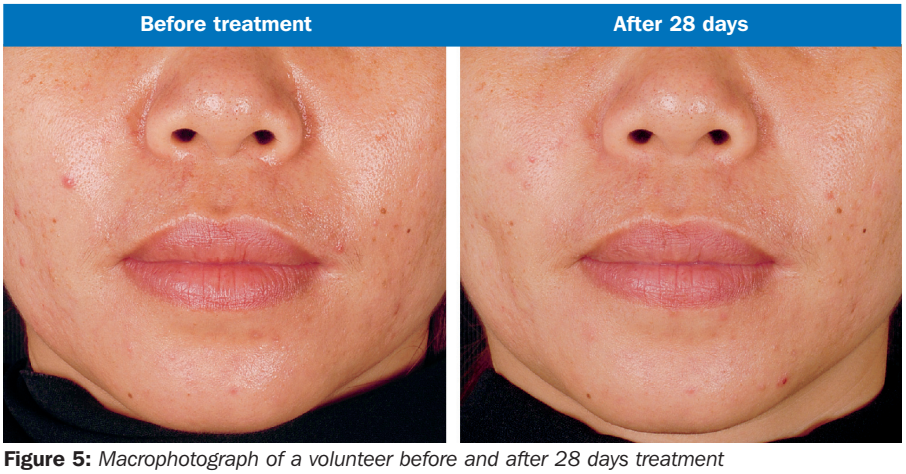

Figure 5: *Macrophotograph of a volunteer before and after 28 days treatment with 2% mastic liposomes.*

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.

Mastic liposome treatment led to a significant pore refinement of more than 8% after 14 days and almost 15% after 28 days (Fig. 3). A refining effect was observed in 95% of volunteers. Pore size was significantly reduced by more than 6% compared to initial conditions (Fig. 4). A reduction of total pore area was observed in 75% of the volunteers.

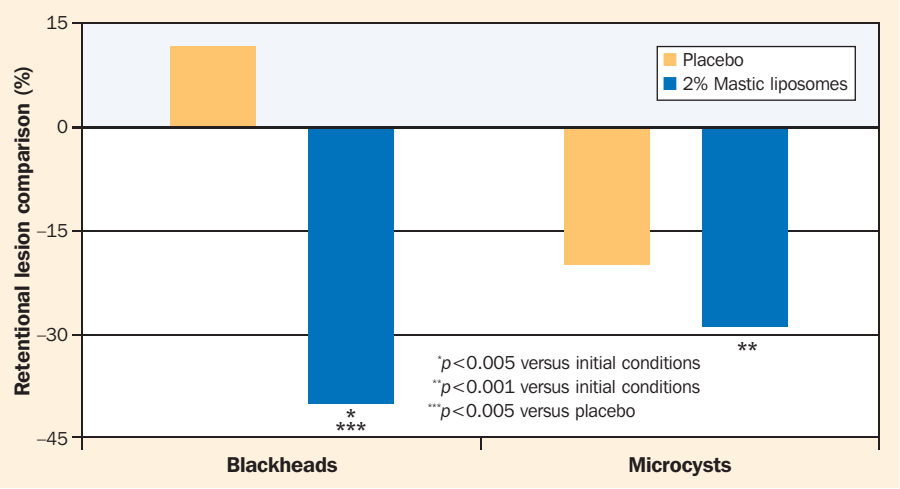

Figure 6: *Evaluation of blackhead and microcyst occurrence compared to initial conditions after 28 days of treatment.*

Reduction of shininess and imperfections

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. For this, 44 volunteers (Thai, female, 30 to 52 years old) 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 (Fig. 5). 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.

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 (Fig. 6). Additionally, 32% of the volunteers treated with mastic compared to placebo exhibited a visible 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 (Fig. 7).

Figure 7: *Macrophotographs of two volunteers before and after treatment with a cream containing 2% mastic liposomes for 28 days.*

Conclusion

The resin of the *Pistacia lentiscus* tree, called mastic, possesses various antioxidant and anti-inflammatory activities, which have been used since ancient times. A liposomal formulation containing mastic was able to inhibit 5α-reductase type I *in vitro*, the enzyme responsible for sebum production in the skin. 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 proves that this new active is efficient in the treatment of blemished, shiny skin and enlarged pores. PC

References

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