

Amaretine® Actives

**NEW**

Bitter-Sweet Synergy for  
Sensitive Skin



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We make beauty natural.

## At a Glance | Amaretine® – Bitter-Sweet Synergy for Sensitive Skin

Sensitive skin, which typically presents as dryness, redness, itching, and an overall sensory discomfort is a sign of an impaired epidermal skin barrier and ongoing inflammatory processes. It is one of the top skin care concerns among consumers worldwide, thus creating a sizable demand for products that minimize skin sensitivity.

With Amaretine®, Lipoid Kosmetik presents the first active ingredient to combine a bitter and a sweet component, in order to synergistically address the symptoms of sensitive skin. The bitter component andrographolide, from the plant 'King of Bitters', specifically binds to bitter receptors in the skin. Bitter receptors are novel and promising targets for skin care as

their activation triggers the regeneration of skin barrier lipids. The sweet component glycyrrhetic acid, derived from licorice roots, is an excellent anti-inflammatory agent. The combination of a bitter component, triggering a novel pathway, with a sweet component, well-known to combat inflammation, makes Amaretine® a unique and innovative skin care active for the cosmetic treatment of sensitive skin.

Taken together, Amaretine® is a COSMOS-approved bitter and sweet complex embedded in a liposomal carrier system. It regenerates an impaired skin barrier, counteracts inflammation and sensory discomfort, and thus offers a unique and all-encompassing approach to the treatment of sensitive skin.

ACTIVE INGREDIENTS	PROVEN EFFICACY	USER BENEFITS
<ul style="list-style-type: none"> <li>• Andrographolide from 'King of Bitters' – activator of barrier lipid production</li> <li>• Glycyrrhetic acid from licorice roots – suppressor of inflammation</li> <li>• Liposomal carrier system – dermal penetration enhancer</li> </ul>	<p><i>in vitro</i></p> <ul style="list-style-type: none"> <li>• Bitter receptor restoration</li> <li>• Rebalancing of atopic skin gene expression</li> </ul> <p><i>in vivo</i></p> <ul style="list-style-type: none"> <li>• Regeneration of skin barrier and redness protection</li> </ul> <p><b>Consumer study</b></p> <ul style="list-style-type: none"> <li>• Relief of sensitive skin</li> </ul>	<ul style="list-style-type: none"> <li>• Strengthening of epidermal barrier</li> <li>• Reduction of inflammatory processes</li> <li>• Alleviation of unpleasant skin sensations</li> <li>• Improvement of skin sensitivity and quality of life</li> </ul>

### Product Details

Amaretine® combines bitter and sweet components for sensitive skin: Bitter andrographolide from *Andrographis paniculata* leaves and sweet glycyrrhetic acid from *Glycyrrhiza glabra* roots activate the skin's bitter receptors and reduce inflammatory responses. The active components are encapsulated in a liposomal carrier system and embedded in propylene-glycolic aqueous matrix of natural origin. COSMOS-approved, preservative-free/ self-preserving.



## Sensitive Skin – A Global Concern and Growing Market

Skin sensitivity is a top skin care concern among consumers globally. Overall, 60–70 % of women and 50–60 % of men report having some degree of sensitive skin, creating a sizable demand for products designed to minimize skin sensitivity <sup>[1]</sup>.

Affected people suffer not only from characteristic sensory perceptions, but also from lower self-confidence due to esthetic concerns relating to skin appearance, often accompanied by the occurrence of anxiety about the recurrence of sensitive skin conditions, finally affecting their quality of life <sup>[2]</sup>.

Therefore, increasing awareness of sensitive skin is changing the beauty industry. According to a Mintel database search, the number of products with sensitive skin claims has increased by 23 % in 2021 alone and by 44 % since 2017. Sensitive skin claims are used across several categories and product formats. The top category with the greatest number of sensitive skin product launches (July 2017 - June 2022) is 'skin care' with the subcategories 'face/neck care' (20 %), followed by 'color cosmetics' (11 %), and 'body care products' (9 %). Thus, sensitive skin claims will show further gains across the globe in major Asian, European, and US skin care markets in the future.



*Fig. 1: Sensitive skin is a major concern and a perfect target for the cosmetic industry. Consumers worldwide are affected by sensitive skin, which typically presents as dryness, redness and unpleasant skin sensations. Cosmetic concepts need to target these aspects to provide an all-encompassing solution.*

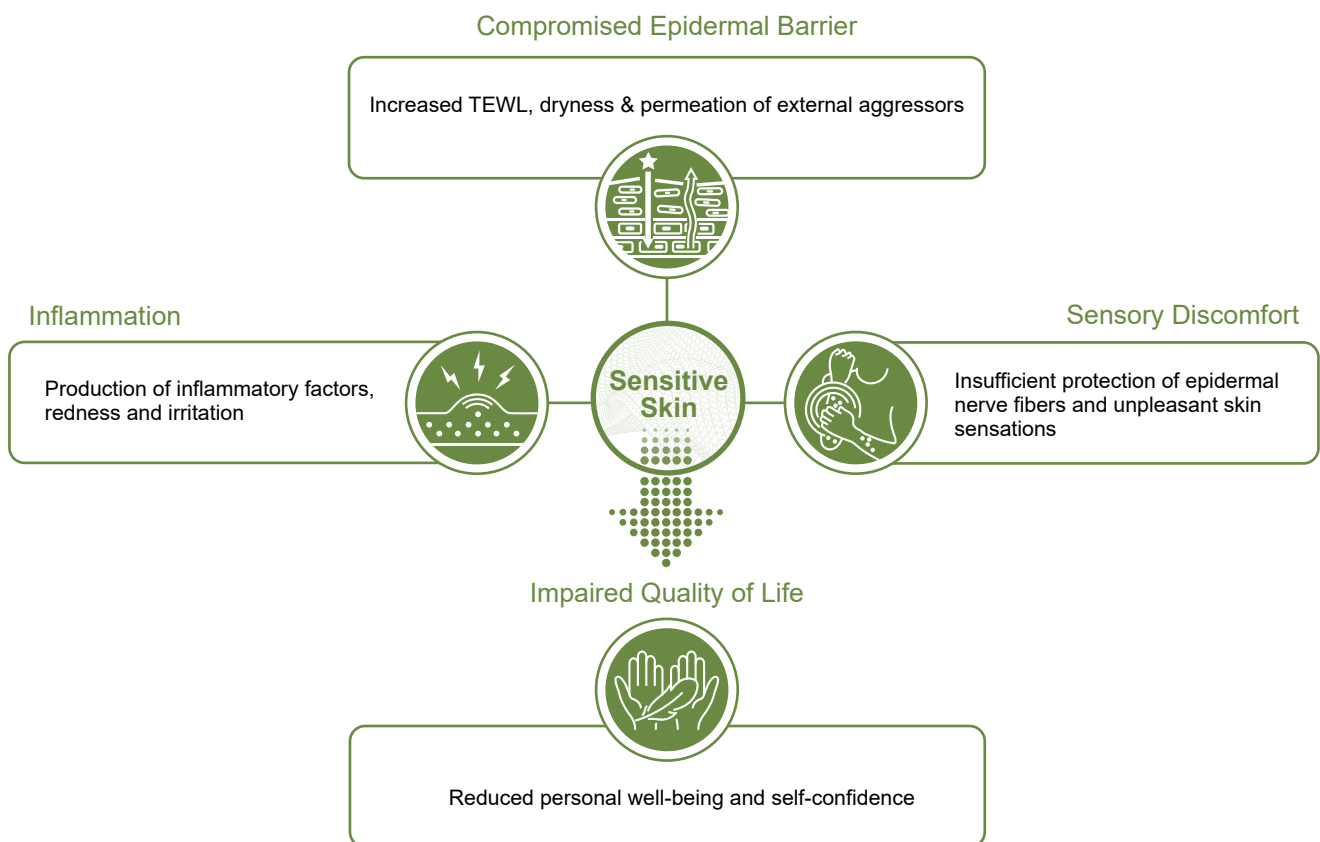
## Sensitive Skin – Diverse Symptoms with an Impact on the Quality of Life

Sensitive skin is typically described as skin with regular occurrences of unpleasant sensations, such as stinging, burning, or itching but also as skin with visible changes, like redness, dryness, scaling, bumps or hives, all caused by forms of stimulation that would not normally create this type of reaction<sup>[1]</sup>. Sensitive skin does not have the same consequences for everyone. Its severity can range from moderate discomfort to severe reactions. Its frequency can fluctuate from occasional flare-ups to more persistent, daily sensitivity. Its underlying cause can range from genetic predisposition to physical, environmental, or chemical stimuli or even overuse of cosmetics<sup>[3]</sup>.

Nevertheless, sensitive skin usually presents with the following characteristics: a compromised epidermal barrier, inflammation, and sensory discomfort. A weak epidermal skin barrier allows the penetration of external irritants, it increases trans-epidermal water loss (TEWL), causing dryness. It is often associated with a disruption of intercellular skin lipids<sup>[3]</sup>.

Sensitive skin is also characterized by inflammatory processes, which go hand-in-hand with the production and release of several pro-inflammatory factors<sup>[1]</sup>. As a result, most people with sensitive skin have to deal with some degree of redness and unpleasant skin sensations. Summarized under the term sensory discomfort, these skin reactions are typically associated with an over-stimulation of epidermal nerve fibers and sensory receptors<sup>[1]</sup>.

Sensitive skin with its various symptoms can significantly influence the quality of life of affected people, which goes beyond simple skin health or esthetics but highlights the overall mental status and well-being of an individual. Hence, to provide an effective and all-encompassing solution, cosmetic strategies for sensitive skin must address all aspects of this condition (Fig. 2). First, the skin barrier requires strengthening and secondly, inflammatory processes must be reduced. These changes then alleviate unpleasant skin sensations and improve overall skin sensitivity and quality of life.



**Fig. 2: Sensitive skin – a few key elements are always present.** Sensitive skin is usually associated with a compromised skin barrier, inflammation, and sensory discomfort. Together, these factors negatively impact the quality of life, which is why they should all be addressed with effective cosmetic treatment.



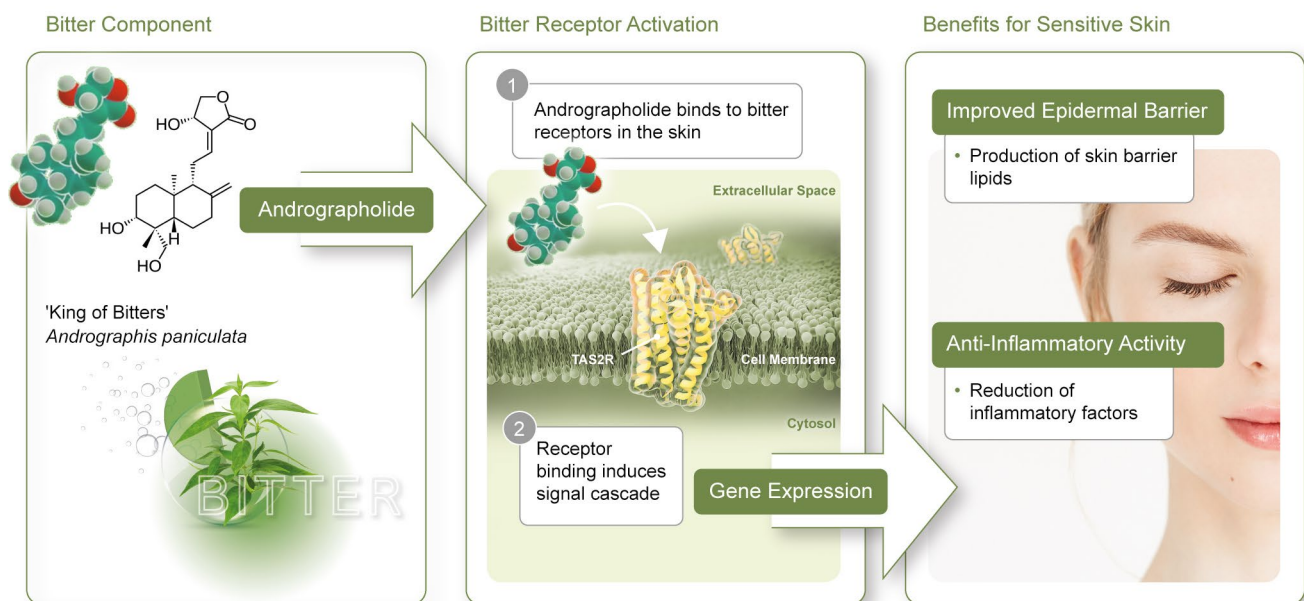
## Andrographolide from the 'King of Bitters' – An Activator of Skin Barrier Lipids

Good medicine tastes bitter, said Confucius <sup>[4]</sup>. Indeed, many active pharmaceutical ingredients taste bitter, supposedly in keeping with the cross-cultural belief that the bitterness of a medicine is correlated with beneficial, pharmacological activity. The database of bitter substances lists more than 1'000 compounds <sup>[5]</sup>, mostly of plant origin. Plants produce these bitter-tasting substances as protection against herbivorous predators.

The recognition of bitter substances in the mouth is mediated by bitter taste receptors belonging to the taste 2 family (TAS2R). Humans have 25 different bitter taste receptors, each specific for a different set of bitter substances. Apart from sensing taste, bitter receptors have more physiological roles. They are also present in extra-oral tissues, for example in the digestive tract, where epithelial cells recognize bitter nutrients, or in the lungs, where bitter substances induce bronchial relaxation <sup>[6]</sup>.

Of interest from a cosmetic perspective - bitter taste receptors of the TAS2R family are also found in skin. Here, they trigger the synthesis of skin barrier lipids and proteins, and they induce anti-inflammatory processes, which makes them novel and interesting targets for the treatment of sensitive skin <sup>[6]</sup>.

An excellent example of a plant-derived bitter substance is andrographolide, an extremely bitter tasting compound isolated from the stems and leaves of *Andrographis paniculata*, also called the 'King of Bitters'. Andrographolide is a diterpene with diverse pharmacological activities that binds and activates bitter taste receptors of the TAS2R family expressed in the skin <sup>[7]</sup>. Receptor activation induces a signal cascade that leads to an enhanced production of skin barrier lipids and reduces inflammatory markers <sup>[8, 9, 10]</sup>. This directly benefits sensitive skin as newly formed lipids strengthen the epidermal barrier and inflammation is reduced.



**Fig. 3: Bitter control of sensitive skin: Andrographolide induces skin lipid synthesis through binding of bitter receptors.** The bitter substance andrographolide binds bitter receptors of the TAS2R family on the skin surface. These receptors are integral membrane proteins that are used by cells to convert extracellular chemical signals into intracellular responses. The activated receptors transmit a signal, which finally triggers the production of skin barrier lipids and skin barrier proteins and reduces inflammatory processes <sup>[9]</sup>.

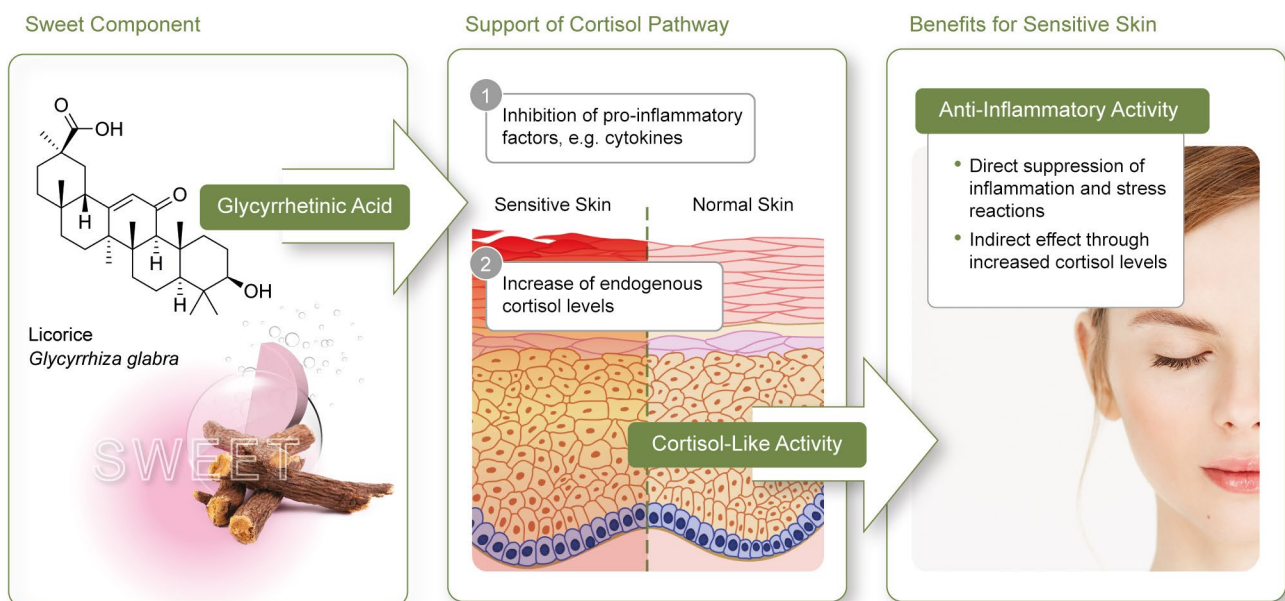
## Glycyrrhetic Acid from Licorice Roots – A Source of Natural Anti-Inflammation

Inflammation is one of the key characteristics of sensitive skin and is associated with skin redness and the production of inflammatory cytokines, chemokines, and interleukins <sup>[11]</sup>. To date, the most effective and widely prescribed compounds to combat inflammation are glucocorticoid derivatives (e.g. cortisol). They exhibit anti-inflammatory effects by suppressing the expression of pro-inflammatory genes and by inhibiting the production of inflammatory cytokines. Hence, topical corticosteroid creams and ointments are the main form of therapy to control acute flares of atopic dermatitis, due to their broad immunomodulatory effects.

The growing trend of natural cosmetics, however, calls for plant-derived solutions as attractive alternatives for the treatment of skin conditions such as sensitive skin or atopic dermatitis. One good example is licorice, the root of *Glycyrrhiza glabra*, which contains the active compound glycyrrhizin

- one of the sweetest substances found in nature. It has 30–50 times the sweetness of sucrose <sup>[12]</sup>, and is, thus, used as natural sweetener, flavoring additive, and food supplement.

Glycyrrhizin is a triterpene glycoside, and its hydrolysate, glycyrrhetic acid (GA), has a cortisol-like activity. It elevates endogenous cortisol levels and reinforces the inhibition of stress reactions and inflammation <sup>[13]</sup>. Moreover, GA inhibits pro-inflammatory factors, thus contributing to its anti-inflammatory activity <sup>[14]</sup>. As a result, GA from licorice root is a natural alternative to cortisol treatments with similar benefits for sensitive skin and an ideal addition to cosmetic actives targeting inflammation.



**Fig. 4: Sweetness for sensitive skin: Glycyrrhetic acid (GA) - A potent anti-inflammatory agent.** Licorice roots are a natural source of the sweet compound glycyrrhetic acid (GA). GA has cortisol-like activity and increases endogenous cortisol levels. At the same time, GA suppresses the expression of pro-inflammatory mediators. Together this leads to a broad anti-inflammatory activity and effective treatment of sensitive skin <sup>[13]</sup>.

## Composition | Amaretine® – The Synergy of Bitter & Sweet for Sensitive Skin

Amaretine® is the first active ingredient combining bitter and sweet components encapsulated in a liposomal carrier system. Bitter receptors are novel targets in the treatment of sensitive skin, their activation induces the production of skin lipids, which strengthens the epidermal barrier. In addition, anti-inflammatory activity is triggered through glycyrrhetic acid, which acts as a

natural, plant-derived alternative to synthetic cortisol. The combination of a bitter component, triggering a novel pathway, with a sweet component, well-known to combat inflammation, makes Amaretine® a unique and innovative skin care active for the cosmetic treatment of sensitive skin.

### Andrographolide

is a natural activator of skin barrier lipid synthesis



### Active Bitter Component

Amaretine® contains andrographolide from the 'King of Bitters' *Andrographis paniculata* that binds to bitter receptors in the skin. Bitter receptors are novel and innovative targets for sensitive skin care. The receptor activation triggers the synthesis of skin barrier lipids and proteins, thus supports the regeneration of a compromised skin barrier.

### Glycyrrhetic Acid

is a natural anti-inflammatory agent



### Active Sweet Component

Amaretine® contains glycyrrhetic acid from the licorice root *Glycyrrhiza glabra*, which shows strong anti-inflammatory activity by providing cortisol-like activity. It represents a natural alternative to synthetic cortisol, one of the most effective substances known to treat even severe forms of sensitive skin.

### Dermal Delivery System based on phospholipids



### Functional Liposomal Carrier

Amaretine® comes with a liposomal carrier system for hydrophilic actives that enhances the natural skin penetration. The delivery system is based on phospholipids, the natural building blocks of cell membranes. This unique delivery system reinforces the epidermal layer while simultaneously enhancing the ability of active compounds to penetrate the skin.

## *in vitro* Activity | Amaretine® Restores Bitter Taste Receptor Level in Atopic Skin

### Objective

- To show that skin keratinocytes contain bitter taste receptors (e.g., TAS2R50). Such bitter taste receptors are specific targets for andrographolide, the bitter component of Amaretine® [7].
- To show that the expression of bitter taste receptors (e.g., TAS2R50) are deregulated in atopic vs. normal skin - and restored by Amaretine®.

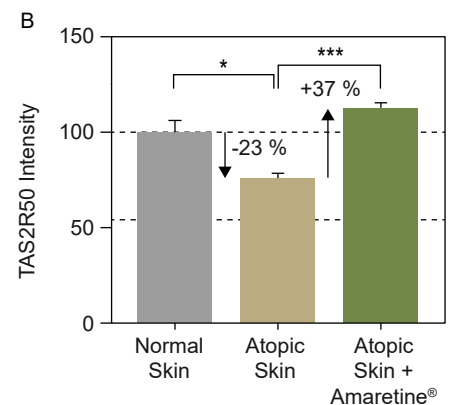
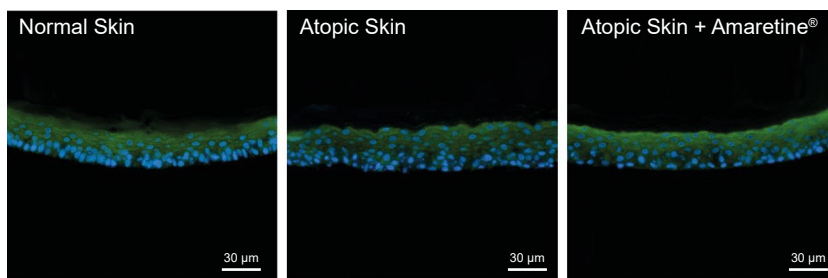
### Technique

A 3D model of a human epidermis was reconstituted, and atopic skin adaptations were induced by adding a cytokine cocktail to the fully differentiated tissue [15]. The expression of bitter taste receptors in the normal and the atopic model was monitored by immunofluorescence microscopy using specific antibodies.

### Study Details

<b>Design</b>	<i>in vitro</i> study
<b>Test Panel</b>	Cell model: 3D reconstituted human epidermis Origin of cells: Normal human epidermal keratinocytes (NHEKs) isolated from 3 Caucasian donors The fully differentiated tissues were stimulated with a cytokine cocktail (IL-4, IL-13, IL-25) to induce alterations reminiscent of atopic skin.
<b>Test Substances</b>	0.003 % Amaretine® was added to the cytokine cocktail or not. Incubation for 48 h. Immunostaining using anti-TAS2R50 antibodies (green) and DAPI cell nucleus staining (blue).
<b>Endpoint</b>	Bitter taste receptor (TAS2R50) level in skin keratinocytes (intensity of fluorescence)

#### A Restoration of Bitter Taste Receptor (TAS2R50)



**Fig. 5: The expression of bitter receptors in human skin is restored by Amaretine®.** (A) Immunofluorescence images of reconstituted human epidermis unstimulated ('Normal Skin'), stimulated with a cytokine cocktail ('Atopic Skin') or upon addition of Amaretine® ('Atopic Skin + Amaretine®'), Scale bar = 30 µm. The green staining refers to labelling of TAS2R50 with specific antibodies. The signal is proportional to the amount of expressed bitter taste receptors. The blue signal highlights the cell nuclei. (B) TAS2R50 fluorescence intensity expressed in percent relative to normal skin. N = 3; Mean + SEM. Student's t-test. \* =  $p < 0.05$ , \*\*\* =  $p < 0.001$ .

### Result

This study confirmed that the bitter taste receptor TAS2R50 is expressed in the human epidermis. The concentration of TAS2R50 (intensity of green fluorescence signal) is significantly deregulated in an atopic skin model. Through addition of Amaretine® expression levels of the receptor were restored.

### Conclusion

Bitter receptors are suggested to play a role in tackling sensitive skin as their activation leads to the production of skin lipids, strengthening the skin barrier [16]. The differential expression pattern and reversal upon treatment with Amaretine® confirms that andrographolide is a ligand of TAS2R50 and portrays bitter receptors as promising, new targets for the treatment of sensitive skin.

**Target receptors of Amaretine® are present and deregulated in sensitive skin. Amaretine® restores receptor expression levels resembling normal skin.**



# in vitro Activity | Amaretine® Reverses Imbalanced Gene Expression of Atopic Skin

## Objective

- To show that Amaretine® can reverse the imbalanced expression of genes associated with atopic skin, including those involved in skin barrier, lipid synthesis, inflammation and hypersensitivity.

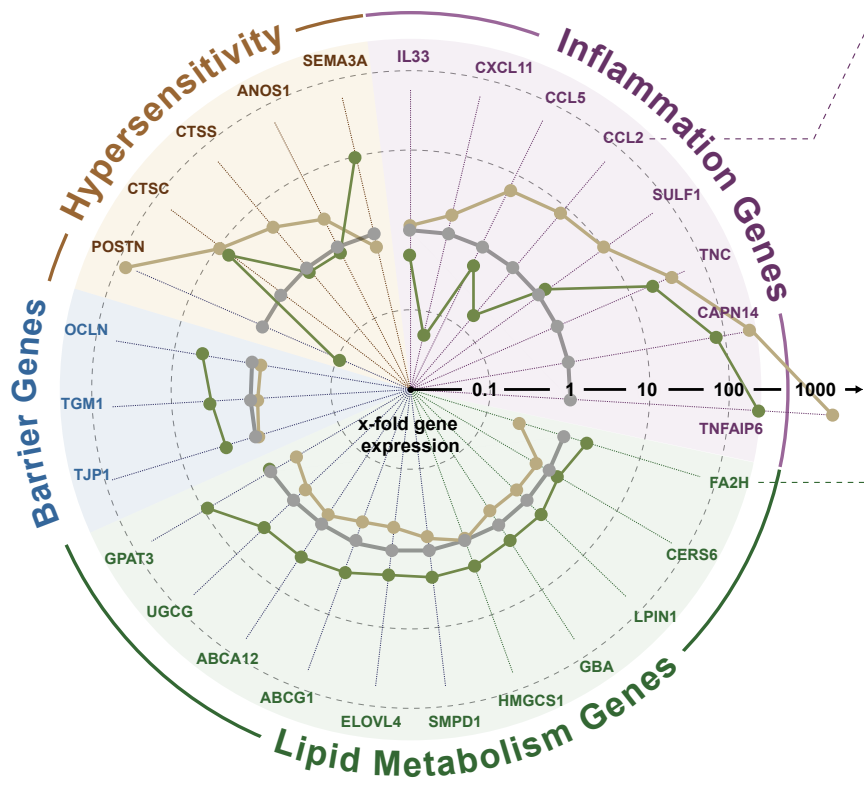
## Technique

A 3D skin model of atopic dermatitis<sup>[15]</sup> was subjected to Amaretine® and a transcriptomic analysis was performed on 93 epidermal gene targets, all related to atopic skin. Changes in gene expression were monitored by real-time quantitative polymerase chain reaction (RT-qPCR) using TaqMan Low Density Arrays and compared to a normal skin model.

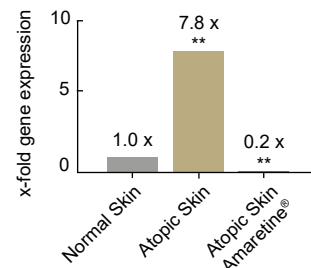
## Study Details

<b>Design</b>	<i>in vitro</i> study
<b>Test Panel</b>	Cell model: 3D reconstituted human epidermis Origin of cells: Normal human epidermal keratinocytes (NHEKs) isolated from 3 Caucasian donors The fully differentiated tissues were stimulated with a cytokine cocktail (IL-4, IL-13, IL-25) to induce alterations reminiscent of atopic skin.
<b>Test Substances</b>	0.01 % Amaretine® was added to the cytokine cocktail or not. Incubation for 48 h.
<b>Endpoint</b>	Changes in expression of 93 gene targets in (i) Normal Skin, (ii) Atopic Skin and (iii) Atopic Skin + Amaretine®

## Rebalancing of Gene Expression

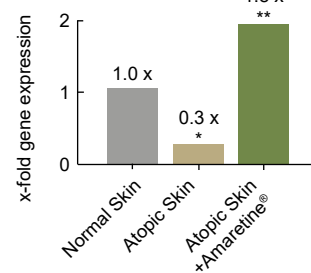


Examples: **CCL2 - Small Inducible Cytokine A2**



**CCL2** is involved in skin inflammation and upregulated in sensitive skin. Amaretine® reduces its expression level.

**FA2H - Fatty Acid 2 Hydroxylase**



**FA2H** is involved in skin lipid synthesis and responsible for strengthening the skin barrier. In atopic skin, its expression is downregulated, which can be reversed by Amaretine®.

- Levels of gene expression in normal skin (set to 1)
- Imbalanced levels of gene expression in atopic skin (x-fold changes)
- Rebalanced levels of gene expression in atopic skin after Amaretine® treatment

**Fig. 6: Amaretine® rebalances sensitive skin-related gene expression.** The radar plot shows gene expressions in normal skin (gray dots) normalized to 0 (baseline levels: fold-change = 1), gene expression after induction of atopic skin (beige dots), and gene expression in atopic skin + Amaretine® (green dots). Genes are grouped according to function (more information about individual genes: [www.genenames.org](http://www.genenames.org)). N = 3; Mean. Student's t-test. \* =  $p < 0.05$ ; \*\* =  $p < 0.01$  (normal skin vs. atopic skin; atopic skin vs. atopic skin + Amaretine®)

## *in vitro* Activity | Amaretine® Reverses Imbalanced Gene Expression of Atopic Skin

### Result

Of the 93 genes screened, 30 genes showed significant disbalance in gene expression in an atopic skin model. As shown in Fig. 6, atopic skin produced huge changes in gene expression up to 2000-fold. Genes affected are coding for components involved in skin barrier function, lipid synthesis, inflammation and hypersensitivity, all of which play a role in the symptomatology of sensitive skin. The addition of 0.01 % Amaretine® inversely modulated the expression of 27 genes and shifted it back towards a healthy skin pattern.

### Conclusion

The effect of Amaretine® on sensitive skin-related genes shows that the ingredient is both active and functional *in vitro*. On a gene expression level, it reverses alterations seen in atopic skin, with a broad impact on different gene groups. As a novel cosmetic active, Amaretine® addresses the major symptoms of sensitive skin by normalizing barrier function, skin lipid metabolism, inflammatory response, and hypersensitivity in an atopic skin model.

**Sensitive skin presents a distinctly imbalanced gene expression pattern compared to normal skin. Amaretine® reverses changes in gene expression levels and shifts them towards a healthy skin pattern.**

## *in vivo* Activity | Amaretine® Regenerates Skin Barrier & Protects from Irritation

### Objective

- To study the capacity of Amaretine® to regenerate a compromised epidermal skin barrier and to protect from skin irritation.

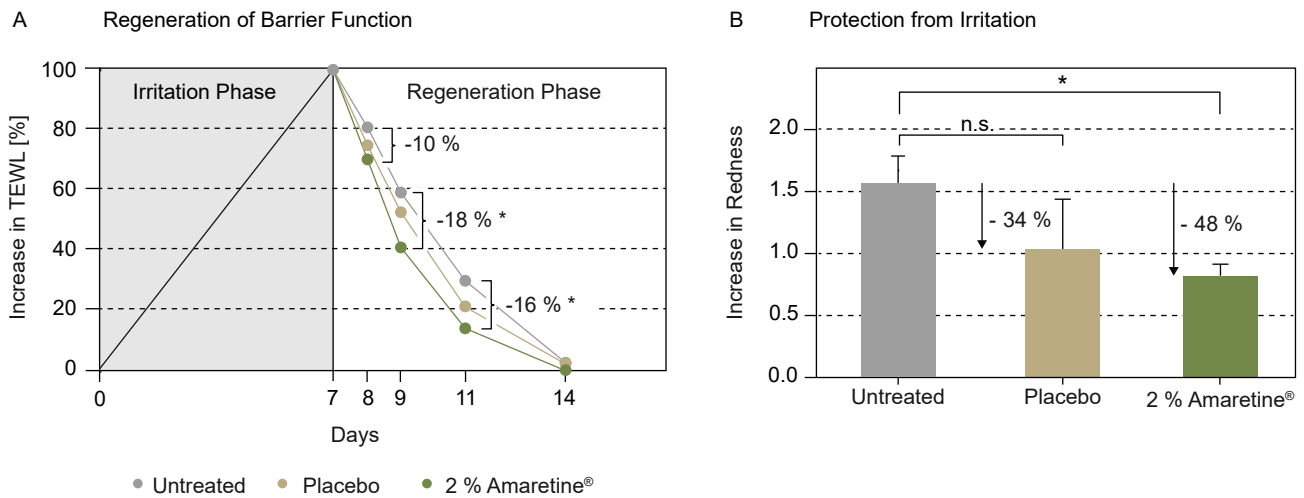
### Technique

SLS-wash test: In a placebo-controlled, double-blind study, a reduced epidermal barrier and irritation was induced by treating the inner arms of healthy volunteers with the aggressive detergent sodium lauryl sulfate (SLS). Regeneration of barrier function was monitored by following trans-epidermal water loss (TEWL) upon SLS stress. Protection from irritation was determined by measuring skin redness before and after SLS stress.

### Study Details

<b>Design</b>	Double-blind, placebo-controlled, randomized <i>in vivo</i> study
<b>Test Panel</b>	20 volunteers (12 females, 8 males) aged between 21 and 61 years
<b>Test Area</b>	Inner sides of forearms
<b>Test Substances &amp; Application Frequency</b>	<u>For barrier function (regeneration):</u> Irritation phase: Washing of inner arms with a 5 % SLS solution twice daily for 7 days. Regeneration phase: No treatment (untreated) or treatment with a cream containing 0 % (placebo) or 2 % Amaretine®, twice daily for another 7 days.  <u>For redness (protection):</u> No treatment of inner arms or treatment with a cream containing 0 % (placebo) or 2 % Amaretine®, twice daily for 7 days. 1 hour after each treatment the arm was washed with SLS solution.
<b>Endpoints</b>	<u>Barrier function:</u> Determination of trans-epidermal water loss (TEWL) with a tewameter. <u>Redness:</u> Determination of skin redness (a*-value) with a colorimeter.

## *in vivo* Activity | Amaretine® Regenerates Skin Barrier & Protects from Irritation



**Fig. 7: Amaretine® regenerates the skin barrier and protects from irritation.** (A) 20 volunteers washed their inner arms with SLS for 7 days, thereby disrupting the skin barrier (increased TEWL in irritation phase). To evaluate the regenerative properties of Amaretine® upon irritation, the skin was treated with a test cream containing 2 % Amaretine® or a placebo, and regeneration of TEWL was monitored for another 7 days. With Amaretine®, regeneration was faster and stronger. (B) To evaluate the protective properties of Amaretine® against irritation, the volunteers applied the test creams 1 hour before SLS washing. After 7 days the skin became irritated (increased redness), which was prevented to a great extent by Amaretine®. N = 20; Mean + SEM. Student's t-test versus untreated; \* = p < 0.05.

### Result

SLS treatment weakens the skin barrier, which leads to dryness and irritation, artificially inducing signs of sensitive skin in a controlled *in vivo* setting. Sensitive skin treated with a test cream containing 2 % Amaretine® showed reduced trans-epidermal water loss (TEWL) by -10 %, -18 % and -16 % after only 1, 2 or 4 days of regeneration, respectively, when compared to untreated (Fig. 7 A). Skin redness, a measure for skin irritation, was significantly less pronounced (-48 %) after 7 days of treatment compared to untreated (Fig. 7 B).

### Conclusion

Amaretine® reduces symptoms of sensitive skin *in vivo* by restoring epidermal barrier integrity and protecting the skin from irritation. The addition of Amaretine® to a simple base formulation is highly effective and acts quickly in treating and preventing major symptoms of sensitive skin.

Amaretine® regenerates the barrier function and soothes irritation in sensitive skin.  
Amaretine® is an effective and rapidly acting ingredient to ease symptoms of sensitive skin.

# in vivo Activity | Amaretine® Eases Sensitive Skin & Improves Quality of Life

## Objective

- To show that a base cream formulation with Amaretine® eases sensitive skin symptoms like dryness, redness and itching.
- To show that sensitive skin directly impacts the quality of life of affected people and that relieving associated skin symptoms can ameliorate skin-related worries and improve overall quality of life.

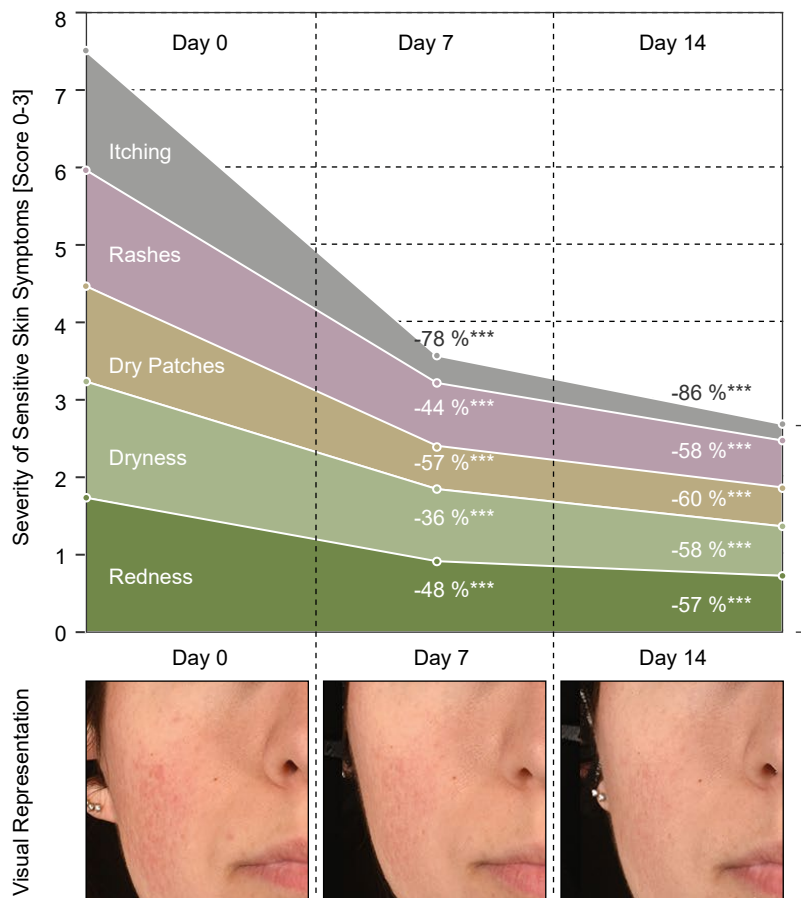
## Technique

In an *in vivo* study, volunteers with sensitive skin identified their own individual problem zone (size and location). Then, over the next 14 days, the volunteers applied a cream with 2 % Amaretine® to their selected area. Improvements in sensitive skin symptoms were objectively measured in a clinical study. Subjective evaluations of product efficacy and changes in quality of life were rated by answering a questionnaire.

## Study Details

<b>Design</b>	<i>in vivo</i> study, comprising a clinical study and a consumer survey
<b>Test Panel</b>	24 volunteers with sensitive skin or tendency to frequent irritation Severity scoring of atopic dermatitis (SCORAD) index < 20 (with visible but minor signs of skin irritation and skin lesions)
<b>Test Area</b>	The application areas of sensitive skin were self-selected by the volunteers (11 % hand, 23 % arm, 32 % face and 34 % body).
<b>Test Substances</b>	Base cream formulation with 2 % Amaretine®
<b>Application Frequency</b>	Twice daily for 14 days
<b>Endpoints</b>	Clinical expert evaluation of sensitive skin symptoms using grading scales Questionnaire monitoring sensitive skin symptoms, product efficacy and changes in quality of life

## Clinical Assessment of Sensitive Skin Symptoms



**Fig. 8: Amaretine® reduces symptoms of sensitive skin.** 24 volunteers with sensitive skin applied a test cream with 2 % Amaretine® for 14 days. Changes in sensitive skin symptoms were evaluated by a clinical expert. The evaluation used pre-established scales ranging from 0 (no symptoms), 1 (low symptoms), 2 (moderate symptoms), to 3 (severe symptoms). The graph shows an additive representation of sensitive skin symptoms. Overall, the symptoms decreased by 52 % and 64 % after 7 and 14 days, respectively.  $N = 24$ . Mean. Student's *t*-test vs. baseline (day 0). \*\*\* =  $p < 0.001$ .

Below: representative pictures of a volunteer show symptom reduction over time.

**-64 %**  
Total Reduction of Symptoms

## in vivo Activity | Amaretine® Eases Sensitive Skin & Improves Quality of Life

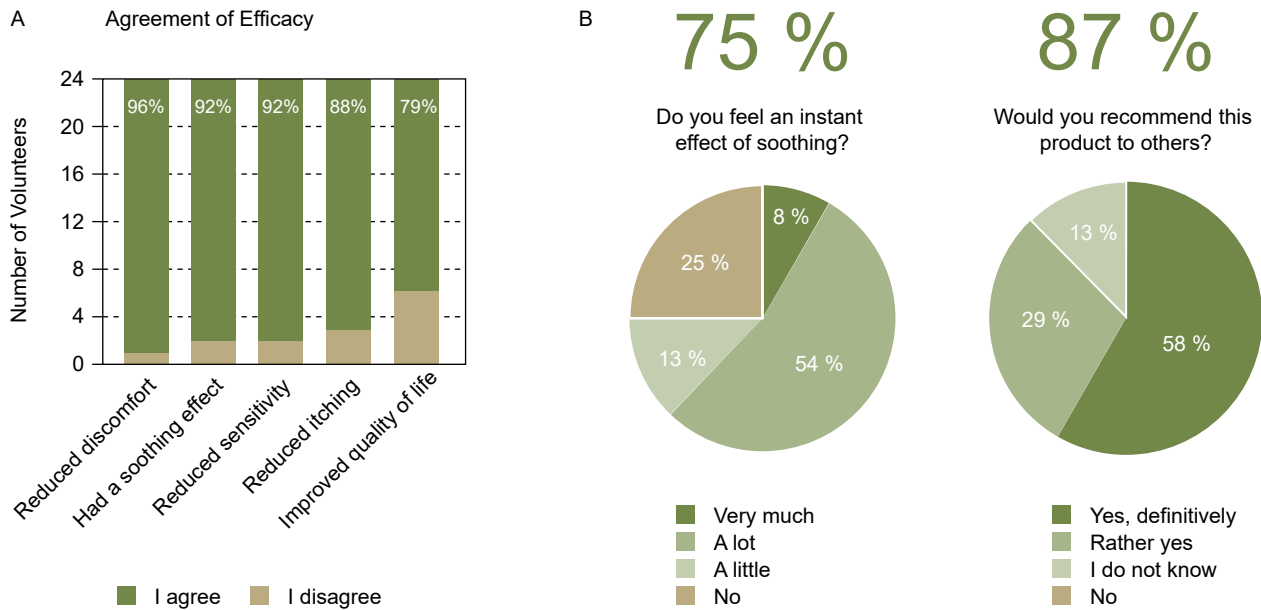


Fig. 9: Consumers experience a 2 % Amaretine® cream as an effective treatment for sensitive skin. Survey in which consumers with sensitive skin used a basic cream formulation with 2 % Amaretine® for 14 days and subsequently answered questions related to product performance. (A) Efficacy agreement of consumers with > 90 % reporting reduced discomfort and sensitivity. (B) In total, 75 % of all volunteers felt an instant soothing effect, and 87 % would recommend the product to others. N = 24.

### The Reduction of Sensitive Skin Symptoms Improves the Quality of Life

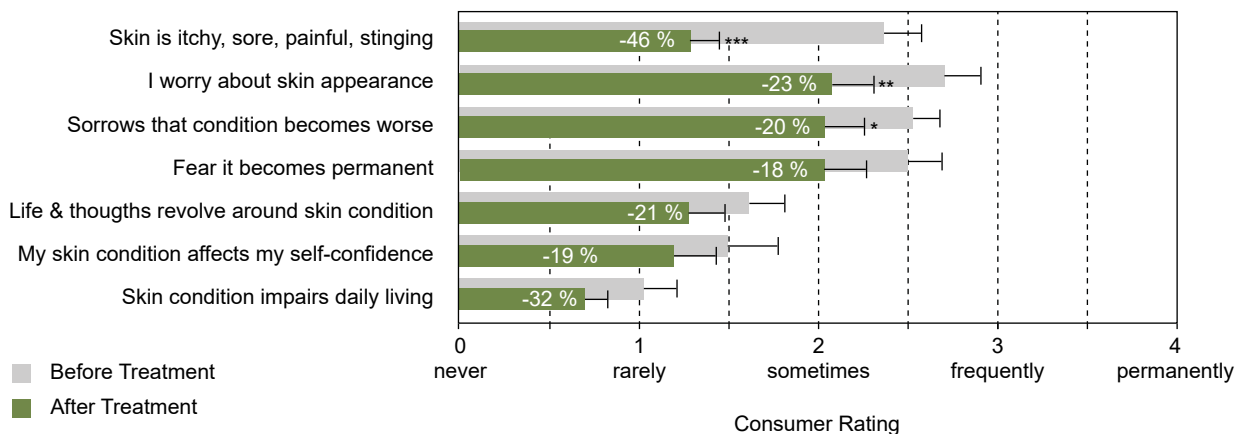


Fig. 10: An Amaretine® test cream improves the quality of life of consumers with sensitive skin. In a consumer study, 24 volunteers with sensitive skin applied a test cream containing 2 % Amaretine® for 14 days. Volunteers rated multiple quality-of-life statements before and after 14 days of treatment, on a scale of 0 to 4 (0 = 'never', 1 = 'rarely', 2 = 'sometimes', 3 = 'frequently', 4 = 'permanently'). At the beginning, volunteers suffered sometimes to frequently from itchy, sore, and painful skin. After treatment, the frequency reduced by 46 % to rarely. Other quality of life parameters were reduced between 18 % and 32 %. Average score + SEM. Changes in scores (before vs. after treatment) are represented in percent changes. N = 24. Student's t-test versus before treatment. \* =  $p < 0.05$ , \*\* =  $p < 0.01$ , \*\*\* =  $p < 0.001$ .



## *in vivo* Activity | Amaretine® Eases Sensitive Skin & Improves Quality of Life

### Result

Clinical expert evaluation determined improvements in all sensitive skin symptoms tested, with an overall reduction of 64 % after 2 weeks (Fig. 8).

This was confirmed by the results of the self-evaluation, where consumers experienced positive effects when using the cream with 2 % Amaretine®. Ranging from 79 % to 96% of volunteers reported less severe skin sensitivity and discomfort as well as a soothing effect and an improvement of life quality (Fig. 9 A). Overall, 75 % of volunteers felt an immediate soothing effect, and 87 % would recommend the product to others (Fig. 9 B).

This improvement of quality of life is expressed in less itchy, sore, painful, and stinging skin (-46 %), less worry about skin appearance (-23 %), less sorrows that it might become worse (-20 %), or fewer thoughts that revolve around the skin condition (-21 %) (Fig. 10).

### Conclusion

The study setup resembles a real-life situation, where users identify their individual problem zones of sensitive skin and critically observe changes in the treated area.

Treatment with a 2 % Amaretine® cream on self-selected areas improved symptoms of sensitive skin – this effect is confirmed by a clinical assessment and is further experienced by the volunteers after self-observation (questionnaire). The effect correlates well with questions related to quality of life, highlighting the importance and benefits of effective treatment, which affects much more than the physical symptoms of skin health or skin esthetics, but is also important for the mental status and overall well-being of an individual.

Further, the effectiveness of Amaretine®, established in this consumer study, is based on cumulative data from face, body, hands, and arms. Therefore, Amaretine® is suitable for a variety of skin care applications.

**Amaretine® eases the physical symptoms of sensitive skin.**

**Amaretine® improves the quality of life of consumers with sensitive skin.**

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## Product Details

### Product Characteristics

- Amaretine® combines bitter and sweet components for sensitive skin: Bitter andrographolide from *Andrographis paniculata* leaves and sweet glycyrrhetic acid from *Glycyrrhiza glabra* roots activate the skin's bitter receptors and reduce inflammatory responses. Encapsulated in a liposomal carrier system and embedded in propylene-glycolic aqueous matrix.
- Propylene glycol is a derived natural ingredient of wholly natural origin.
- Vegan, COSMOS-approved raw material
- Preservative-free/ self-preserving
- Brown, viscous liquid

### Recommended Applications

- Sensitive skin care
- Calming face care
- Comforting body lotion

### Recommended Usage

- Recommended use level: 0.5-5 %
- Final cosmetic products with Amaretine® can be claimed as e.g., 'contains Swiss manufactured ingredient'.

### Formulation Recommendations

- Amaretine® is suitable for o/w, w/o emulsions, water-based gels, and surfactant-based products. It can be easily incorporated due to its liquid form. We recommend adding this active after emulsification below 40 °C or during cold processes at any suitable step.
- For detailed information, please ask for our report 'stability and formulation recommendations' (info@lipoid-kosmetik.com).

### Safety

- Non-phototoxic (OECD 432), when tested at a concentration of 10%
- Non-irritating for skin (HRIPT, repeated human patch test), when tested undiluted on 51 volunteers
- Non-sensitizing for skin (HRIPT, repeated human patch test), when tested undiluted on 51 volunteers

- Non-mutagenic and non-pro-mutagenic (AMES test – OECD 471)
- No allergens (as per current EU Cosmetic Regulation)
- Non-irritating for eyes (BCOP – OECD 437), when tested at a concentration of 10%

### Sustainability - Corporate Level

- Award-winning company and top 1 % supplier according to the EcoVadis sustainability rating
- Efficient energy consumption and reduction process
- Climate-neutral according to Scope 1/2; CO<sub>2</sub>-offset with myclimate Gold Standard
- Sustainable use of biodiversity
- Green product portfolio with documented naturalness and sustainability information
- Certified according to the RSPO Supply Chain Standard, Mass Balance
- For more details, please visit the [sustainability section](#) on our website.

### Sustainability - Process Level

- Sophisticated supplier/ raw material qualification system against a comprehensive set of sustainability criteria.
- Energy-efficient and environment-friendly cold process technology.
- Controlled under cosmetic GMP ISO 22716.
- Readily biodegradable product from renewable sources.
- Excellent material and waste management programs.

### Sustainability - Raw Materials

#### Andrographis Paniculata Leaves

- Cultivated, GMO-free
- [Sustainability Score 2/3](#)

#### Glycyrrhetic Acid

- Plant-derived, 100 % non-GMO

#### Propylene Glycol

- Plant-derived, 100 % non-GMO

## Regulatory *(Further regulatory documents upon request)*

INCI	Propylene Glycol, Aqua (Water), Glycyrrhetic Acid, Sodium Bicarbonate, Lecithin, Glycerin, Andrographis Paniculata Leaf Extract, Pentylene Glycol, Sodium Hydroxide, Tocopherol
EU Cosmetic Regulation	The product complies to the EU Cosmetic Regulation (EC) No 1223/2009.
China INCI	All INCI are listed in the current Inventory of Existing Cosmetic Ingredient China (IECIC). CSAR Ingredient Submission Code is available.
EU REACH	The product, i.e. its substances, conforms to the Regulation (EC) No 1907/2006.
China REACH	The ingredient Andrographis Paniculata Leaf Extract is not listed in the current Inventory of Existing Chemical Substances China (IECSC).
Allergen	No allergens (as per current EU Cosmetic Regulation: <10 ppm for leave-on/<100 ppm for rinse-off).
CMR	The product is not known to contain substances classified as CMR under the Regulation (EC) No 1272/2008 (CLP).
ABS	The product complies with the requirements of Access and Benefit Sharing (ABS) as derived from the Nagoya Protocol.
COSMOS	Amaretine® is a raw material approved by ECOCERT Greenlife that conforms to the COSMOS Standard. The raw material is of 100 % natural origin. Raw material verified by ECOCERT GREENLIFE, conforms to the COSMOS Standard.
ISO 16128	The product has a Natural Origin Content (Cno) of 100 %.
Halal	The product conforms to HALAL requirements, considering the following: Traces of ethanol remaining in Amaretine® at the end of the manufacturing process are technically unavoidable. The ethanol is plant-derived and non-GMO. Its concentration is less than 0.1 %.
Vegan	The product can be used in vegan formulations.
Non-GMO	The product is non-GMO. It meets the non-GMO standards set by Regulation (EC) No 1829/2003 and EC (No) 1830/2003.
Palm oil	The product does not contain palm/ palm kernel oil or its derivatives.



COSMOS  
APPROVED

## Sustainability *(Please refer to page 15 for detailed information)*

Corporate	Top 1 % supplier according to the EcoVadis sustainability rating.
Process	Sophisticated supplier/ raw material qualification system and sustainable process technology.

Raw Material



2/3 Sustainability Score

This product is developed and manufactured in Switzerland.

For more information: [www.lipoid-kosmetik.com/en/sourcing-raw-material](http://www.lipoid-kosmetik.com/en/sourcing-raw-material)

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