

Focus on the product

Dandruff and Malassezia

Dandruff is a common scalp condition characterised by oily-yellow flakes and an itchy scalp, often accompanied by inflammation. A primary contributor to dandruff is the overgrowth of *Malassezia*, a genus of lipid-dependent yeasts that thrive in sebaceous areas of the skin. While these yeasts are normally part of the skin's microbiota, they can become problematic when environmental factors disrupt the balance.¹

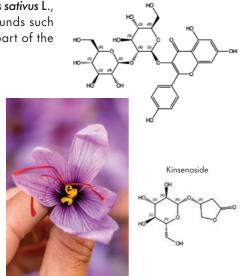
Malassezia consists of 18 species that act as both commensals and transient pathogens, with Malassezia restricta and Malassezia globosa being the most prevalent on the skin.\(^1\) These yeasts produce enzymes like lipases and phospholipases, which contribute to scalp disorders, itch and inflammation.\(^2\) Nearly 50% of adults experience dandruff at some point, especially those aged 20 to 50. Factors such as increased sebum production, stress, climate changes and prolonged head covering (hat, hijab, bandana, turban etc.), can predispose or worsen the condition, leading to inflammation and discomfort.\(^3\) Additionally, an immune response dysregulation to Malassezia can worsen dandruff and scalp condition, activating pro-inflammatory pathways,\(^4\) and even affecting self confidence and mood.

Revealing Nature's Gold: the preciousness and efficacy of saffron flower

Saffron: From the vibrant landscape of Morocco to the Active Beauty Centre of Excellence in Green Fractionation in France, researchers have explored the remarkable properties of *Crocus sativus L.*, commonly known as saffron. This plant is characterised by unique bioactive compounds such as flavonoids (like Kaempferol-3-O-sophoroside), and rare molecules identified as part of the phytocomplex (like Kinsenoside, Goodyeroside and 3-hydroxyubutyrolactone).

DandEraseTM: An extract obtained from *Crocus sativus* L. petals, by-products of saffron spice production. The flowers are harvested at dawn and, after removal of stigmas, are extracted only with water, optimised with the NaDES (Natural Deep Eutectic Solvents) technology to further enhance the solubilisation and stabilisation of these valuable compounds, enhancing their efficacy and skin tolerance.

A LCA (Life Cycle Analysis) was performed by an independent third party according to ISO 14040/14044 and assessed a low carbon footprint (2.7 kgCO $_2$ eq) thanks to the valorisation of the flowers, no use of pesticides, low fertilisers and little mechanisation. The resulting phytocomplex is rich with potent and rare molecules. This blend of cutting-edge science and sustainability positions DandErase $^{\text{TM}}$ as a powerful ingredient in cosmetic formulations aimed at effectively addressing dandruff and scalp itch and inflammation.



Kaempferol-3-O-sophoroside

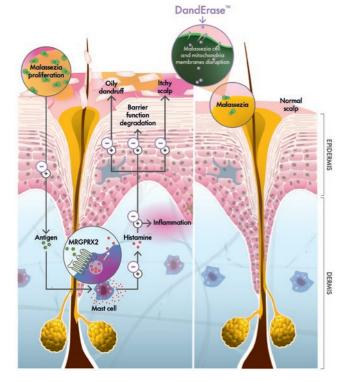
DandErase™ selectively reduces *Malassezia* and dandruff

DandErase™ inhibits Malassezia spp. hyperproliferation:

- Disrupting the Malassezia cell membrane.
- Depolarising the Malassezia mitochondrial membrane.

This decrease in *Malassezia spp.* hyperproliferation, brings the following benefits:

- Decreasing inflammatory markers (TNF- α) and erythema.
- Mitigating itch (histamine via the MRGPRX2 receptor).7
- Restoring the skin/scalp barrier function (desmoglein-1).
- Balancing the microbiome (healthy scalp, long lasting antidandruff effect).



Biological activity

DandErase™: as good as synthetic benchmarks on *Malassezia* growth inhibition

1. Malassezia spp. growth reduction

Malassezia globosa cultures were resuspended to 10^6 CFU/mL to evaluate the growth inhibition potential of DandEraseTM compared to well known anti-dandruff benchmarks: climbazole, ketoconazole and piroctone olamine after 24 hours.

Results: The benchmarks effectively inhibits M. globosa growth, while DandEraseTM at a lower dose (dry matter) shows equivalent efficacy, underscoring its promise as a dandruff-fighting agent.

2. The power of the phytocomplex

The efficacy of DandEraseTM against M. globosa was evaluated in comparison to its carrier (NaDES Eutectys BLA) and key biologically active compounds in the extract: kaempferol-3-O-glucoside (astragalin or K30G), kaempferol-3-O-sophoroside (K30S) and kinsenoside, all at equivalent doses. Cultures of Malassezia were resuspended to a final concentration of 10^6 CFU/mL to assess growth inhibition after 24 hours.

Results: DandEraseTM exhibits significant growth inhibition, highlighting the synergistic power of the phytocomplex in its antifungal activity against M. globosa. This suggests that Malassezia species are less likely to develop resistance when exposed to such a complex matrix.

DandErase™: soothing benefit

1. Promotion of anti-inflammatory balance

The soothing effect of DandEraseTM was assessed on Normal Human Epidermal Keratinocytes (NHEK), pretreated for 24 hours with DandEraseTM or with anti-dandruff benchmarks climbazole, or piroctone olamine. After inducing chemical stress (Phorbal miristate acetate, PMA) for an additional 24h, cytokines release was measured by Multiplex assay (anti-inflammatory: IL-1Ra, pro-inflammatory: TNFα, IL-6).

Results: DandErase™ significantly reduces pro-inflammatory cytokines release, demonstrating its ability to alleviate inflammation linked to scalp disorders. In contrast, piroctone olamine showed neutral effects, and climbazole exhibited even pro-inflammatory potential, as also respresented in literature.8

2. Reduction of Malassezia-triggered pro-inflammatory markers

Scalp inflammation is normally associated to dandruff and Malassezia hyperproliferation.

Reconstructed Human Epidermis (RHE) containing Langerhans cells was pre-treated overnight with DandEraseTM at 0.6%. The RHE was then exposed to an inactivated inoculum of *Malassezia spp.* (10^4 CFU/mL) for 2 hours. After rinsing, the product was reapplied for 24 hours, and the culture medium was collected to quantify the pro-inflammatory marker TNF-a (ELISA assay).

Results: DandEraseTM significantly reduces the inflammatory marker TNF- α triggered by Malassezia spp. by -25%**.

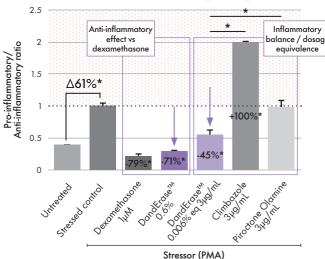
Inhibition of Malassezia **T** Equivalence 80 Inhibition (%) 60 40 20 DandErase™ Ketoconazole Piroctone Climbazole Olamine 0.5% 0.3% eq. 0.5% 0.5% (dry matter) (dry matter) (dry matter) dry matter

Mann-Whitney test: *p<0.05

The phytocomplex on Malassezia globosa 80 Lower risk 60 of microbial Inhibition (%) 20 0 Kinsenoside K30G + K30S Eutectvs DandErase¹ K30G K30S eq. dose eq. dose eq. dose ea. dose

Mann-Whitney test: *p<0.05

DandErase™ basal soothing activity



Mann Whitney test: *p<0.05

Reduction of TNF-α 150 Δ34%* 100 T T T T T Addition of TNF-α Labeled a stressed control Untreated Stressed control DandEraseTM 0.6% + Malassezia species

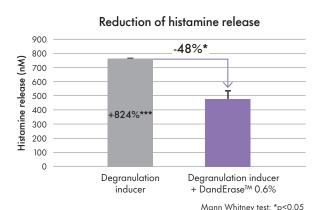
Student t-test: *p<0.05; **p<0.01

Biological activity

DandEraseTM: anti-itching activity

The hyperproliferation of *Malassezia* not only leads to dandruff and inflammation but also triggers itching. This response is mediated by the MRGPRX2 receptor on mast cell membranes, which induces histamine release. In this study, human mast cells were pre-incubated for 15 minutes with a medium containing DandErase[™] at 0.6%, without it and with Cromoglycate 10 mM (positive control). Following this, an inducer (compound 48/80 at 5 μg/mL) was added to induce histamine release via degranulation. Histamine release was quantified in the cell media using an EIA kit.

Results: DandErase™ significantly reduces histamine release by 48%* demonstrating its effectiveness in modulating the MRGPRX2 pathway, the primary receptor associated with itch.



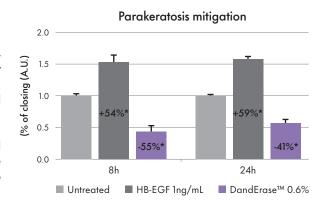
DandErase™: skin barrier repair

Maintaining a healthy skin barrier is essential for overall scalp health and preventing conditions such as greasiness, irritation, and inflammation. DandErase™ plays a crucial role in protecting and strengthening the skin barrier through its holistic mechanism of action.

1. Inhibition of keratinocytes migration (8h and 24h)

Normal Human Epidermal Keratinocytes (NHEKs) were pre-treated for 24 hours with DandErase™ (0.6%). A scratch was then created on the cellular layer to simulate an injury, and the treatment with the active was renewed. After an additional 24 hours of incubation, wound closure was quantified using image analysis.

Results: DandErase™ limits keratinocyte migration by 55% at 8 hours and by 41% at 24 hours. This reduction helps mitigate parakeratosis (incomplete maturation of epidermal keratinocytes) commonly observed in scalp disorders related to Malassezia infection.

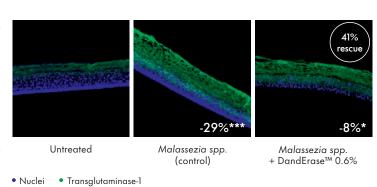


ANOVA of Kruskal-Wallis followed by Mann-Whitney test : * p<0.05

2. Reduction of epidermal hyperdifferentiation

Reconstructed Human Epidermis (RHE) containing Langerhans cells was pre-treated overnight with DandEraseTM at 0.6%. An inactivated inoculum of M. furfur, M. globosa, and M. restricta (10^4 CFU/mL) was then applied for 2 hours. After rinsing, the product was reapplied for 24 hours. Transglutaminase-1 expression, a marker of keratinocytes terminal differentiation, was measured through immunofluorescence (IF).

Results: DandEraseTM significantly reduces the hyperdifferentiation provoked by Malassezia spp. measured by Transglutaminase-1 expression, playing a key role in skin barrier function.



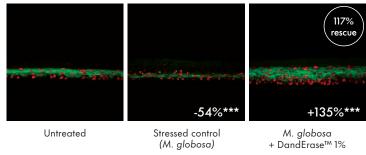
Student's t-test: *p<0.05 vs control and ***p<0.001 vs untreated

3. Reinforcement of desmosomes

The presence of *Malassezia spp.* induces barrier impairment, leading to a decrease in desmoglein-1 expression at the desmosomes level.

Reconstructed Human Epidermis (RHE), activated with sebum, was topically pre-treated with DandErase™ at 1% for 30 minutes before inoculation with M. globosa (2.10^5 CFU/mL). After rinsing, the product was reapplied for a total treatment of 48 hours. At the end of the culture period skin explants were fixed, tissue processing was done and immunostaining against Desmoglein-1 were performed by IF.

Results: DandErase™ significantly reactivates desmoglein-1 expression by 135%* and promotes the improvement of skin barrier integrity.



Nuclei
 Desmoglein-1 (desmosomes)

Mann-Whitney test: ***p<0.001 vs stressed control (Malassezia)

Clinical efficacy #1

Anti-dandruff efficacy: as good as the benchmark, long-lasting effect

DandErase™ as effective as #1 anti-dandruff shampoo

This study aimed to evaluate the anti-dandruff effects of a DandErase[™]-containing shampoo in a diverse population of 70 volunteers having dandruff (>300 C Cube), and itchy and sensitive scalp. The study was organised as follows:

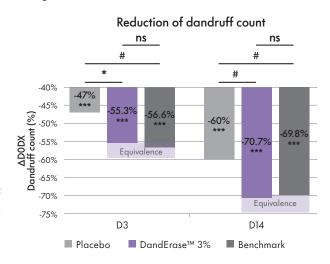
- 30 volunteers using DandErase™ 3% shampoo > 15 switching to placebo shampoo D14 to D28 (long lasting efficacy evaluation).
- 20 volunteers using placebo shampoo.
- 20 volunteers using benchmark shampoo.

Use of shampoo 3 times per week. Measurements were carried out at D-7 (before the wash out period), and at D0, D3, D14.

Dandruff evaluation was performed with C Cube and Dandruffmeter.

Results 1/3: After just 3 days (with only 2 shampoo applications), DandErase™ reduces dandruff count as effectively as the #1 anti-dandruff shampoo in the market, achieving up to a 95% reduction in dandruff by day 3, efficacy was shown in 100% of volunteers.

After 2 weeks, the average decrease in dandruff count was -71% compared to baseline, with results **up to -97**%, demonstrating equivalent efficacy to the benchmark.



Wilcoxon test vs D0: ***p<0.001
Mann Withney test vs placebo: #p<0.1; *p<0.05; **p<0.01



Results 2/3: Erythema was reduced by 4.8x (D3) to 5x at D14 versus placebo.

Results 3/3: DandEraseTM induces a long-lasting effect on microbiome stabilisation with the reduction of dandruff continuing to decrease even two weeks after stopping the treatment.

Erythema continues to decrease as well.

Scalp stabilisation: maintenance of results

0

Switch with placebo

Switch with placebo

-75%***

-80

D0

D3

D14

D28

Wilcoxon test vs D0 and Mann Whitney test vs placebo: ***p<0.001

Clinical efficacy #2

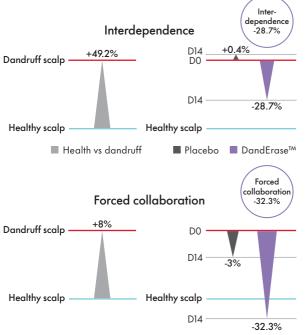
DandErase™ protects and restores the scalp Interabiome

Interabiome: microflora interactions, stability and resilience

A diverse panel of 20 volunteers aged 18-70 with oily, itchy scalps and 210-1400 dandruff counts participated in a double-blind study in France. After a 2-week washout, 10 participants used a 3% DandErase™ shampoo, while the other 10 used a placebo, applying it three times a week for 2 weeks. The scalp microbiome evolution was monitored through Real-Time PCR focusing on 20 specific targets*, compared to the same evaluation on 10 volunteers with a healthy scalp.

Results: DandErase™ optimises two parameters: interdependence and forced collaboration that should be low to ensure that the disruption of one strain does not compromise the others. Interdependence is almost 50% higher in a dandruff scalp compared to health population, and DandErase™ in 2 weeks reduces interdependence by 28.7% and forced collaboration by 32.3%. DandErase™ enhances scalp health fostering interabiome stability and resilience.

DandErase™ effectively reduces all Malassezia species over two weeks without altering bacterial balance, confirming its targeted selectivity.



^{*3} Cutibacterium species (+ genus), 4 Staphylococcus species (+ genus), Corynebacterium, Enterococcus, Lactobacillus, Prevotella, Streptococcus, Lawsonella clevelandensis, Pseudomonas aeruginosa, 3 Malassezia species (+ genus)

Anti-dandruff, soothing and scalp rebalancing activity

DandErase™ reduces dandruff towards a healthier scalp

In the same group of volunteers, dandruff and erythema were measured to confirm the benefits observed by a rebalanced Interabiome.

Results: DandErase™ significantly reduces dandruff up to 95.4% (D14) compared to baseline (D0), with 90% of participants experiencing improvement. Additionally, the erythema index decreases by 2.6x compared to the placebo, benefiting 80% of the volunteers.

Consumers Home Usage test (HUT) () 💿



DandErase™ confirms its anti-dandruff efficacy while promoting well-being

The product was tested for 14 days on consumers with dandruff and were users of a market-leading shampoo brand (126 French and 150 Chinese consumers, 50:50 men / women aged 19~59). They responded to 3 questionnaires at DO, D7 and D14, using Mood Portraits™ 2.0¹ and Finger Tracking².

1 Givaudan proprietary non-verbal neuroscience method using pictures to measure consumers' mood and emotional responses; 2 Neuroscience method measuring both implicit & explicit results.

Results: DandErase™ sets new standards in just one week: consumers massively perceived a strong anti-dandruff efficacy, performing better than their current shampoo (benchmark) and featuring an amelioration of well-being.

Dandruff reduction



notice an improvement of their well-being with a significant increase of positive emotions*

Well-being improvement

*relaxation, de-stress, and mindfulness / radiance

Better than benchmark



of consumers acknowledge the DandErase™ shampoo outperforms their current benchmark

fewer severe dandruff sufferers in just 7 days

Summary













Technical information

INCI: Water (and) Betaine (and) Potassium Lactate (and) Lactic Acid (and) Crocus Sativus

Flower Extract

Origin: Green fractionation

Preservation: None

Appearance: Light brown to brown liquid

Solubility: Hydrosoluble

Dosage: 3%

Processing: Can be added at the end of the formula process at a pH between 4 and 8 and a temperature below 40°C.

Benefits

Claims: Anti-dandruff*, itching reduction, redness reduction, scalp soothing, microbiome balancing, Malassezia spp.

reduction, long lasting effect, improves the appearance of the scalp, reduces flakiness, maintains a healthy

scalp**, optimal tolerability

Applications: Hair and scalp care, shampooing, rinse off and leave on scalp lotions, long lasting / maintenance scalp care

*The Givaudan Active Beauty product «DandEraseTM» is intended to be used only for cosmetic application. Anti-dandruff claim is allowed in cosmetic applications in Europe. Note that in the USA, anti-dandruff is considered OTC, in Korea as Drug, in Japan as Quasi-Drug. In China, despite there is no positive list of anti-dandruff agents, the concentration in finished products needs to be tested as well as the efficacy. It is the customer's responsibility to assess which claims are compliant with cosmetic regulation in the countries where the final product is launched.

** Claim not applicable in the US market.



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