

Bibliography report on how ingredients of ANTI-AGING CREAM can benefit skin health

CALENDULA OFFICINALIS

[A systematic review of Calendula officinalis extract for wound healing](#) Or Givol et al.

[Wound Repair and Regeneration 2019, 27 \(5\): 548-561.](#)

This systematic review **evaluates the role of *Calendula officinalis* flower extract as monotherapy compared to control for wound healing in vivo.** Searches were conducted in PubMed, EMBASE, Cochrane Central Register of Controlled Trials, CINAHL, and Scopus (up to April 2018) with 14 studies meeting the inclusion criteria, comprising 7 animal experiments and 7 clinical trials. Findings from the **review on acute wound healing showed faster resolution of the inflammation phase with increased production of granulation tissue in the test groups treated with extract.** These findings were consistent in five animal studies and one randomized clinical trial. Chronic wound healing studies were varied. Two clinical control studies on venous ulcers demonstrated decreased ulcer surface area compared to controls. Another randomized clinical trial demonstrated no improvement for the calendula group in diabetic leg ulcer healing. Burn healing similarly showed mixed results. Two animal studies demonstrated a prophylactic effect for the administration of calendula extract prior to burn injury. A randomized clinical trial of patients suffering from partial to full thickness burns demonstrated no benefit for topical application of calendula extract compared to controls. Two randomized clinical trials assessed the potential for extract to prevent acute post radiation dermatitis, with one study showing improvements compared to trolamine, while the other found no improvement compared to aqua gel cream. Animal studies provide moderate evidence for improved recovery from the inflammation phase and increased production of granulation tissue in calendula extract treatment groups. **This review identified some evidence for the beneficial effects of *C. officinalis* extract for wound healing, consistent with its role in traditional medicine.**

[Development of lamellar gel phase emulsion containing marigold oil \(Calendula officinalis\) as a potential modern wound dressing](#) C H Okuma et al.

[European Journal of Pharmaceutical Sciences 2015 April 25, 71: 62-72.](#)

Appropriate therapeutics for wound treatments can be achieved by studying the pathophysiology of tissue repair. Here we develop **formulations of lamellar gel phase**

(LGP) emulsions containing marigold (*Calendula officinalis*) oil, evaluating their stability and activity on experimental wound healing in rats. LGP emulsions were developed and evaluated based on a phase ternary diagram to select the best LGP emulsion, having a good amount of anisotropic structure and stability. The selected LGP formulation was analyzed according to the intrinsic and accelerated physical stability at different temperatures. In addition, in vitro and in vivo studies were carried out on wound healing rats as a model. The LGP emulsion (15.0% marigold oil; 10.0% of blend surfactants and 75.0% of purified water [w/w/w]) demonstrated good stability and high viscosity, suggesting longer contact of the formulation with the wound. No cytotoxic activity (50-1000 µg/mL) was observed in marigold oil. In the wound healing rat model, the LGP (15 mg/mL) showed an increase in the leukocyte recruitment to the wound at least on days 2 and 7, but reduced leukocyte recruitment after 14 and 21 days, as compared to the control. Additionally, collagen production was reduced in the LGP emulsion on days 2 and 7 and further **accelerated the process of re-epithelialization of the wound itself.** The methodology utilized in the present study has produced a potentially useful formulation for a **stable LGP emulsion-containing marigold, which was able to improve the wound healing process.**

[Extracts from *Calendula officinalis* offer in vitro protection against H₂O₂ induced oxidative stress cell killing of human skin cells](#)

[Abdullah M Alnuqaydan et al.](#)

[Phytotherapy Research: PTR 2015, 29 \(1\): 120-4.](#)

The in vitro safety and antioxidant potential of *Calendula officinalis* flower head extracts was investigated. The effect of different concentrations (0.125, 0.5, 1.0, 2.0 and 5.0% (v/v)) of *Calendula* extracts on human skin cells HaCaT in vitro was explored. Doses of 1.0% (v/v) (0.88 mg dry weight/mL) or less showed no toxicity. Cells were also exposed to the *Calendula* extracts for either 4, 24 or 48 h before being exposed to an oxidative insult (hydrogen peroxide H₂O₂) for 1 h. Using the MTT cytotoxicity assay, it was observed that two independent extracts of *C. officinalis* gave time-dependent and concentration-dependent H₂O₂ protection against induced oxidative stress in vitro using human skin cells. Pre-incubation with the *Calendula* extracts for 24 and 48 h increased survival relative to the population without extract by 20% and 40% respectively following oxidative challenge. The antioxidant potential of the *Calendula* extracts was confirmed using a complimentary chemical technique, the DPPH(●) assay. *Calendula* extracts exhibited free radical scavenging abilities. This study demonstrates that ***Calendula* flower extracts contain bioactive and free radical scavenging compounds that significantly protect against oxidative stress in a human skin cell culture model.**

[In vitro studies to evaluate the wound healing properties of *Calendula officinalis* extracts](#)

[Christoph Nicolaus et al.](#)

[Journal of Ethnopharmacology 2017 January 20, 196: 94-103.](#)

Calendula officinalis (pot marigold) flower extracts have a long-lasting tradition in ethnopharmacology. Currently, the **European Medicines Agency (EMA) has approved its lipophilic and aqueous alcoholic extracts as traditional medicinal products for the treatment of minor inflammation of the skin and as an aid in the healing of minor wounds.** The purpose of this study was to analyse the molecular mechanism of the

wound healing effects of *Calendula* extracts, which may reflect the phytomedicines currently used in the market. The effect of three different extracts from *Calendula* flowers (n-hexanic, ethanolic, aqueous) on the inflammatory phase of wound healing was studied in human immortalized keratinocytes and human dermal fibroblasts. An electrophoretic mobility shift assay on NF- κ B-DNA binding, qRT-PCR and ELISA experiments were performed. The effect of *Calendula* extracts on the new tissue formation phase of wound healing was evaluated by studying the migratory properties of these extracts, triterpene mixtures and single compounds in human immortalized keratinocytes using the scratch assay. Finally, the effect of the extracts on the formation of granulation tissue in wound healing was studied using bacterial collagenase isolated from *Clostridium histolyticum* and the determination of soluble collagen in the supernatant of human dermal fibroblasts. The n-hexanic and the ethanolic extracts from *Calendula* flowers influence the inflammatory phase by activating the transcription factor NF- κ B and by increasing the amount of the chemokine IL-8, both at the transcriptional and protein level, in human immortalized keratinocytes. The migration of the keratinocytes during the new tissue formation phase was only marginally influenced in the scratch assay. However, it can be assumed that **the granulation tissue was affected, as the ethanolic extract inhibited the activity of collagenase in vitro and enhanced the amount of collagen in the supernatant of human dermal fibroblasts**. Our results contribute to a better understanding of the **wound healing properties of the traditional medicinal plant *Calendula officinalis***. However, further studies are necessary to evaluate which of its known constituents are responsible for these effects. **Triterpenes seem to play only a marginal role, but carotene and xanthophyll derivatives should garner more attention in future studies.**

[Anti-Inflammatory Activity of *Calendula officinalis* L. Flower Extract.](#)
[Silva D et al.](#)
[Cosmetics 2021, 8, 31](#)

The use of calendula for its lenitive properties' dates to the XII century. This **plant contains several bioactive compounds, including terpenoids, terpenes, carotenoids, flavonoids and polyunsaturated fatty acids**. Calendula flower extract is used in soothing cosmetics, such as after-sun, sensitive skin and eye contour products. The anti-inflammatory properties of this ingredient were demonstrated in an animal model, but the mechanism of action is poorly understood. Therefore, our work explored the **effect of a calendula flower extract on NO production, a pro-inflammatory radical produced by nitric oxide synthase (iNOS) and highly released by innate immune cells in inflammatory-related pathologies**. NO production was evoked by the Toll-like receptor 4 agonist lipopolysaccharide (LPS) in macrophages, using concentrations that did not compromise cells viability. This ingredient exhibited a dose-dependent NO inhibition, reaching 50% at 147 μ L/mL without cytotoxicity. Together with previous literature, these results provide **experimental evidence on the anti-inflammatory properties of calendula flower extract, as well as its usefulness in cosmetics with soothing properties and adjunctive skin care in the treatment of the diseases associated with dysregulation of the NO signaling cascade.**

[Use of calendula ointment after episiotomy: a randomized clinical trial](#)
[Carlo De Angelis et al.](#)
[Journal of Maternal-fetal & Neonatal Medicine 2020, 27: 1-5.](#)

Episiotomy is associated with an increased risk of postpartum pain, bleeding, and dyspareunia. The hypothesis of this trial was that in women with singleton pregnancy, and spontaneous labor at term, **use of calendula ointment would reduce pain after episiotomy**. This was a single-center parallel group randomized trial of women with singleton pregnancies and spontaneous labor at term who were randomized to either use of calendula ointment (i.e. intervention group) or standard care (i.e. control group) after episiotomy. Eligible women were those with singleton gestations in spontaneous labor and vertex presentation at term. Women with premature rupture of membranes were excluded from the study. Women in the intervention group were recommended use of calendula ointment 4 h after the episiotomy and then every 8 h for 10 days. The primary outcome was the pain level. Pain level was self-reported and recorded using the verbal rating scale (VRS). The effect of the calendula ointment was quantified as mean difference (MD) with 95% confidence interval (CI). During the study, 100 women agreed to take part in the study, underwent randomization, and were enrolled in this trial. Of the 100 randomized women, 50 were randomized to the calendula ointment group, and 50 to the control group. No women were excluded after randomization or lost to follow up. **Women who received calendula ointment after episiotomy compared to standard care had a significantly lower pain level starting from day two and during all the follow-up. Calendula ointment also improve wound healing in terms of redness and edema. Use of calendula ointment significantly reduce pain after episiotomy.**

[Protective effect of Calendula officinalis extract against UVB-induced oxidative stress in skin: evaluation of reduced glutathione levels and matrix metalloproteinase secretion](#)

[Yris Maria Fonseca et al.](#)

[Journal of Ethnopharmacology 2010 February 17, 127 \(3\): 596-601.](#)

Calendula officinalis flowers have long been employed time in folk therapy, and more than 35 properties have been attributed to decoctions and tinctures from the flowers. The main uses are as **remedies for burns (including sunburns), bruises and cutaneous and internal inflammatory diseases of several origins**. The recommended doses are a function both of the type and severity of the condition to be treated and the individual condition of each patient. Therefore, the present study investigated the potential use of ***Calendula officinalis* extract to prevent UV irradiation-induced oxidative stress in skin**. Firstly, the physico-chemical composition of **marigold extract (ME)** (hydroalcoholic extract) was assessed and the in vitro antioxidant efficacy was determined using different methodologies. Secondly, the cytotoxicity was evaluated in L929 and HepG2 cells with the MTT assay. Finally, the in vivo protective effect of ME against UVB-induced oxidative stress in the skin of hairless mice was evaluated by determining reduced glutathione (GSH) levels and monitoring the secretion/activity of metalloproteinases. The polyphenol, flavonoid, rutin and narcissin contents found in ME were 28.6 mg/g, 18.8 mg/g, 1.6 mg/g and 12.2mg/g, respectively and evaluation of the in vitro antioxidant activity demonstrated a dose-dependent effect of ME against different radicals. Cytotoxicity experiments demonstrated that ME was not cytotoxic for L929 and HepG2 cells at concentrations less than or equal to of 15 mg/mL. However, concentrations greater than or equal to 30 mg/mL, toxic effects were observed. Finally, **oral treatment of hairless mice with 150 and 300 mg/kg of ME maintained GSH levels close to non-irradiated control mice. In addition, this extract affects the activity/secretion of matrix metalloproteinases 2 and 9 (MMP-2 and -9) stimulated by exposure to UVB irradiation**. However, additional studies are required to have a complete understanding of the **protective effects of ME for skin**.

Effectiveness of nursing interventions in preventing and treating radiotherapy side effects in cancer patients: a systematic review

Aline Moraes de Abreu et al.

Revista da Escola de Enfermagem da USP 2021, 55: e03697

To synthesize the best available evidence on the **effectiveness of nursing interventions in radiotherapy patient care and to summarize the evidence on the experience and acceptability of interventions reported by health professionals involved in the prevention and treatment of side effects**. A mixed-method systematic review.

Quantitative and qualitative studies are presented. Twelve studies published between 2013 and 2017 were included. Most interventions found focused on skin care, oral care, nausea and vomiting and nursing consultation. In accordance with high level of evidence and recommendation grade of the studies, the use of *Calendula officinalis* and thyme honey were considered **effective for preventing and treating radiodermatitis and mucositis**, respectively.

Treatment of acute wounds in hand with Calendula officinalis L.: A randomized trial

Giana Silveira Giotri et al.

Tissue Barriers 2021 October 21, : 1994822.

Most injuries in the hand and fingers, especially on the digital pulps, are suited for healing by secondary intention. Nevertheless, delay in epithelization seems to unfavorably restrict this technique. The purpose of this controlled randomized clinical trial is to **analyze by means of photo planimetry the progression of the healing process by secondary intention in acute wounds of the hand using the standardized extract of *Calendula officinalis* L. (SEC)**. The cohort of eligible participants included two groups of 20 patients with skin loss in the hand and fingers treated by secondary intention. Control group (CG) used mineral oil and **intervention group (IG) received SEC**. Wound pictures were captured at each outpatient assessment until epithelization was achieved and measured with ImageJ. Intervention group (IG) and control group (CG) with 19 wounds each, primarily formed by men in their 40's with wounds in their index and ring fingers on the left side, showed homogeneous variables and similar initial wound areas.

Epithelization time was shorter and healing speed was faster in IG

(IG = 8.6 ± 4.7 days and $9.5 \pm 5.8\%$ day versus CG = 13.2 ± 7.4 days and $6.2 \pm 2.9\%$ day, $p < 0.05$), leading to the **conclusion that healing by secondary intention in acute wounds of the hand and fingers with SEC led to a faster epithelization**.

Biological Activities of Oleanolic Acid Derivatives from Calendula officinalis Seeds

Ahmed Zaki et al.

Phytotherapy Research: PTR 2016, 30 (5): 835-41.

Phytochemical examination of butanol fraction of *Calendula officinalis* seeds led to the isolation of **two compounds identified as 28-O- β -D-glucopyranosyl-oleanolic acid 3-O- β -D-glucopyranosyl (1 \rightarrow 3)- β -D-glucopyranosiduronic acid (CS1) and oleanolic acid 3-O- β -D-glucopyranosyl (1 \rightarrow 3)- β -D-glucopyranosiduronic acid (CS2)**.

Biological evaluation was carried out for these two compounds such as melanin biosynthesis inhibitory, hyaluronic acid production activities, anti obesity using lipase inhibition and adipocyte differentiation as well as evaluation of the protective effect against hydrogen peroxide induced neurotoxicity in neuro-2A cells. The results showed that, **compound CS2 has a melanin biosynthesis stimulatory activity**; however, compound **CS1 has a potent stimulatory effect for the production of hyaluronic acid on normal human dermal fibroblast from adult** (NHDF-Ad). Both compounds did not show any inhibitory effect on both lipase and adipocyte differentiation. Compound CS2 could protect neuro-2A cells and increased cell viability against H₂O₂. These activities (melanin biosynthesis stimulatory and protective effect against H₂O₂ of CS2 and hyaluronic acid productive activities of these triterpene derivatives) have been reported for the first time.

Calendula extract: effects on mechanical parameters of human skin

Naveed Akhtar et al.

Acta Poloniae Pharmaceutica 2011, 68 (5): 693-701.

The aim of this study was to evaluate the effects of newly **formulated topical cream of *Calendula officinalis* extract on the mechanical parameters of the skin** by using the cutometer. The Cutometer 580 MPA is a device that is designed to measure the mechanical properties of the skin in response to the application of negative pressure. This non-invasive method can be **useful for objective and quantitative investigation of age related changes in skin, skin elasticity, skin fatigue, skin hydration, and evaluation of the effects of cosmetic and antiaging topical products**. Two creams (base and formulation) were prepared for the study. **Both the creams were applied to the cheeks of 21 healthy human volunteers for a period of eight weeks**. Every individual was asked to come on week 1, 2, 3, 4, 5, 6, 7, and 8 and measurements were taken by using Cutometer MPA 580 every week. Different mechanical parameters of the skin measured by the cutometer were; R0, R1, R2, R5, R6, R7, and R8. These were then evaluated statistically to measure the effects produced by these creams. Using ANOVA, and t-test it was found that R0, and R6 were significant ($p < 0.05$) whereas R1, R2, R5, R7, R8 were insignificant ($p > 0.05$). The instrumental measurements produced by formulation reflected **significant improvements in hydration and firmness of skin**.

Anti-inflammatory action of a group of plant extracts

T Shipochliev et al.

Veterinarno-meditsinski Nauki 1981, 18 (6): 87-94.

Use was made of Wistar albino rats in which an inflammation was induced via the simultaneous injection of caraginan and prostaglandin E1 in order to evaluate the **antiinflammatory activity of 6 freeze dried plant extracts**. It was found that with such model of inflammation the inflammatory effect of caraginan was strongly enhanced, which was accompanied by the rapid and prolific white blood cell extravasates. The freeze-dried extracts of St. John's-wort (*Hypericum perforatum* L.), **potmarigold calendula (*Calendula officinalis* L.)**, camomile (*Matricaria chamomilla* L.) and plantain (*Plantago lanceolata* L. et *Pl. major* L.) were found to **suppress both the inflammatory effect and the leukocyte infiltration**. The extracts of symphytum (*Symphytum officinale* L.) and those of flax seed (*Linum usitatissimum* L.) did not inhibit the inflammation, however, they suppressed the leukocyte infiltration at the 3rd and 4th hour of the induced inflammation.

Antioxidant and Skin Anti-Aging Effects of Marigold Methanol Extract

Chul Ho Kang et al.

Toxicological Research 2018, 34 (1): 31-39

The objective of this study was to evaluate the **antioxidant and anti-aging effects of marigold methanol extract (MGME) in human dermal fibroblasts**. Total polyphenolic and flavonoid contents in MGME were 74.8 mg TAE (tannic acid equivalent)/g and 85.6 mg RE (rutin equivalent)/g, respectively. MGME (500 µg/mL) increased 1,1-diphenyl-2-picryl hydrazyl (DPPH) and 2,2'-azino-3-ethylbenzothiazoline-6-sulfonic acid (ABTS) radical-scavenging, and superoxide dismutase (SOD)-like antioxidant activities by 36.5, 54.7, and 14.8%, respectively, compared with the control. At 1,000 µg/mL, these activities increased by 63.7, 70.6, and 20.6%, respectively. MGME (100 µg/mL) significantly increased the synthesis of type 1 procollagen by 83.7% compared with control treatment. It also significantly decreased Matrix Metalloproteinase-2 (MMP-2) activity and MMP-1 mRNA expression by 36.5% and 69.5%, respectively; however, it significantly increased laminin-5 mRNA expression by 181.2%. **These findings suggest that MGME could protect human skin against photo-aging by attenuating oxidative damage, suppressing MMP expression and/or activity as well as by stimulating collagen synthesis.**

Extraction and Clinical Application of Calendula officinalis L. Flowers Cream

Khulood M. Alsaraf et al.

IOP Conf. Series: Materials Science and Engineering 571 (2019) 012082

The results of the HPLC analysis indicated that marigold flowers extract contain nine different active compounds, including Vitexin 11.40%, Rutin 12.29%, Quercetin-3-3galactosid 12.64%, Luteolin-7-glucose 9.27%, Quercetin-3glucoside 7.38%, Quercitrin 9.83%, Myricetin 10%, Luteolin 10.72%, Apigenin 7.08% and kampferol 9.37%. The results of a clinical study showed the effect of marigold flowers extract cream as an antioxidant which protected the skin in particular from oxidative damage after sunburn and reduced the symptoms of skin aging. This effect was evident in both concentrations 10% and 15% when compared with control. Control response rate, 10% of marigold flowers cream and 15% of flowers extract cream were reached to 76%, 85% and 92% within two weeks of treatment respectively. **The Conclusion of this study showed the importance of marigold flowers extract as a source of bioactive compounds such as rutin and quercetin derivatives, vitexin, luteoline, apigenin and kampferol which act as an antioxidant to restore skin health and aging resistance. This study approved that marigold flowers extract characteristics can make it the main ingredients in the preparation of topical agents for the treatment of various skin diseases.**

Herbal anti-inflammatory agents for skin disease

J Graf

Skin Therapy Letter 2000, 5 (4): 3-5.

Herbs have been used in clinical medicine for thousands of years. However, it is only in recent times that we have been able to employ scientific methods to prove the efficacy of many of these herbs and to give us a better understanding of their mechanisms of action. This article will focus on the use of herbs in various dermatological conditions characterized by inflammation and pruritus. Topical preparations of many of these herbs

are more commonplace in Europe. However, their availability is increasing in the US. As this is occurring we are witnessing a growing marriage between alternative and traditional medicines. **Calendula (*Calendula officinalis*)**, derived from the marigold plant, is quite widely used in topical skin and hair preparations as a soothing ingredient. Its **anti-inflammatory effects are a result of triterpene flavonoids and saponins**. It has been used topically as an antiseptic agent and applied to poorly healing wounds.

Characterization of Biologically Active Substances from *Calendula officinalis*

Petra Lovecka et al.

Current Pharmaceutical Biotechnology 2017, 18 (14): 1167-1174.

The aim of this work was to compare **water and organic extracts, infusions and tinctures from flowers and leaves of *Calendula officinalis* in terms of their biological activity and composition**. The purpose of work was investigation whether the leaves and stems are really the waste or they contain interesting substances which could be utilized. **Antimicrobial, antifungal, antioxidant and anti-inflammatory activities were studied**. Then, the ability to inhibit collagenase was studied as well. Cytotoxicity was tested for all the samples on **mammalian cell lines**. To determine the composition of extracts, infusions and tinctures phytochemical analysis (the set of colour reactions for the detection of groups of biologically active compounds) was carried out and showed that samples from flowers and leaves contain the same groups of biologically active substances (**proteins and amino acids, reducing sugars, flavonoids, saponins, phenolics, terpenoids, steroids, glycosides**). The **antimicrobial activity of tested samples was proved**, where the most sensitive bacterium was *Micrococcus luteus* and the most sensitive yeast was *Geotrichum candidum*. The study of anti-collagenase activity has shown that the enzymatic reaction of collagenase was affected by all tested samples and their effect was concentration dependent. Using cell line RAW 264.7, **antiinflammatory activity of all samples was observed**. Tincture of leaves was the most effective.

Anti-inflammatory, anti-tumor-promoting, and cytotoxic activities of constituents of marigold (*Calendula officinalis*) flowers

Motohiko Ukiya et al.

Journal of Natural Products 2006, 69 (12): 1692-6.

Ten oleanane-type triterpene glycosides, 1-10, including four new compounds, calendulaglycoside A 6'-O-methyl ester (2), calendulaglycoside A 6'-O-n-butyl ester (3), calendulaglycoside B 6'-O-n-butyl ester (5), and calendulaglycoside C 6'-O-n-butyl ester (8), along with five known flavonol glycosides, 11-15, were **isolated from the flowers of marigold (*Calendula officinalis*)**. Upon evaluation of compounds 1-9 for inhibitory activity against 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced inflammation (1 microg/ear) in mice, **all of the compounds, except for 1, exhibited marked anti-inflammatory activity**, with ID50 values of 0.05-0.20 mg per ear. In addition, when 1-15 were evaluated against the Epstein-Barr virus early antigen (EBV-EA) activation induced by TPA, compounds 1-10 exhibited moderate inhibitory effects (IC50 values of 471-487 mol ratio/32 pmol TPA). Furthermore, upon evaluation of the cytotoxic activity against human cancer cell lines in vitro in the NCI Developmental Therapeutics Program, **two triterpene glycosides, 9 and 10, exhibited their most potent cytotoxic effects against colon cancer, leukemia, and melanoma cells**.

[European Union herbal monograph on *Calendula officinalis* L., flos](#)
[27 March 2018 EMA/HMPC/437450/2017](#)
[Committee on Herbal Medicinal Products \(HMPC\)](#)

Therapeutic indication:

- 1) Traditional herbal medicinal product for the **symptomatic treatment of minor inflammations of the skin (such as sunburn) and as an aid in healing of minor wounds.**
- 2) Traditional herbal medicinal product for the symptomatic treatment of minor inflammations in the mouth or the throat. The product is a traditional herbal medicinal product for use in the specified indication exclusively based upon long-standing use.

[Assessment report on *Calendula officinalis* L., flos](#)
[27 March 2018 EMA/HMPC/603409/2017](#)
[Committee on Herbal Medicinal Products \(HMPC\)](#)

Based on the documentation found in handbooks, as listed above and the actual market data received from the Competent Authorities **sufficient information was found for the herbal substance, comminuted herbal substance, liquid extracts and tincture to justify at least 30 years of medicinal use including at least 15 years of the EU for the herbal substance *Calendula* flower. All above mentioned preparations are for cutaneous use and some for oromucosal use, have a specified strength and posology and have indications suitable to meet the legal requirements in the relevant route of administration.**

[Health Claim 4369 - *Calendula officinalis*-marigold-*Calendulae* flowers - Skin and mucosal healing agent - due to polysaccharides, triterpene flavonoids and saponins content](#)
EFSA-Q-2010-00322 | Status: Intake

Last updated: 15/12/2016

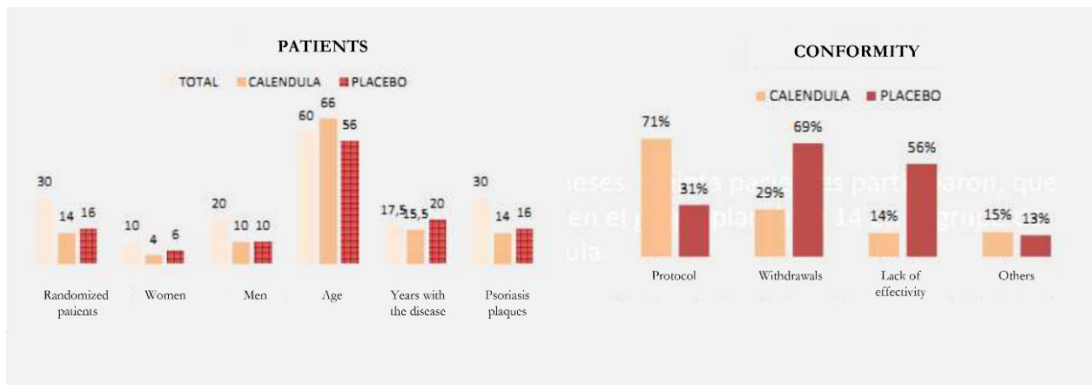
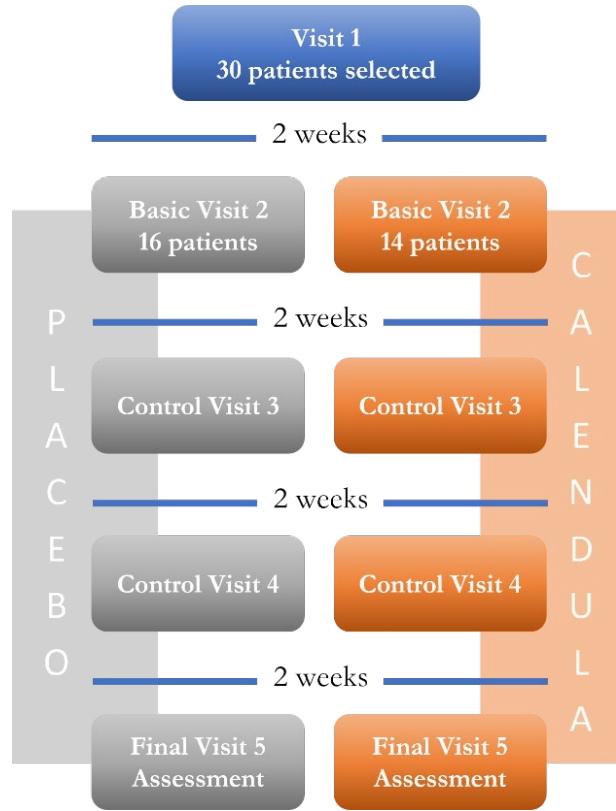
No Output has been formed yet for this question.

[Prospective, randomized, double-blind, placebo-controlled study on the effectiveness and tolerability of the active calendula extract in patients with flaking and mild to moderate skin alterations](#)

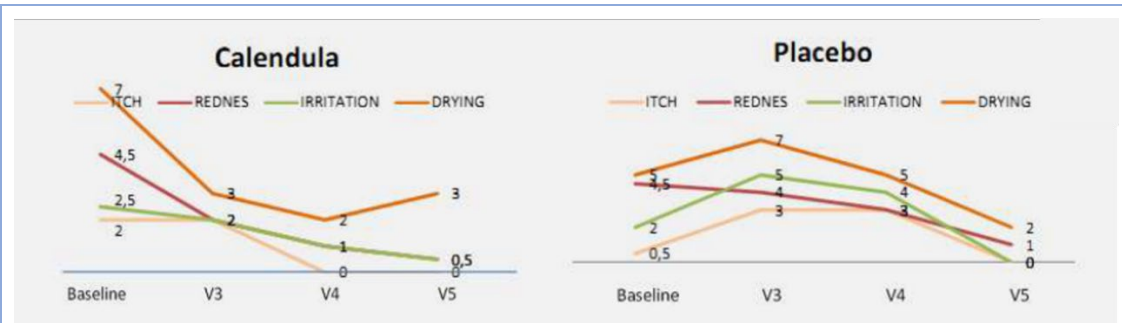
[Nuria Lamas Doménech, Manuel Sánchez Regaña, María José Aldunce Soto, Vicente Expósito Serrano, Cristian Fischer Levancini, Helena Collgros, Montse Salleras Redonnet. Salleras Redonnet.](#)
[Sagrat Cor University Hospital, Dermatology Service. Service. Barcelona.](#)

Inclusion criteria	Exclusion criteria
<p>Male or female, aged 18 to 70 years.</p> <p>Able and willing to give written informed consent to participate in the study.</p> <p>Diagnostic criteria for mild (PASI <3%) and stable psoriasis.</p> <p>Stable plaque psoriasis: involvement of at least 10% of the body surface.</p> <p>Guttate psoriasis.</p> <p>Susceptible to respond to topical treatment.</p> <p>Willing and able to understand and comply with all study requirements.</p>	<p>Known hypersensitivity to calendula extract or any ingredient in the formulation.</p> <p>History of alcohol or illicit drug use within 2 years prior to V1 (screening visit).</p> <p>Subjects who received an investigational product (or medical device) within 3 months prior to screening, or who are participating in a clinical trial to investigate a product (or medical device).</p> <p>Pregnant or breastfeeding.</p> <p>Other inflammatory skin disease that is not primarily due to psoriasis.</p> <p>Subjects who have received systemic treatments for psoriasis within 6 weeks prior to V1 (screening visit) and/or are unwilling to refrain from using topical or systemic treatments for psoriasis during the study.</p> <p>Subjects who received phototherapy within 4 weeks prior to V1 (screening visit) and/or who are unwilling to abstain from phototherapy throughout the study.</p>
<p>Methods</p> <ul style="list-style-type: none"> - Single-center, prospective, randomized, double-blind, placebo-controlled, parallel-group study in 30 patients with mild to moderate stable psoriasis. - Product: cream containing a special extract of marigold flower, supplied by Phytocutan S.L. (Barcelona, Spain). - Placebo: cream without extract, but with the same characteristics of the product. - Two-week washout period. - The product was applied twice a day for eight weeks. - Control visits were performed every two weeks during which overall PASI and target plaque evolution were assessed using the visual analog scale for erythema, infiltration, desquamation and pruritus. - Scores were assessed using the Psoriasis Area Severity Index (PASI) and Patient Global Impression of Change (PGIC). 	

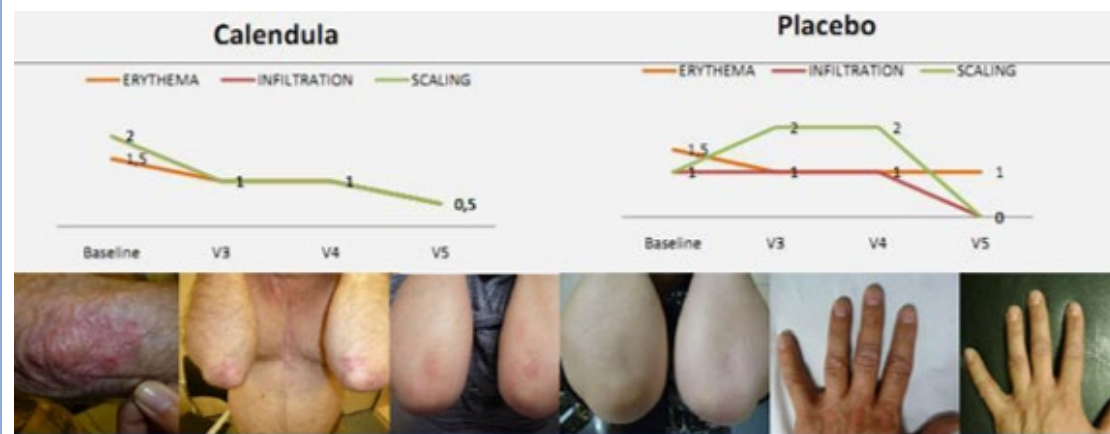
Study design



No adverse effects were reported.



The evolution of edges and symptoms in the target psoriasis plaque showed a decrease in the group treated with calendula, while in the placebo group there was a clear deterioration. An improvement was observed in the placebo, but only between visits 4 and 5, when 69% of patients had dropped out, mainly due to lack of efficacy (56%).



CONCLUSIONS

- The results of the study showed an improvement in patients treated with the cream containing calendula flower extract compared to those treated with placebo.
- The cream containing special calendula flower extract was very well tolerated by the patients because it is natural. It works best in water-soluble form.
- Our calendula active ingredient improves and cares for skin disorders.
- The clinical trial described is an example of what is described in the properties of the beneficial effects of calendula on the skin.

OLEA EUROPAEA OIL L. - OLIVE OIL

[Effects of Olive Oil on Striae Gravidarum in Primiparous Women: A Randomized Controlled Clinical](#)
[Ayça Solt Kırca, Derya Kanza Gül](#)

Alternative Therapies in Health and Medicine 2021 September 24.

The development of **striae gravidarum (SG), stretch marks, is one of the most common skin changes during pregnancy.** The number of studies conducted on the reduction or prevention of SG, especially on the effects of olive oil, is limited. The study intended to **evaluate the clinical efficacy of olive oil in reducing the severity and preventing the progression of SG when used from the third trimester of pregnancy to the child's birth.** Participants were 156 Turkish women having their first pregnancies and in their third trimester. Participants were randomly assigned to either the intervention or the control group. Women in the intervention group applied olive oil to their abdomens twice a day, in the morning and evening. The control group used no intervention. The participants' striae levels were assessed using the Fitzpatrick Skin Type Scale and Davey's Severity Score. A statistically significant difference existed between the intervention and the control groups in terms of incidence and type of striae gravidarum, with the intervention group having a 50% incidence and 85.9% type 2 striae compared to the control group's 69.2% incidence and 35.9% type 4 striae. According to Davey's Severity Score, **the severity of striae was significantly lower in the intervention group compared to the control group, with the scores being 2 and 4, respectively. Using olive oil was very effective in reducing the severity and preventing the progression of striae gravidarum.**

Novel antibacterial and emollient effects of coconut and virgin olive oils in adult atopic dermatitis

Vermén M Verallo-Rowell et al.

Dermatitis 2008, 19 (6): 308-15.

Atopic dermatitis (AD) skin is dry and readily colonized by *Staphylococcus aureus* (SA). **Coconut and olive oils are traditionally used to moisturize and treat skin infections.** The aim of the study was to **compare virgin coconut oil (VCO) and virgin olive oil (VOO) in moisturizing dryness and removing SA from colonized AD skin.** This was a double-blind controlled trial in two outpatient dermatology clinics with adult AD patients who were diagnosed by history, pattern, evolution, and skin lesions and who were randomized to apply VCO or VOO twice daily at two noninfected sites. SA cultures, photography, and objective-SCORAD severity index (O-SSI) scoring were done at baseline and after 4 weeks. Twenty-six subjects each received VCO or VOO. Of those on VCO, 20 were positive for SA colonies at baseline versus 12 on VOO. Post intervention, only 1 (5%) VCO subject remained positive versus 6 (50%) of those on VOO. Relative risk for VCO was 0.10, significantly superior to that for VOO (10:1, $p = .0028$; 95% CI, 0.01-0.73); thus, the number needed to treat was 2.2. For the O-SSI, the difference was not significant at baseline ($p = .15$) but was significantly different post treatment ($p = .004$); this was reduced for both oils ($p < .005$) but was greater with VCO. **VCO and monolaurin's O-SSI reduction and in vitro broad-spectrum activity against SA (given clinical validity here), fungi, and viruses may be useful in the proactive treatment of AD colonization.**

Topical use of olive oil preparation to prevent radiodermatitis: results of a prospective study in nasopharyngeal carcinoma patients

Zhaoyang Cui et al.

International Journal of Clinical and Experimental Medicine 2015, 8 (7): 11000-6.

Radiodermatitis is a common side effect of radiotherapy. The purpose of this study was to **evaluate the effectiveness of topical olive oil in the prevention of acute radiodermatitis in patients with nasopharyngeal carcinoma (NPC) who were undergoing concurrent chemoradiotherapy.** A prospective study was conducted in patients with NPC. The patients were randomized into the intervention (n = 47) and control (n = 47) groups. Patients in the control group were treated with a general skin care regimen (placebo), whereas patients in the intervention group were treated with olive oil thrice daily for 7 weeks during chemoradiotherapy and for two weeks thereafter. On a weekly basis for a total duration of 9 weeks, a blinded observer assessed the severity of dermatitis, which was graded from 0 to 4 according to the Radiation Therapy Oncology Group (RTOG) criteria and the Visual Analog Scale (VAS) score. Mild reactions due to radiation (grades I and II) occurred in 93.6% of the intervention group and in 72.3% of the control group. **Patients in the intervention group encountered significantly less severe dermatitis during chemoradiotherapy compared with patients in the control group (P < 0.01).** A multivariate analysis revealed that the use of olive oil (P < 0.01) was significantly associated with a decrease in skin injuries. **The prophylactic use of olive oil was associated with a significant decrease in the intensity of acute dermatitis in NPC patients. The results of this trial indicate that olive oil holds promise as a safe and effective prophylactic treatment for radiodermatitis.**

[Olive oil-induced reduction of oxidative damage and inflammation promotes wound healing of pressure ulcers in mice](#)

[Aline Donato-Trancoso et al.](#)

[Journal of Dermatological Science 2016, 83 \(1\): 60-9.](#)

The **overproduction of reactive oxygen species (ROS) and exacerbated inflammatory response are the main events that impair healing of pressure ulcers.** Therefore, **olive oil may be a good alternative to improve the healing of these chronic lesions due to its anti-inflammatory and antioxidant properties.** This study investigated the effect of olive oil administration on wound healing of pressure ulcers in mice. Male Swiss mice were daily treated with olive oil or water until euthanasia. One day after the beginning of treatment, two cycles of ischemia-reperfusion by external application of two magnetic plates were performed in skin to induced pressure ulcer formation. The olive oil administration accelerated ROS and nitric oxide (NO) synthesis and reduced oxidative damage in proteins and lipids when compared to water group. The inflammatory cell infiltration, gene tumor necrosis factor- α (TNF- α) expression and protein neutrophil elastase expression were reduced by olive oil administration when compared to water group. The re-epithelialization and blood vessel number were higher in the olive oil group than in the water group. The olive oil administration accelerated protein expression of TNF- α , active transforming growth factor- β 1 and vascular endothelial growth factor-A when compared to water group. **The collagen deposition, myofibroblastic differentiation and wound contraction were accelerated by olive oil administration when compared to water group.** Olive oil administration improves cutaneous wound healing of pressure ulcers in mice through the acceleration of the ROS and NO synthesis, which **reduces oxidative damage and inflammation and promotes dermal reconstruction and wound closure.**

[Natural Oils for Skin-Barrier Repair: Ancient Compounds Now Backed by Modern Science](#)

[Alexandra R Vaughn et al.](#)

[American Journal of Clinical Dermatology 2018, 19 \(1\): 103-117.](#)

Natural plant oils are commonly used as topical therapy worldwide. They are usually easily accessible and are relatively inexpensive options for skin care. **Many natural oils possess specific compounds with antimicrobial, antioxidant, anti-inflammatory, and anti-itch properties, making them attractive alternative and complementary treatments for xerotic and inflammatory dermatoses associated with skin-barrier disruption.**

Unique characteristics of various oils are important when considering their use for topical skin care. Differing ratios of essential fatty acids are major determinants of the barrier repair benefits of natural oils. Oils with a higher linoleic acid to oleic acid ratio have better barrier repair potential, whereas oils with higher amounts of irritating oleic acid may be detrimental to skin-barrier function. Various extraction methods for oils exist, including cold pressing to make unrefined oils, heat and chemical distillation to make essential oils, and the addition of various chemicals to simulate a specific scent to make fragranced oils. The method of oil processing and refinement is an important component of selecting oil for skin care, and cold pressing is the preferred method of oil extraction as the heat- and chemical-free process preserves beneficial lipids and limits irritating byproducts. **This review summarizes evidence on utility of natural plant-based oils in dermatology, particularly in repairing the natural skin-barrier function, with the focus on natural oils, including *Olea europaea* (olive oil), *Helianthus annuus* (sunflower seed oil), *Cocos nucifera* (coconut oil), *Simmondsia chinensis* (jojoba oil), *Avena sativa* (oat oil), and *Argania spinosa* (argan oil).**

[Multiple Biological Effects of Olive Oil By-products such as Leaves, Stems, Flowers, Olive Milled Waste, Fruit Pulp, and Seeds of the Olive Plant on Skin](#)

[Asuka Kishikawa et al.](#)

[Phytotherapy Research: PTR 2015, 29 \(6\): 877-86.](#)

As olive oil production increases, so does the amount of olive oil by-products, which can cause environmental problems. Thus, new ways to utilize the by-products are needed. In the present study, **five bioactive characteristics of olive oil by-products were assessed, namely their antioxidant, anti-bacterial, anti-melanogenesis, anti-allergic, and collagen-production-promoting activities.** First, the extracts of leaves (May and October), stems (May and October), flowers, olive milled waste, fruit pulp and seeds were prepared using two safe solvents, ethanol and water. According to HPLC and LC/MS analysis and Folin-Ciocalteu assay, the ethanol extracts of the leaves (May and October), stems (May and October) and flowers contained oleuropein, and the ethanol extract of the stems showed the highest total phenol content. **Oleuropein may contribute to the antioxidant and anti-melanogenesis activities of the leaves, stems, and flowers.** However, **other active compounds or synergistic effects present in the ethanol extracts** are also likely to contribute to the **anti-bacterial activity of the leaves and flowers**, the anti-melanogenesis activity of some parts, the anti-allergic activity of olive milled waste, and the **collagen-production-promoting activity of the leaves, stems, olive milled waste and fruit pulp.** This study provides evidence that the by-products of olive oil have the potential to be further developed and used in the skin care industry.

Design and evaluation of novel topical formulation with olive oil as natural functional active

Ana Henriques Mota et al.

Pharmaceutical Development and Technology 2018, 23 (8): 794-805.

Currently, the innovative skin research is focused on the development of novel topical formulations loaded with natural functional actives. The health benefits of olive oil are unsurpassed and many others are revealed as research studies allow the understanding of its unlimited properties. **Olive oil has a protective toning effect on skin**, but it is not transported effectively into its layers. Aiming the **development of a cosmetic formulation for skin photoprotection and hydration**, we have prepared and characterized macro-sized particles, made of a hydrogel polymer, loaded with olive oil. Alginate beads were uniform in shape, with minimal oil leakage, offering interesting prospects for encapsulation of lipophilic and poorly stable molecules, like olive oil. In vitro photoprotection and in vivo tolerance tests were in favor of this application. Thus, this study suggests that the **incorporation of the olive oil-loaded particles into a cream formulation provides strong moisturizing properties and a photoprotective potential, when applied to healthy subjects.**

Observer-blind randomized controlled study of a cosmetic blend of safflower, olive and other plant oils in the improvement of scar and striae appearance

S Bielfeldt, J Blaak et al.

International Journal of Cosmetic Science 2018, 40 (1): 81-86.

The normal process of skin tissue repair following injury invariably results in visual scarring. It is known that topical treatment with hydrophobic cosmetics rich in silicone and mineral oil content can improve the appearance of scars and striae. Given lifestyle preferences of many cosmetic consumers towards so-called natural treatments, the objective of this controlled randomized study was to investigate the efficacy of a **plant body oil rich in oleic and linoleic acids (Bio Skin Oil®) for improving the appearance of scars and striae**. A panel of 80 volunteers with non-hypertrophic scars (40) or stretch marks (40) not older than 3 years applied a cosmetic face and body oil for 8 weeks. Compared to an untreated scar/stretch mark region, a blinded investigator as well as volunteer assessments with given observed parameters demonstrated the efficacy of the oil under test. On the Observer Scar Assessment Scale (OSAS), the mean score was reduced on the product-treated area by approximately 5% ($P = 0.006$). The untreated area remained unchanged. Observed effects by volunteers were more pronounced - Patient Scar Assessment Scale (PSAS) giving a reduction of approximately 20% on the treated area, and on the control untreated area a reduction of approximately 6%. The overall product effect of 14% was shown to be clearly significant ($P = 0.001$). All statements relating to product traits achieved higher frequencies of agreements than of non-agreements and were therefore assessed positively by the volunteers. Highest frequencies of agreements occurred in statements that the test product provides a long-lasting, soft and supple skin feeling (93%); caring effect (87%); and quick absorbance (84%). Agreement was also found for statements that the product improves the skin appearance (61%) and that scars/striae appear less pronounced (51%). Only 17% of volunteers felt the oil had no benefit to the

appearance of their scars/striae. The **oil blend under test is effective in improving the appearance of non-keloid scars and striae.**

Scientific Opinion on the substantiation of health claims related to polyphenols in olive and protection of LDL particles from oxidative damage (ID 1333, 1638, 1639, 1696, 2865), maintenance of normal blood HDL cholesterol concentrations (ID 1639), maintenance of normal blood pressure (ID 3781), “anti-inflammatory properties” (ID 1882), “contributes to the upper respiratory tract health” (ID 3468), “can help to maintain a normal function of gastrointestinal tract” (3779), and “contributes to body defences against external agents” (ID 3467) pursuant to Article 13(1) of Regulation (EC) No 1924/2006

EFSA

On the basis of the data presented, the Panel concludes that: The food constituent, polyphenols in olive (olive fruit, olive mill waste waters or olive oil, *Olea europaea* L. extract and leaf) standardised by their content of hydroxytyrosol and its derivatives (e.g. oleuropein complex), which is the subject of the health claims, is sufficiently characterised in relation to the claimed effects.

Protection of LDL particles from oxidative damage (ID 1333, 1638, 1639, 1696, 2865)

The claimed effects are “reduces oxidative stress”, “antioxidant properties”, “lipid metabolism”, “antioxidant activity, they protect body cells and LDL from oxidative damages”, and “antioxidant properties”. The target population is assumed to be the general population. In the context of the proposed wordings, the Panel assumes that the claimed effects refer to the protection of low-density lipoprotein (LDL) particles from oxidative damage. Protection of LDL particles from oxidative damage may be a beneficial physiological effect.

A cause and effect relationship has been established between the consumption of olive oil polyphenols (standardised by the content of hydroxytyrosol and its derivatives) and protection of LDL particles from oxidative damage.

The following wording reflects the scientific evidence: **“Consumption of olive oil polyphenols contributes to the protection of blood lipids from oxidative damage.”**

In order to bear the claim, 5 mg of hydroxytyrosol and its derivatives (e.g. oleuropein complex and tyrosol) in olive oil should be consumed daily. These amounts, if provided by moderate amounts of olive oil, can be easily consumed in the context of a balanced diet. The concentrations in some olive oils may be too low to allow the consumption of this amount of polyphenols in the context of a balanced diet. The target population is the general population.

Maintenance of normal blood HDL-cholesterol concentrations (ID 1639)

The claimed effect is “lipid metabolism”. The target population is assumed to be the general population. In the context of the proposed wording, the Panel assumes that the

claimed effect refers to maintenance of normal blood HDL-cholesterol concentrations. Maintenance of normal blood HDL-cholesterol concentrations (without increasing LDL-cholesterol concentrations) is a beneficial physiological effect.

The evidence provided is insufficient to establish a cause and effect relationship between the consumption of olive oil polyphenols (standardised by their content of hydroxytyrosol and its derivatives) and maintenance of normal blood HDL-cholesterol concentrations.

Maintenance of normal blood pressure (ID 3781)

The claimed effect is “contributes to the maintenance of a normal blood pressure”. The target population is assumed to be the general population. Maintenance of normal blood pressure is a beneficial physiological effect.

A cause and effect relationship has not been established between the consumption of polyphenols in olive (olive fruit, olive mill waste waters or olive oil, *Olea europaea* L. extract and leaf) standardised by the content of hydroxytyrosol and its derivatives (e.g. oleuropein complex) and maintenance of normal blood pressure.

“Anti-inflammatory properties” (ID 1882)

The claimed effect is “a potent source of olive biophenols with anti-inflammatory properties”. The target population is assumed to be the general population. In the context of the proposed wordings, the Panel considers that the claim refers to diseases such as osteoarthritis or rheumatoid arthritis, in which a reduction of inflammation would be a therapeutic target for the treatment of the disease.

Reduction of inflammation in the context of diseases such as osteoarthritis or rheumatoid arthritis is a therapeutic target for the treatment of the disease, and does not comply with the criteria laid down in Regulation (EC) No 1924/2006.

“Contributes to the upper respiratory tract health” (ID 3468)

The claimed effect is “contributes to the upper respiratory tract health”. The target population is assumed to be the general population.

The claimed effect is general and non-specific, and does not refer to any specific health claim as required by Regulation (EC) No 1924/2006.

“Can help to maintain a normal function of gastrointestinal tract” (3779)

The claimed effect is “can help to maintain a normal function of gastrointestinal tract”. The target population is assumed to be the general population.

The claimed effect is general and non-specific, and does not refer to any specific health claim as required by Regulation (EC) No 1924/2006.

“Contributes to body defences against external agents” (ID 3467)

The claimed effect is “contributes to body defences against external agents”. The target population is assumed to be the general population.

The claimed effect is general and non-specific, and does not refer to any specific health claim as required by Regulation (EC) No 1924/2006.

RAPHANUS SATIVUS L.

[A Novel Compound Rasatiol Isolated from *Raphanus sativus* Has a Potential to Enhance Extracellular Matrix Synthesis in Dermal Fibroblasts](#)

[Seok-Seon Roh et al.](#)

[Annals of Dermatology 2013, 25 \(3\): 315-20](#)

The **fibrous proteins of extracellular matrix (ECM) produced by dermal fibroblast contributes to the maintenance of connective tissue integrity**. This study is carried out to identify the bioactive ingredient from natural products that enhances ECM production in dermal fibroblasts. Bioassay-directed fractionation was used to isolate the active ingredient from natural extracts. The **effects of rasatiol (isolated from *Raphanus sativus*) on ECM production in primary cultured human dermal fibroblasts was investigated** by enzyme linked immunosorbent assay and western blot analysis. **Rasatiol accelerated fibroblast growth in a dose-dependent manner and increased the production of type 1 collagen, fibronectin and elastin**. Phosphorylation of p42/44 extracellular signal-regulated kinase, p38 mitogen-activated protein kinase, and Akt was remarkably increased by rasatiol, indicating that enhanced ECM production is linked to the activation of intracellular signaling cascades. These results indicate that **rasatiol stimulates the fibrous components of ECM production, and may be applied to the maintenance of skin texture**.

[Study of the refirming effect of a plant complex](#)

[A Benaiges et al.](#)

[International Journal of Cosmetic Science 1998, 20 \(4\): 223-33](#)

Loss of skin elasticity is one of the main problems of ageing. This is a mechanical property influenced by elastin, a protein in the dermis which, together with collagen and glycosaminoglycans, makes up the connective tissue. This tissue is affected by a large number of events (such as cutaneous ageing, pregnancy, slimming processes and cellulitis) which eventually cause it to change. At the same time, the metabolism of the proteins of the connective tissue decreases and there is an ever greater presence of enzymes, principally elastases and collagenases, which are responsible for breaking down the elastin and the collagen. One way to **prevent such a loss of elasticity is to use active ingredients that are able to inhibit elastase enzymes**. A plant complex was prepared using the following plants: lady's thistle (*Silybum marianum* GAERTN), alchemilla or yarrow (*Alchemilla vulgaris* L.), horsetail (*Equisetum arvense* L.) as well as germinated seeds (*Glycine soja* Siebold and Zucc., *Triticum vulgare* Vilars, *Medicago sativa* L., *Raphanus sativus* L.). The complex was standardized to give the corresponding active principles, silybin, tannins, silicon and peptides, respectively, and in vitro enzymatic tests were carried out to **establish its ability to inhibit elastase**. The study of enzymatic inhibition was carried out using two enzymes: (1) porcine pancreatic elastase (PPE), and (2) human leukocyte elastase (HLE). The results showed that the plant complex presents non-competitive inhibition in the order of 41.0% against PPE and 50.0% against HLE. An in vivo test was made alongside the in vitro test using an SEM 474 Cutometer (Courage &

Khazaka) to study the elasticity of the skin, and positive effects were obtained when applying a cosmetic formulation containing 5% of the plant complex. **Image analysis of duplicates of the cutaneous surface, before and after treatment began with a product containing 5% of plant complex and showed that wrinkles were decreased by 36.7%.**

[The Effects of Reducing Skin Wrinkles and Improving Skin Elasticity from Korean Radish Extract](#)

[Hyun-Kyoung Kim](#)

[International Journal of Advanced Smart Co Vol. 8 No 113-125 \(2019\)](#)

The radish skin and radish greens are an edible part of the radish. But they are removed before eating the radish and used as a byproduct or an animal feed material because of their tough and rough texture. This study was **conducted to investigate the effect of supercritical heat-treated radish-extract on UV-induced HRM-2 wrinkled mouse animal model on anti-aging wrinkles. Supercritical heat-treated radish-extract was applied on the back of seven-weeks old HRM-2 mice. The effect of HRE on skin thickness, elasticity and wrinkle formation of the mice was observed by using UVB lamp to induce melanogenesis and wrinkle formation.** As the result, increased depth of wrinkles was observed in the negative control group in comparison to the normal group. In contrast, decreased depth of wrinkles was observed in the radish-extract-free group compared to the negative control group. In the study of the effect of radish-extract on wrinkle-formation related gene expression and protein what protein expression, MMP-2 and MMP-9 gene expression significantly increased in the negative control group compared to the normal group. The gene expression reduced in dependence to the mass of radish-extract treated. Similar to quantitative results of mRNA expression, the expression of MMP-2 protein increased as a result of UVB-irradiation. The MMP-2 expression was inhibited in dependence to the mass of radish-extract treated. In conclusion, the supercritical heat-treated radish-extract has an effect on **improving skin wrinkles not only when it is applied to the skin but also when orally ingested.** Thus, it can be effectively used as a composition to health functional products. Therefore we can also conclude that radish a food that does not show any side-effects even upon long-term intake **can reduce wrinkle formation as well as improve skin elasticity when taken regularly for a long period.**

ORYZA SATIVA L.

[Antioxidant and Anti-Inflammatory Properties of Anthocyanins Extracted from *Oryza sativa* L. in Primary Dermal Fibroblasts](#)

[Pakhawadee Palungwachira et al.](#)

[Oxidative Medicine and Cellular Longevity 2019, 2019: 2089817](#)

Flavonoids are naturally active substances that form a large class of phenolic compounds abundant in certain foods. **Black rice (*Oryza sativa* L.) contains high levels of**

anthocyanin polyphenols, which have beneficial effects on health owing to their antioxidant properties. The breakdown of collagenous networks with aging or skin deterioration results in the impairment of wound healing in the skin. Accordingly, **reviving stagnant collagen synthesis can help maintain dermal homeostasis during wound healing.** This study presents an **assessment of the cellular activity of anthocyanins (ANT) extracted from *Oryza sativa* L., providing information necessary for the development of new products that support natural healing processes.** The relative composition of ANT from *Oryza sativa* L. was determined by high-performance liquid chromatography/diode array detection. ANT promoted the migration of rat dermal fibroblasts (RDFs) and demonstrated antioxidant properties. ANT increased the mRNA expression of collagen type I alpha 2 (COL1A2) and upregulated type I collagen protein levels in H₂O₂-stimulated RDFs without cytotoxicity. Compared with the untreated group, treatment of RDFs with ANT in the presence of H₂O₂ led to the activation of signaling pathways, including the extracellular signal-regulated protein kinases 1 and 2 (ERK1/2) and Akt, whereas it significantly ($p < 0.001$) inhibited the phosphorylation of I κ B α and suppressed the activation of the nuclear factor-kappa B (NF- κ B) subunits, p50 and p65, which are transcription factors responsible for inflammation. Taken together, our findings suggest that **ANT from *Oryza sativa* L. have anti-inflammatory properties and antiaging potential by modulating type I collagen gene expression and suppressing H₂O₂-induced NF- κ B activation in skin fibroblasts.**

[Black rice \(*Oryza sativa* L.\) extract modulates ultraviolet-induced expression of matrix metalloproteinases and procollagen in a skin cell model](#)

[Mira Han et al.](#)

[International Journal of Molecular Medicine 2018, 41 \(5\): 3073-3080](#)

Exposure of the skin to **ultraviolet (UV) radiation causes extracellular matrix (ECM) collapse in the dermis, owing to an increase in matrix metalloproteinase (MMP) production in both the epidermis and dermis, and a decrease in type I collagen expression in the dermis.** Recently, black rice (*Oryza sativa* L.) was reported to have a wide range of pharmacological effects in various settings. However, the effects of black rice extract (BRE) on UV-irradiated skin cells have not yet been characterized. BRE treatment did not affect cell morphology and viability of HaCaT and human dermal fibroblasts (HDF). We demonstrated that **BRE downregulated basal and UV-induced MMP-1 expression in HaCaT cells. Furthermore, BRE significantly increased type I procollagen expression, and decreased MMP-1 and MMP-3 expression in UV-irradiated HDF.** The underlying mechanisms of these results involve a decrease in p38 and c-Jun N-terminal kinase activity, and suppression of UV-induced activation of activator protein-1 (AP-1). **BRE reduced UV-induced reactive oxygen species production in HaCaT cells in a dose-dependent manner.** Indeed, mass spectrometry revealed that **BRE contained antioxidative flavonoid components such as cyanidin-3-O- β -D-glycoside and taxifolin-7-O-glucoside.** These findings suggest that BRE attenuates UV-induced ECM damage by modulating mitogen-activated protein kinase and AP-1 signaling, and could be used as an **active ingredient for preventing photoaging of the skin.**

[New Functional Ingredients Based on Microencapsulation of Aqueous Anthocyanin-Rich Extracts Derived from Black Rice \(*Oryza sativa* L.\)](#)

[Iuliana Aprodu et al.](#)

[Molecules: a Journal of Synthetic Chemistry and Natural Product Chemistry 2019](#)

[September 18, 24 \(18\)](#)

The **aqueous anthocyanin-rich extract derived from black rice (*Oryza sativa* L.)** was encapsulated by freeze drying using milk proteins and peptides as coating materials. The molecular modelling approach indicated that all major casein fractions and whey proteins were able to bind at least one anthocyanin molecule. The hydrophobic interactions and hydrogen bonding across the interfaces appeared to be mainly responsible for the stabilizations of the complexes formed between the coating material and bioactive compounds. Two dark purple colored powders, differentiated by the ratio of the encapsulation materials used, rich in phytochemicals were obtained, with an encapsulation efficiency of up to 99%. The **powders were tested for antioxidant activity**, cytocompatibility, and thermal stability. The morphological structure of the powders highlighted the **presence of encapsulated anthocyanins**. Both powders showed a remarkable **antioxidant activity** of about 46 mM Trolox/g D.W., and cytocompatibility on the L929 fibroblast culture. At certain concentrations, both powders **stimulated cell proliferation**. The powders showed a good thermal stability between 75 and 100 °C for 15 min. The powders were tested in a food model system and checked for stability of phytochemicals during storage. The **added value of the powders was demonstrated throughout the antioxidant activity**, which remained unchanged during storage.

[Anti-aging efficacy of topical formulations containing niosomes entrapped with rice bran bioactive compounds](#)

[Aranya Manosroi et al.](#)

[Pharmaceutical Biology 2012, 50 \(2\): 208-24](#)

Rice [*Oryza sativa* L. (Gramineae)] bran is a rich source of phytochemicals. Its oil also contains several bioactive components that exhibit antioxidative properties such as ferulic acid (F), γ -oryzanol (O), and phytic acid (P) which can be a new source of cosmetic raw materials. To **evaluate the anti-aging effects of the gel and cream containing niosomes entrapped with the rice bran bioactive compounds**. The semi-purified rice bran extracts containing F, O, and P which indicated the growth stimulation of human fibroblasts and the inhibition of MMP-2 by sulforhodamine B and gelatin zymography, respectively, were entrapped in niosomes by supercritical carbon dioxide fluid (scCO₂) and incorporated in gel and cream formulations. **The skin hydration, elasticity, thickness and roughness, and pigmentation in human volunteers after treated with these gel and creams were investigated** by corneometer, cutometer, visiometer, and mexameter, respectively. Gel and cream containing the semi-purified rice bran extracts entrapped in niosomes gave no sign of erythema and edema detected within 72 h on the shaved rabbit skin by the closed patch test investigated by mexameter and visual observation, respectively. These **formulations also demonstrated higher hydration enhancement and improvement of skin lightening, thickness, roughness, and elasticity on the skin of 30 human volunteers** within the 28-day treatment not more than 9, 27, 7, 3, and 3 times, respectively. The formulations containing niosomes entrapped with the rice bran bioactive compounds gave superior clinical anti-aging activity which can be applied as a novel skin product.

[Amended final report on the safety assessment of Oryza Sativa \(rice\) Bran Oil, Oryza Sativa \(rice\) Germ Oil, Rice Bran Acid, Oryza Sativa](#)

(rice) Bran Wax, Hydrogenated Rice Bran Wax, Oryza Sativa (rice) Bran Extract, Oryza Sativa (rice) Extract, Oryza Sativa (rice) Germ Powder, Oryza Sativa (rice) Starch, Oryza Sativa (rice) Bran, Hydrolyzed Rice Bran Extract, Hydrolyzed Rice Bran Protein, Hydrolyzed Rice Extract, and Hydrolyzed Rice Protein

(no author information available yet)

International Journal of Toxicology 2006, 25 Suppl 2: 91-120

This report addresses the **safety of cosmetic ingredients derived from rice, *Oryza sativa***. Oils, Fatty Acids, and Waxes: Rice Bran Oil functions in cosmetics as a conditioning agent--occlusive in 39 formulations across a wide range of product types. Rice Germ Oil is a skin-conditioning agent--occlusive in six formulations in only four product categories. Rice Bran Acid is described as a surfactant-cleansing agent, but was not in current use. Rice Bran Wax is a skin-conditioning agent--occlusive in eight formulations in five product categories. Industry did not directly report any use of Rice Bran Wax. Hydrogenated Rice Bran Wax is a binder, skin-conditioning agent--occlusive, and viscosity-increasing agent--nonaqueous in 11 formulations in six product categories. Rice Bran Oil had an oral LD50 of > 5 g/kg in white rats and Rice Wax had an oral LD50 of > 24 g/kg in male mice. A three-generation oral dosing study reported no toxic or teratologic effects in albino rats fed 10% Rice Bran Oil compared to a control group fed Peanut Oil. Undiluted Rice Bran Oil, Rice Germ Oil, and Hydrogenated Rice Bran Wax were not irritants in animal skin tests. Rice Bran Oil was not a sensitizer. Rice Bran Oil, Rice Germ Oil, Rice Wax, and Hydrogenated Rice Bran Wax were negative in ocular toxicity assays. A mixture of Rice Bran Oil and Rice Germ Oil had a ultraviolet (UV) absorption maximum at 315 nm, but was not phototoxic in a dermal exposure assay. Rice Bran Oil was negative in an Ames assay, and a component, gamma-oryzanol, was negative in bacterial and mammalian mutagenicity assays. Rice oils, fatty acids, and waxes were, at most, mildly irritating in clinical studies. Extracts: Rice Bran Extract is used in six formulations in four product categories. Rice Extract is a hair-conditioning agent, but was not in current use. Hydrolyzed Rice Extract is used in four formulations and current concentration of use data were provided for other uses. Hydrolyzed Rice Bran Extract, described as a skin-conditioning agent--miscellaneous, is used in two product categories. Use concentrations are in the 1% to 2% range. Rice Bran Extract is comprised of proteins, lipids, carbohydrates, mineral ash, and water. The content includes palmitic, stearic, oleic, and linoleic acids. Other components include antioxidants such as tocopherols. Rice Extract reduced the cytotoxicity of sodium chloride in male rats. Bran, Starch and Powder: Rice Bran (identified as rice hulls) is an abrasive and bulking agent in one formulation. Rice Starch is an absorbent and bulking agent in 51 formulations across a wide range of product categories. Rice Germ Powder is an abrasive and one manufacturer described an exfoliant use, but it was not reported to be used in 2002. Oral carcinogenicity studies done on components of Rice Bran (phytic acid and gamma-oryzanol) were negative. Rice Bran did not have an anticarcinogenic effect on 1,2-dimethylhydrazine-induced large bowel tumors. In cocarcinogenicity studies done using 1,2-dimethylhydrazine and other agents, with Rice Bran Oil and Rice Bran-derived hemicellulose and saccharide, tumor inhibition was observed; gamma-oryzanol did not inhibit the development of neoplasms. A decrease in cutaneous lesions in atopic dermatitis patients was reported following bathing with a Rice Bran preparation. Proteins: Hydrolyzed Rice Bran Protein and Hydrolyzed Rice Protein function as conditioning agents (hair or skin), but only the latter was reported to be used in a few products. An in vitro phototoxicity assay using UVA light found no photochemical toxicity. Rice bran protein hydrolysates are not acutely toxic, are not skin or ocular irritants in animals, are not skin sensitizers in guinea pig maximization tests, and are not irritating or

sensitizing in clinical tests. Isolated cases of allergy to raw rice have been reported, but rice, in general, is considered non allergenic. The Cosmetic Ingredient Review (CIR) Expert Panel considered that safety test data available on certain of these ingredients could be extrapolated to the entire group. Although Rice Bran Extract does contain UV absorbing compounds at low concentrations, clinical experience suggested no phototoxicity would be associated with such materials. Rice derived ingredients generally are considered to be non allergenic. There were no safety test data available for Hydrolyzed Rice Extract and Hydrolyzed Rice Bran Extract, but their safety may be inferred from that of the extracts from which they are derived. Current levels of polychlorinated biphenyls (PCBs) and heavy metals in rice-derived ingredients used in cosmetics are not a safety concern. The Panel was concerned, however, that contaminants such as pesticides have been reported in Rice Bran Oil used for cooking. Pesticides and heavy metals should not exceed currently reported levels for rice-derived cosmetic ingredients. **The CIR Expert Panel concluded that these rice-derived ingredients are safe as cosmetic ingredients in the practices of use and concentrations as described in this safety assessment.**

[Effect of Rice \(*Oryza sativa* L.\) Ceramides Supplementation on Improving Skin Barrier Functions and Depigmentation: An Open-Label Prospective Study](#)

[Teik Kee Leo et al.](#)

[Nutrients 2022 June 30, 14 \(13\)](#)

Ceramides plays a crucial role in maintaining skin barrier function. Although foregoing evidence supported beneficial effects of topical ceramides for restoration of the skin barrier, studies on oral ceramides are extremely scarce, with most published data collected from in vivo and in vitro models. Thus, this study aimed to **evaluate the efficacy of rice ceramides (RC) supplementation to improve skin barrier function and as a depigmenting agent through comprehensive clinical assessments.** This study investigated the beneficial effects of **orally administered RC supplementation in 50 voluntary participants.** **Skin hydration, firmness and elasticity, transepidermal water loss (TEWL), melanin index (MI), erythema index (EI), sebum production, pH, and wrinkle severity were assessed at baseline and during monthly follow-up visits.** RC supplementation was found to significantly ($p < 0.01$) improve skin hydration, sebum production, firmness and elasticity, and wrinkle severity for three assessed areas, namely the left cheek, dorsal neck, and right inner forearm. Additionally, RC significantly ($p < 0.01$) reduced the rates of TEWL, levels of MI and EI. Analyses of data indicated that participants at older age were more responsive towards the effect of RC supplementation. Our findings suggest that **RC supplementation can effectively improve skin barrier function, reduce wrinkle severity, and reduce pigmentation.**

[Evaluating the effect of rice \(*Oryza sativa* L.: SRNC05053-6-2\) crude extract on psoriasis using in vitro and in vivo models](#)

[Sumate Ampawong et al.](#)

[Scientific Reports 2020 October 19, 10 \(1\): 17618](#)

Psoriasis is mainly caused because of inappropriate immune responses in the epidermis. **Rice (*Oryza sativa* L.: SRNC05053-6-2) consists of anthocyanin, which exhibits strong antioxidative and anti-inflammatory properties.** This study aimed to evaluate the role of this black-coloured rice crude extract in alleviating the symptoms of

psoriasis using human psoriatic artificial skin and an imiquimod-induced rat psoriasis model. Psoriasis-related genes, cytokines and chemokines were examined; in addition, the antioxidative and anti-inflammatory properties and the immunohistopathological features of this condition were studied. The results showed that the rice extract reduced the severity of psoriasis by (1) decreasing the epidermal thickness, acanthosis, hyperkeratosis, epidermal inflammation and degree of apoptosis induction via caspase-3, (2) increasing the expression levels of anti-inflammatory cytokines (IL-10 and TGF- β), (3) reducing the levels of pro-inflammatory cytokines (IL-6, IL-8, IL-20, IL-22 and TNF- α), chemokines (CCL-20) and anti-microbial peptides (psoriasin and β -defensin), (4) enhancing the antioxidative property (Nrf-2), (5) downregulating the levels of psoriasis-associated genes (psoriasin, β -defensin, koebnerisin 15L and koebnerisin 15S) and (6) upregulating the levels of psoriasis-improving genes (caspase-14, involucrin and filaggrin). Thus, the extract appears to exert **therapeutic effects on psoriasis through its antioxidative and immunomodulatory properties.**

[Evaluating the Antioxidants, Whitening and Antiaging Properties of Rice Protein Hydrolysates](#)

[Hui-Ju Chen et al.](#)

[Molecules: a Journal of Synthetic Chemistry and Natural Product Chemistry 2021 June 12, 26 \(12\)](#)

Plant-derived protein hydrolysates have potential applications in nutrition. **Rice protein hydrolysates (RPHs), an excellent source of proteins, have attracted attention for the development of cosmeceuticals.** However, few studies have reported the potential application of RPH in analysis, and this **study examined their antioxidant activities and the inhibitory activities of skin aging enzymes.** The results indicated that the total phenolic and flavonoid concentrations were 2.06 ± 0.13 mg gallic acid equivalent/g RPHs and 25.96 ± 0.52 μ g quercetin equivalent/g RPHs, respectively. RPHs demonstrated dose-dependent activity for scavenging free radicals from 1,1-diphenyl-2-picrylhydrazyl [half-maximal inhibitory concentration (IC₅₀) = 42.58 ± 2.1 mg/g RPHs] and 2,2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) (IC₅₀ = 2.11 ± 0.88 mg/g RPHs), dose-dependent reduction capacity (6.95 ± 1.40 mg vitamin C equivalent/g RPHs) and oxygen radical absorbance capacity (473 μ mol Trolox equivalent/g RPHs). The concentrations of the RPH solution required to achieve 50% inhibition of hyaluronidase and tyrosinase activities were determined to be 8.91 and 107.6 mg/mL, respectively. This study demonstrated that **RPHs have antioxidant, antihyaluronidase, and antityrosinase activities for future cosmetic applications.**

[Rice bran supplement prevents UVB-induced skin photoaging in vivo](#)

[Su Jeong Ha et al.](#)

[Bioscience, Biotechnology, and Biochemistry 2018, 82 \(2\): 320-328](#)

Although rice bran consumption is reportedly has numerous beneficial effects on human health, the relationship between rice bran and the prevention of photoaging has not been investigated in detail. We sought to **investigate whether consumption of rice bran supplement (RBS) can elicit preventive effects against UVB-induced photoaging in vivo.** Dorsal skin sections of hairless mice were exposed to UVB over 16 weeks. **RBS consumption suppressed UVB-induced wrinkle formation and inhibited the loss of water content and epidermal thickening in the mouse skin.** Western blot and immunohistochemical analyses revealed that repeated exposure to UVB upregulated matrix

metalloproteinase-13 (MMP-13) and cyclooxygenase-2 (COX-2) expression, while consumption of RBS suppressed MMP-13 and COX-2 expression, as well as mitogen-activated protein kinase (MAPK) signaling pathways. These findings suggest that RBS could be a potential **bioactive ingredient in nutricosmetics to inhibit wrinkle formation and water content loss via the suppression of COX-2 and MMP-13 expression.**