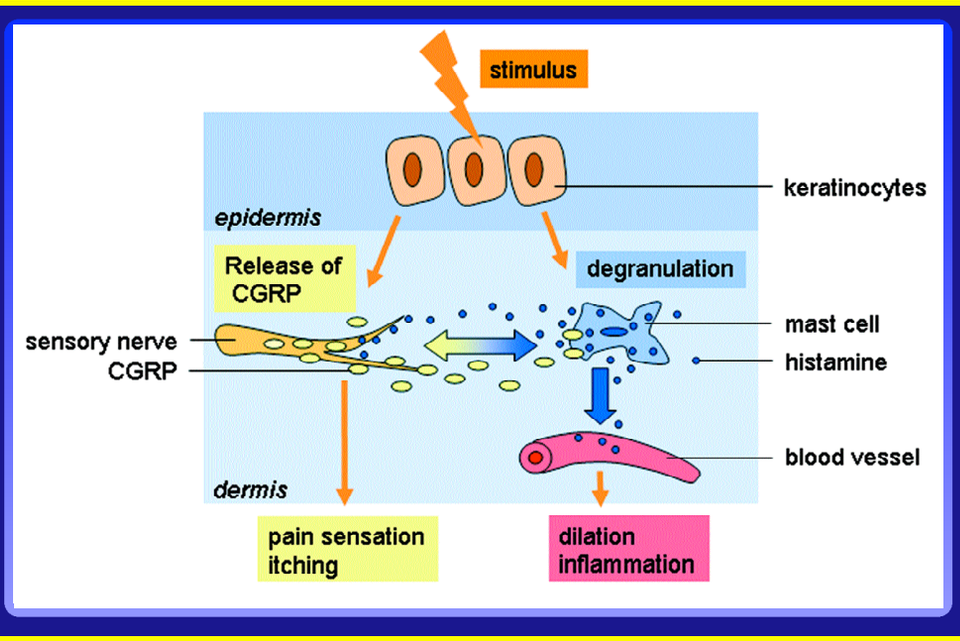
SÖFW Journal

International Journal for Applied Science

Personal Care ■ Detergents ■ Specialities



Reprint from 11-2005

D. Schmid, F. Suter, F. Zülli

Soothing Factor from Opuntia Cactus for Sensitive Skin

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Keywords: Opuntia, Nopal, soothing, hydration, sensory neurons, CGRP

Introduction

Sensitive skin tends to be more susceptible to some environmental factors. People with sensitive skin report exaggerated reactions such as redness, itching or rashes when their skin is in contact with certain cosmetics, plants or fabrics, hot or cold, or insect bites. Normally, people with sensitive skin show quicker an erythemal reaction against ultraviolet irradiation. Skin that is sensitive to sun, typically shows allergic reactions, induced by ultraviolet radiation alone or in combination with chemical ingredients in skin care products. The most important factors for sensitive skin are skin dryness and atopic skin, means skin that is hyper reacting towards allergens. This article describes a preparation of the Opuntia cactus that helps against sensitive skin in two different ways: it increases skin hydration and it specifically reduces the itch sensation and local inflammation. The latter phenomena are the consequence of a »crosstalk« between the stratum corneum, free sensory afferent nerve endings and mast cells **(Fig. 1)**. A stimulus such as a pruritogenic substance or inflammatory mediators or cytokines produced by keratinocytes act either directly on a subset of specialized nerve endings, called C-fibers, inducing an action potential or on mast cells inducing degranulation. The action potential leads to the evocation of nociceptive reflexes and pain behaviour and to the re-lease of neuropeptides such as substance P and the calcitonin gene-related peptide (CGRP). These neuropeptides induce dilation of the surrounding capillaries and local inflammation and also degranulation of mast cells. Degranulation liberates histamine, which, in turn, initiates itch and local inflammation by stimulating the C-fiber nerve endings.

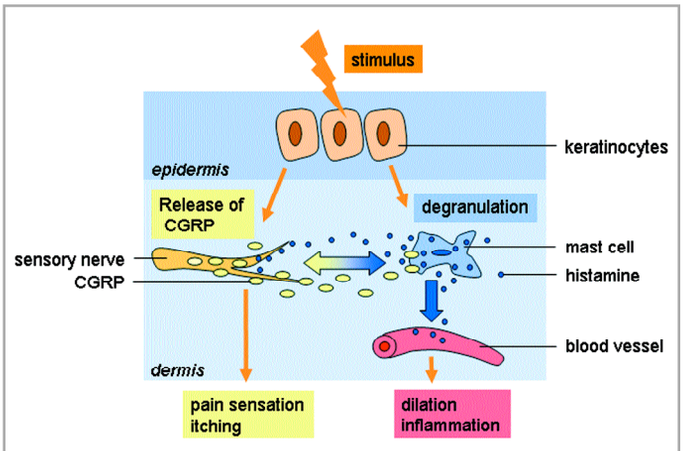

Fig. 1 Sensory system of the skin

The cactus Opuntia

To the genus Opuntia belong about 200 – 300 cactus species that grow all over the world in arid and semi-arid zones. Commercial cultivation is carried out in Italy, Spain, Mexico, Brazil, Chile, Argentina and California. Traditionally Opuntia cactus plants serve as sources for fruits and vegetables and for medicinal and cosmetic purposes. The term »nopales« is used for the flattened stem segments that are morphologically incorrectly designated as cactus leaves. The dried powdered cactus leaves are used as nutritional supplement. They are a rich source of minerals, pectins and flavonoids (1). The nopal extract was found in several studies to reduce glucose plasma level which explains its positive contribution to overall health in diabetes mellitus type II. Saponins are assumed to exert this antidiabetic effect. Others studies with Opuntia stem extract showed a general anti-hyperlipidemic effect that most probably comes from the especially high pectin content. There are several scientific publications that report about an analgesic action and anti-inflammatory properties of nopal extract (2).

Materials and Methods

Preparation of the cactus elixir »AquaCacteen«: Leaves of the species Opuntia *Streptacantha Platyopuntia* that have been carefully dried at relatively low temperatures served as source material. The material was taken up in a phosphate buffer solution and digested with a special enzyme mixture. The final product was obtained after passage through different filter devices and cross flow filtration through a 10 kDa membrane.
Protection against UVA irradiation: Human keratinocytes (HaCaT) were irradiated with UVA for 25 minutes at a dose of 1125 kJ/cm² ± »AquaCacteen«. Cell growth was measured 24 and 48 hours later with the MTT assay.
Study on protection against UV irradiation: Emulsions with different concentrations of »AquaCacteen« were tested in a study over 17 days with 20 women of the age of 18 to 60. The test products were applied twice daily for 14 days on the inner side of the forearms. After 14 days the test areas were irradiated with 1 MED. Skin firmness was determined with the Cutometer SEM 475 (Courage & Khazaka GmbH, Cologne) at the beginning of the study, at day 14 and day 17.
Coculture model with sensory neurons and keratinocytes: Rat sensory neurons were cultivated in 96 wells plate in coculture medium. After 10 days, normal human keratinocytes were seeded in each well. After 2 days of coculture, supernatants were changed by coculture medium alone or with the test compound and cells were incubated for 30 minutes. At the end of this incubation, the cells were stimulated during 20 minutes with 10^{-6} M capsaicin. Then the supernatants were recovered and frozen to analyze CGRP by ELISA. Lidocaine at 10^{-6} M was used as positive control.
Study on skin hydration: Shower gels with different concentrations of »AquaCacteen« were tested in a study over 1 week with 20 women of the age of 23 to 49. The products were applied once daily on separate areas on the inner side of the forearm. Hydration was measured with the Corneometer CM 825 PC (Courage & Khazaka GmbH, Cologne).

Results and Discussion

The nopal preparation »AquaCacteen« was first studied *in vitro* with keratinocytes. The human cell line HaCaT was used to verify if nopal contains antioxidants that confer a protective effect against irradiation with UVA. The MTT-assay was used to measure the concentration of metabolically active cells (3). The applied irradiation dose and irradiation time normally leads to a cell death of about 50%. In this experiment the survival rate in the normal cell medium was 42% after 1 day and 25% after 2 days **(Fig. 2)**. Keratinocytes in the medium with 1% »AquaCacteen« clearly showed a higher resistance against UVA treatment and after 2 days regeneration. Survival after 1 day was at 53% and then the culture started to growth again reaching 61% of the amount of metabolically active cells that were present before irradiation. Thus in opuntia cactus ingredients are present that help keratinocytes to better tolerate UVA. This UV protection could also be demonstrated *in vivo*. Emulsions with 0.5 and 2% »AquaCacteen« were tested in a study with 20 female subjects. A pretreatment period of 2 weeks showed that the product with 2% nopal clearly improved the firmness of the skin **(Fig. 3)**. The test areas on the inner side of the forearm were then irradiated with 1 MED. Three days later skin firmness was found to be reduced in the zone with the placebo emulsion whereas firmness in the zones treated with the nopal emulsions remained the same or even improved further. The mechanism of this UV pro-

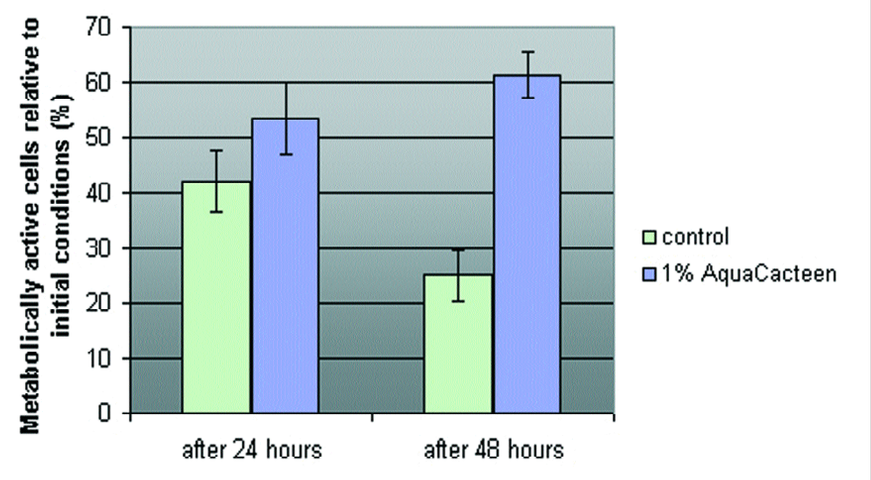

Fig. 2 Protection of keratinocytes after UVA irradiation. Human keratinocytes (HaCaT) were irradiated with a LD50 dose of UVA. After 1 and after 2 days the amount of metabolically active cells was measured by the MTT assay

tection might be part of a soothing, anti-inflammatory effect that could be shown in a cell culture test system with sensory nerve cells and keratinocytes. C-fiber nerve cells are cultured together with keratinocytes. Capsaicin, the pungent active in chile pepper, is a strong skin irritant and was therefore used in this test system as stimulus to induce an action potential. Stimulation of the C-fiber nerve endings is recorded by measuring the concentration of the released neuropeptide calcitonin gene-related peptide (CGRP). Reduced CGRP liberation in presence of capsaicin indicates a soothing activity. Lidocaine, a local anesthetic that blocks the signal at the endings of sensory nerves, is used as positive control. Stimulation of the coculture with capsaicin resulted in a prominent release of the neuropeptide CGRP **(Fig. 4)**. The positive control lidocaine reduced CGRP release by 61% and a solution of 0.3% nopal preparation by 42%.

Dry skin favours the development of sensitive skin reactions. The nopal preparation was therefore tested for beneficial effects on skin hydration. To show a moisturizing effect even in a rinse off product, different concentrations of »AquaCacteen« were tested in shower gels. A distinct dose-dependent increase in skin hydration was obtained **(Fig. 5)**. The product with 2% »AquaCacteen« increased hydration by 16% after 1 week application.

■ Conclusion

Members of the cactaceae family are biologically adapted to resist strong sunlight, extreme drought and big differences in day / night temperatures. The commercially available Opuntia cactus was used as source material to exploit this extraordinary protective activity. The final product »AquaCacteen« was found to protect skin cells in culture as well as *in vivo* against UV light. Skin hydration could be increased with »AquaCacteen« and a soothing effect could be demonstrated in a cell culture model for sensitive skin.

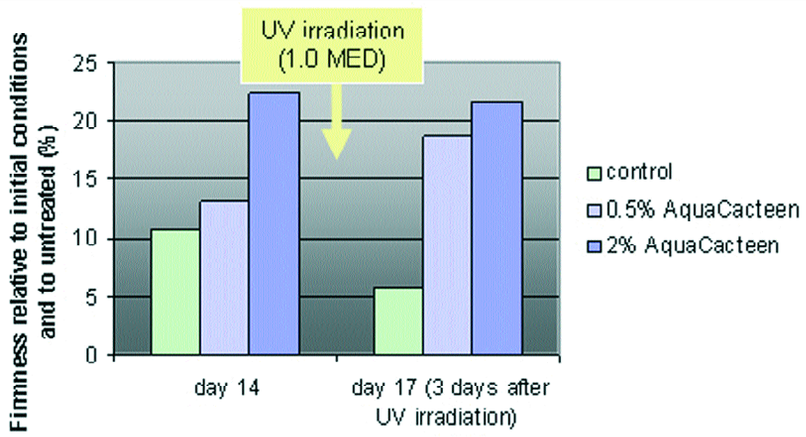

Fig. 3 Increase in firmness and UV protection. The inner side of the forearm was pretreated during 2 weeks. The test areas were then irradiated with 1 MED of UV light and 3 days later skin firmness was analyzed again

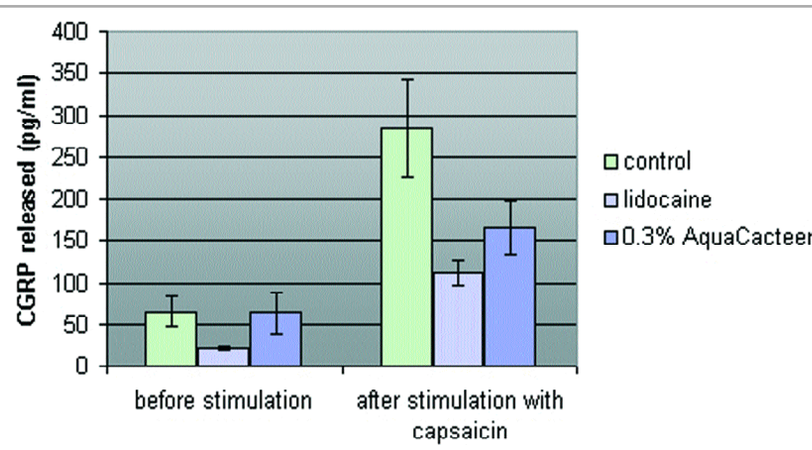

Fig. 4 Soothing effect of AquaCacteen in a coculture model with sensory nerve cells and keratinocytes. The concentration of the neuropeptide CGRP in the culture supernatant was measured before and after stimulation with capsaicin. The analgesic lidocaine was used as positive control

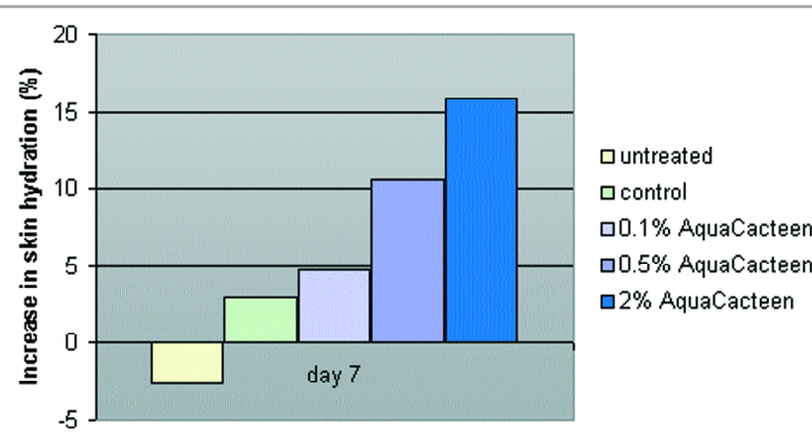

Fig. 5 Improvement of skin hydration. Shower gels with different concentrations of AquaCacteen were used during 7 days

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* *Author's address:*
Dr. Daniel Schmid
Franz Suter
Dr. Fred Zülli
Mibelle AG Biochemistry
Bolimattstrasse 1
5033 Buchs
Switzerland
Email: Daniel.Schmid@Mibelle.ch