
An Opuntia Cactus Extract to Treat Sensitive and Dry Skin

Dr. Daniel Schmid, Franz Suter and Dr. Fred Züllli

Mibelle Biochemistry, Switzerland

May 2007

Abstract

The pads of the cactus *Opuntia* are known as nopales and are used in Mexico as dietary supplement to promote weight loss and as medicine to treat inflammation and pain. Purified components of the *Opuntia* cactus were used for the development of a cosmetic ingredient that provides long-lasting hydration to skin even in rinse-off applications. This ingredient has also remarkable soothing properties which could be shown in a fascinating cell culture system with nerve cells. The *Opuntia* cactus ingredient was found to inhibit the depolarisation of sensory nerve cells upon stress. The ingredient can be used in sun care products and skin care products to soothe sensitive and dry skin.

Introduction

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 itch sensation and local inflammation.

The latter two phenomena are the consequence of a "crosstalk" between the stratum corneum, free sensory afferent nerve endings and mast cells (figure 1). A stimulus such as a pruritogenic sub-

degranulation of mast cells. Degranulation liberates histamine, which, in turn, initiates itch and local inflammation by stimulating the C-fiber nerve endings.

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" or "nopal" is used for the flattened stem segments that are morphologically incorrectly designated as cactus leaves. The dried powdered nopales are used as nutritional supplement. They are a rich source of minerals, pectins and flavonoids (1).

There are several scientific publications that report on an analgesic action and anti-inflammatory properties of nopal extract (2).

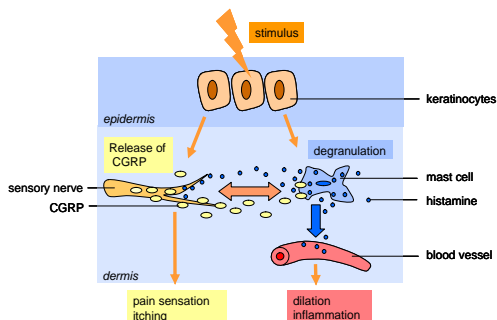


Figure 1: Sensory system of the skin

stance 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 release 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

Materials and Methods

Preparation of the cactus extract "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. For standardisation of the extract the lead substance piscidic acid (figure 2) was analysed by HPLC-MS

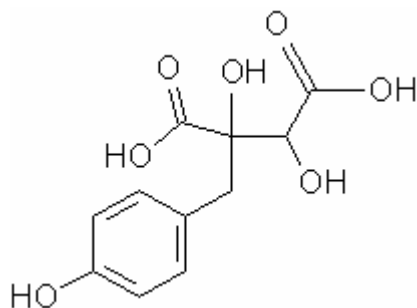


Figure 2: Lead substance piscidic acid that was used for standardisation of the extract.

and NMR. Piscidic acid is a chelator of free iron ions.

Protection against UVA irradiation: Human keratinocytes (HaCaT) were irradiated with UVA for 25 minutes at a dose of $1125 \text{ kJ/cm}^2 \pm$ "AquaCacteen". Cell growth was measured 24 and 48 hours later with the MTT assay.

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 (figure 3). Keratinocytes in the medium with 1 %

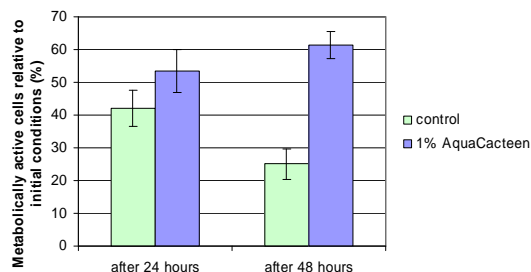


Figure 3: Protection of keratinocytes after UVA irradiation. Human keratinocytes (HaCaT) were irradiated with a LD50 dose of UVA. After 1 and after 2 days the amount of metabolically active cells was measured by the MTT assay.

"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 grow 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. Also the Opuntia lead substance, piscidic acid, could contribute to this protective effect. Piscidic acid neutralizes free iron ions that otherwise would initiate the formation of hydroxyl radicals through the Fenton reaction. Ferritin, the body's own iron chelator, is decomposed upon UV-radiation.

A cell culture test system with sensory nerve cells and keratinocytes was used to demonstrate a soothing, anti-inflammatory effect. 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 (figure 4). The positive control lidocaine

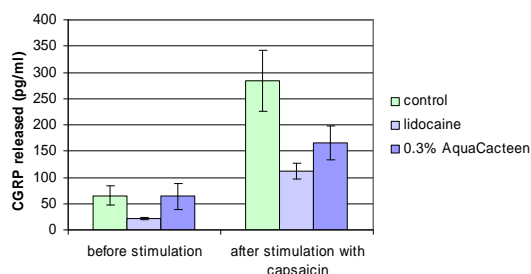


Figure 4: Soothing effect of AquaCacteen in a coculture model with sensory nerve cells and keratinocytes. The concentration of the neuropeptide CGRP in the culture supernatant was measured before and after stimulation with capsaicin. The analgesic lidocaine was used as positive control.

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 (figure 5). The product with 2 % "AquaCacteen"

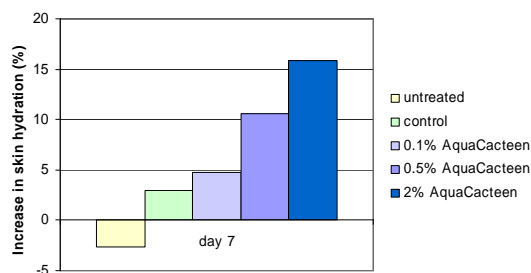


Figure 5: Improvement of skin hydration. Shower gels with different concentrations of AquaCacteen were used during 7 days.

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 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.

References

- (1) Stintzing F. C. and Carle R. (2005) Cactus stems (*Opuntia* spp.): A review on their chemistry, technology, and uses. *Mol. Nutr. Food Res.* 49: 175 – 194
- (2) Park E.-H., Kahng J.-H., Paek E.-A. (1998) Studies on the pharmacological actions of cactus: Identification of its anti-inflammatory effect. *Arch. Pharm. Res.* 21: 30 – 34
- (3) Mosmann T. (1983) Rapid colorimetric assay for cellular growth and survival: application to proliferation and cytotoxicity assays. *J. Immunol. Methods* 65: 55 – 63

monitors for success

mibellebiochemistry

Bolimattstrasse 1, 5033 Buchs / Switzerland
Phone: +41 62 836 17 31 Fax: +41 62 836 14 05
info@mibellebiochemistry.com, www.mibellebiochemistry.com