

LEXICON

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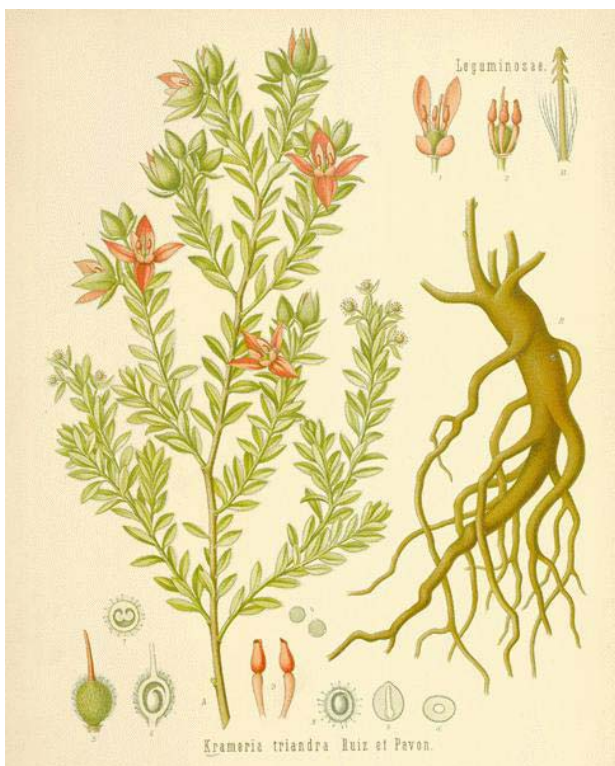
VEVY EUROPE

Nr 2 November 2007

AntiCytoStressor®

The best opportunity to redefine the action of a cosmetic product

One of our scientific confirmations of basic importance, highlighted that the cells of *surface cutis* (keratynocytes of the epidermis) can produce stress hormones. Stress [ancient English: "stresse", short for "distresse" (from the Latin word "district(us)" past participle of the verb "distringere" i.e. to grip here and there) meaning an effort]. Stress is a factor or a combination of physical, chemical or psychological factors modifying the homeostasis or the well-being of an organism and causing a defence reaction, such as – for instance – a physical or emotional trauma or an infection. See next paragraphs.



In detail, the epidermis autonomously reacts to stress-causing stimuli and produces catecholamines (noradrenalin, adrenaline, and dopamine), causing the epidermis to become stressed, also due to local factors (*idiopathic stress*); this situation is completely different from the cutis reaction due to general stress ("cutis of a person subject to stress").

An emotionally stressed person, due to increased circulation of stress-hormones, may develop cutis phenomena such as the peripheral vasoconstriction, vasodilatation, hyperhidrosis, itching, increased capillary brittleness, immunologic phenomena (release of catecholamine influences the production of immunocomplexes and may cause cell-mediated reactions). Having thus ascertained that the epidermis can locally produce stress-hormones as a protection against local insults, it may be easily deduced that all cutis pathology due to general stresses may be locally reproduced even in idiopathic stress.

We have identified the metabolic phase of this particular transformation in the human cutis.

The presence of stress-related hormones in the cutis modulates the triggering of many adverse, even immunologic phenomena. More recently, other researchers have proven the presence of adrenergic cutaneous receptors (which react to the stress-hormones) in a second category of cutis cells, Langerhans cells (LC). It is known that these cells play an important role in showing antigens within the immune-system and are connected with nerve fibres passing through the epidermis. The fact that LC have adrenergic receptors is an additional confirmation of the concept of mutual connection of the nervous and immune systems, and suggests the hypothesis that the stress hormones can modulate at cutis level triggering of immune phenomena and/or

International information on dermo-pharmaceutics cosmetics and toiletries

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vice versa. Some substances can induce stress-giving stimuli, or act as *stressors* for cutis (therefore cause unfavourable reaction phenomena, or idiopathic stress): *unsuitable substances applied on cutis, unsuitable substances taken by os or by nose, dietary factors, environment agents, occupational mechanical agents, underwear, sun radiation, indirect light, genetic factors, sex factors, psychosocial factors, antigen factors, time factors, and infectious factors.*

Absorption of ultraviolet and chiefly visible light triggers formation of electrically excited molecules. Dissipation of this energy can cause a phototoxic effect on cells. At sub cellular level primary targets of phototoxic reaction are polynucleotides, proteins, cytoplasm membranes as well as some cell bodies. Some of these molecular alterations can be related to cell toxicity and to mutagenesis (it is known that cutis cancer risk is greatly connected to exposure to sun rays and although these tumours mostly appear in old age, the damage causing those tumours may happened some decades before, due to critical gene mutation even of one cell). It is worthy to remember that a keratinocyte also produces opioid substances (endorphins) related to stimuli such as sun rays, contact, etc. Therefore one can deduce that epidermis in all ways offers resistance to noxious stimuli.

Stress-hormones, defence substances, change normal cutis physiology and lead to morphology changes (dimorphism).

Among these changes there is cutis ageing, a part from age. After having identified in laboratory formation steps of stress-hormones, we designed a substance inhibiting such formation in a specific end-point of it. This substance has been obtained by synthesis from natural molecules (sequence of aminoacids). It is not subject to any restrictive limit imposed by European and North American chemical and pharmaceutical standards. This substance has been marked with the trade name **Anticytostressor®**.

ACS-Anticytostressor (Vevey codex 13.4566) is an active ingredient for products earmarked for skin health such as functional, hygiene and decorative cosmetics, excipients for dermatologic remedies and for OTC, pharmaceutical cicatrizing, anti-burn repairing pomades. ACS, when applied to the cutis, helps normalizing those noxious phenomena caused by the release of stress-hormones including vasomotor phenomena (for instance: cold-related vasoconstriction, vasodilatation due to exposure to UV rays, and chemical insults which release oxidizing radicals). ACS prevents local stress due to injury, among which interventions of plastic surgery (cicatrization without keloids). The application of ACS is resolute in all three local treatment types: i.e. anti-ageing, reconstituting-healing and protection-prevention.

The use of ACS is also decisive for the preparation of excipients or vehicles for dermatologic

and cosmetic purposes, to prevent any stress caused by chemical ingredients. Any natural or synthetic substance may provoke a negative reaction on the cutis. It is a **dose-dependent** reaction in which cutaneous symptoms are closely related to the pharmacotoxicological action developed by this substance. The in-house Cell Dermo-pharmacology Laboratory of Vevy Europe highlighted local cytotoxic and enzymo-toxic phenomena that are strongly dose-dependent for a large number of

iodotrat® (vevy codex 18.0364)

On the market since 1978, it is a safe, stable and active iodate amine with local action for the prevention and the treatment of the Hydro-Lipidic District Dystrophia (Cellulitis).

Iodotrat® is a water-soluble low molecular weight molecule, purified by double crystallization and therefore devoid of free iodine, as confirmed by extremely severe trials. Topical treatment with Iodotrat® promotes mast cells stimulation mediated by beta-receptors of the membrane by inducing an increase in the number of mast cells and their granules. Improvement of blood circulation sets up lipid motion at adipocyte level on the beta-oxidation cycle (degradation pathway of fatty acids). The progressive regression of the interstitial oedema together with an objective cutaneous improvement in terms of appearance and size reduction of the treated zone and on palpation is demonstrated by histological and clinical tests. Extensive pharmacotoxicological and efficacy tests clearly demonstrated that it is a safe and effective active for the topical treatment of the appearance of tissue distortion of cellulite (abnormal concentration of fatty tissues especially in thighs, hips, buttock and waist). Cosmetics containing Iodotrat®, also in association with Zedomine® (Vevy codex 13.1250) promote day after day visible and encouraging slimming and smoothing results, while skin spongy texture and tone (*orange peel* appearance) are effectively diminished. Iodotrat® is used in emulsions and gels at very low concentrations (up to 0.8%).

ACS (Vevy codex 13.4566)



- The epidermis produces the stress hormones autonomously
- The substance that allows us to modulate this activity has been found
- A new era for the topical treatment of cutaneous stress

cosmetic ingredients, including the sensitization reactions [(IgE mediate and non IgE mediate) allergies, idiosyncrasies].

In the fight against skin-**ageing** (and against free radicals aggravating it) ACS offers the best opportunity to redefine actions of cosmetic products in rational dermatologic cosmetology. The term "cosmetic products" means «the preparations developed for application on human external surfaces (epidermis, pilonidal system and hair, nails, lips, external reproductive organs) or on teeth and the mucosa of mouth, to clean, perfume, protect, keep them in good condition, modify their appearance and/or amend body odours» (Art. 1, paragraph 1 of the VI Directive of the Council of the Ministers of the European Community, amending the EEC Directive n. 76/768). **This new definition of cosmetic products acknowledges that cosmetics have a primary function.** The fact that lawmakers recognize the cosmetic functions is of course wel-

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Vevy Europe will present:

iodotrat®

comed by the cosmetics industry and is at the same time an official "consecration" of a rational and innovative cosmetology grounded on interdisciplinary character, which Vevy Europe has always sustained and pursued, free from the confusing action of allospecialists (Lexicon Vevy Europe Skin Care Instant Report: Skin Ageing, 1988, 2: 13-15).

Stress may have numerous causes and many unfavourable situations. ACS intervention is a skin treatment of total bio regulation. On one side it prevents cutaneous dismorphism, while on the other side it stops this *trend* – triggered by stress-hormones – even when it is already present. ACS is the ingredient allowing to protect, keep in good condition, and favourably change skin *appearance*.

The users are:

- Pharmaceutical Industries: production of dermatologic products, involved in the production of *optimum excipients* (inhibition of stresses caused by chemical substances) or to coadjuvate the active principle with local stress inhibitors in case of skin disease;
- OTC Industries: the same considerations above mentioned;

Bioemulgoids. This term refers to emulgators for cutaneous application which not only meet the prerequisites for absolute pharmacotoxicologic harmlessness, including cryptotoxicologic parameters, but also do not inhibit cutaneous glycolytic scission phases or certain other specific enzymatic actions which represent a basic energetic instant of the skin tissue. Their use assures complete dermal tolerance and no biochemical interference with the active principles incorporated in the emulsion.

Bioemulgoidi. Corrispondono a questa denominazione quegli emulsionanti per uso cutaneo che oltre a rispondere ai requisiti di assoluta innocuità farmacotossicologica, ivi compresi i parametri criptotossicologici, hanno la proprietà di non inibire le tappe della scissione glicolitica cutanea e di alcune altre attività enzimatiche specifiche che rappresentano una istanza energetica fondamentale del tessuto cutaneo. Il loro impiego garantisce la totale tollerabilità dermica e la non interferenza biochimica con i principi attivi incorporati nell'emulsione.



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- Pharmaceutical Industries with production of Cosmetic products: the same considerations for excipients and for cosmetic active principles. The cosmetic products are split in Decorative Cosmetics, Hygiene Cosmetics, and Functional Cosmetics;
- Cosmetic Industries: the same considerations. In this case ACS may be a strong point for all three categories.
 - Hygiene Product Industries: detergents (syndets, milks, cleansing agents). The same considerations are valid especially concerning chemical stresses caused by surfactants.
 - Industries of Decorative Cosmetics (*maquillage*): chemical and physical stresses (occlusion caused by covering materials).

La fatigue d'éclaircir les difficultés

As Jean Racine (1639-1699) wrote in the preface to his tragedy Berenice: "*qu'ils se reposent sur nous de la fatigue d'éclaircir les difficultés (...)*" (It is up to us to find a solution for the difficulties). In our case, fatigue to create a perfect emulsion without any physical or biological incompatibility is entrusted to Xalifin-15® (Vevy codex 02.0151). This means that it must quickly form O/W emulsions which remain stable even at 55°C; Xalifin-15® does not inhibit the enzymic activity of normal skin and it is even well tolerated by scraped skin.

Scriveva Jean Racine (1639-1699) nella prefazione della sua tragedia Berenice: "*qu'ils se reposent sur nous de la fatigue d'éclaircir les difficultés (...)*" (Sta a noi trovare una soluzione alle difficoltà). Nel nostro caso, la fatica di creare una emulsione perfetta, senza incompatibilità fisiche e biologiche è affidata a Xalifin-15® (Vevy codex 02.0151) Questo significa che Xalifin-15® forma rapidamente emulsioni del tipo olio in acqua stabili anche a 55°C, che non inibisce l'attività enzimatica della cute normale e che è ben tollerato anche dalla cute abrasa.