

Triple Action



mesotech

DEFEND

Solar Radiation

Solar radiation have on human being two conflicting functions: on one hand, a beneficial effect for their caloric, antirachitic and antidepressant action, and on the other hand, a negative action for their significant influence on ageing and on the risk of skin cancer.

Considerable amount of radiation reach the Earth's surface in the form of ultraviolet radiation, visible light and infrared rays. ¹

Such radiation can be divided into five categories according to their wavelength (Fig. 1):

- UV-C rays between 100 and 290 nm
- UV-B rays between 290 and 320 nm
- UV-A rays between 320 and 400 nm. UV-A is further divided into UV-AI (λ = 340-400 nm) and UV-AII (λ = 320-340 nm)
- Visible light rays between 400 and 750 nm
- Infrared rays between 750 and 3000 nm

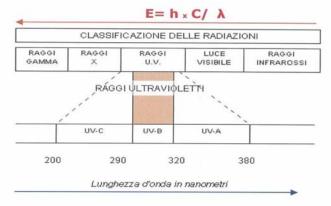


Fig. 1

UV RAYS ACTION

UV-C rays (100-290 nm) are the most energetic but being absorbed by atmospheric ozone they do not reach the Earth.

UV-B rays (290-320 nm) are very energetic, they are absorbed by the epidermis, where they unload all their energy (Fig. 2).

UV-A rays (320-400 nm) are less energetic than UV-B, but they penetrate more deeply into the skin.

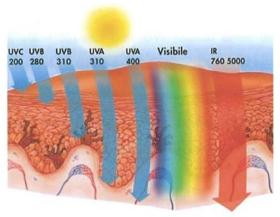


Fig. 2: Cutaneous penetration of UV-C, UV-B and UV-A radiation.

PHOTOTYPE

This term classifies each person's predisposition to have a greater or lesser erythema response to sun exposure.

Phototypes, which are grouped into six different categories, are defined by the following characteristics: skin pigmentation, eyes color, hair, quantity of freckles and the ability to acquire a protective tan.

Then there are people extremely photosensitive because of vascular problems, or elderly sick and weakened. For these people it is advisable having an intense skin protection and a lot of caution and care in sun exposure because their acclimatization time is quite long.²

Therefore, in accordance with the characteristics of each one, i.e. its own phototype, it is necessary to use an adequate sun protection before sun exposure.



Fototipo	Caratteristiche
1	Pelle color latte (rossiccia), numerose macchie rosse
II	Pelle molto chiara, numerose macchie rosse
III	Pelle da chiara a ambrata, qualche macchia di rossore
IV	Pelle ambrata
V et VI	Pelle scura o nera

Effects of radiation on the skin

The biological effects of the UV radiation on human skin appear immediately after the absorption of photons in skin tissues. 3 The epidermis is hardly hit and it reacts realizing defense mechanisms which work at different times. At first are released mediators, irritating bodies, which spread gradually inside the skin until reaching the blood vessels of the dermal papillary area. Within 12-24 hours appears sunburn, the so-called "solar erythema", vasodilatation occurs, with an increase of skin temperature and redness. At the same time with the release of the mediators, the UV rays

start in special epidermal cells called melanocytes, an enzymatic reaction which produces a dark pigment, the melanin.

Melanin is transferred into the normal epidermal cells and begins the migration towards the surface. In this way the granules of melanin create a barrier against further UV-B ray preventing them to penetrate inside the epidermis. In parallel with the formation of melanin, the skin cells called keratinocytes, are stimulated by the UV-B rays to reproduce, and within 72 hours, they double the superficial stratum corneum. This too, like melanin, reduces the penetration of UV-B rays, and it's thanks to its thickening and thanks to the presence of the pigment, that the skin of a normal subject, starting from the third days of exposure, is self – protected by UV-B rays.

The UV-A rays pass through the epidermis and go into extinction in the dermis (Fig.2); they cause the "maturation" of the preformed melanin completing in this way the oxidation process, increasing its brown tone. UV- A rays run down into the dermis, where they meet protein fibers such as collagen and elastin. An overdose of such radiation produces irreversible transformations in the collagen and elastic structures of the dermis causing collagenase and elastosis, i.e. "skin aging" 4. Free radicals formed when natural defense becomes insufficient, are attacked by some enzymatic systems, from vitamins E and C, β -carotene in addition to trace elements such as selenium, zinc, copper and manganese.

If the exposure is excessive or too brutal, the skin becomes inelastic, yellowish, opaque and embellished only for short periods by a temporary tan. Our skin's natural defenses are not unlimited, but are reduced to each exposure until they are exhausted.

SKIN AGING FOR UV IRRADIATION

Excessive doses of UV irradiation cause deep changes in the metabolism of melanocytes, real mutations which are definitive and irreversible. Generally the violent or continuous UV irradiation cause an uncontrolled multiplication of the melanocytes and the ensuing melanosis should be considered as a real precancerous stages.

The second action of UV rays is manifested by an increased activity of nuclear DNA synthesis, which results in increased cell mitosis. ⁵ In few days, with the increased number of epidermal cells through the subsequent keratinization, the stratum corneum is practically doubled in thickness.

The main agents of the damage induced by chronic photo exposure are the free radicals, but the photo – aging is caused also by the modifications that the UV radiation determines on the immune system and on the biochemical functionality of the skin. Also the dermis is affected by the action of UV rays, especially the UV-A which are more penetrating. Their protracted absorption causes dermis ageing with break of elastic fibers and denaturation of collagen fibers, causing in this way elastosis and collagenase. ^{6,7}



Fig.4 Difference of skin status in two identical Brazilian twin with different approaches to sun exposure.

DEFEND



Defend is the result of Mesotech's Research and Development Laboratories.

Company mission is to develop highly effective products, in order to meet customers 's needs who are looking for very high performance products, without losing sight of the toxicological profile of the raw materials used.

Defend is a photoprotector suitable for everyday use. Ideal for dry hyper-reactive skin, photodermatosis, photosensitivity due to certain drugs, pigment spots, premature skin aging and immunological alterations. Helps prevent dermatological disordes caused by excess UVB and UVA (SPF 50+) radiation, including solar allergies, stains, elastosis, premature aging and the consequences of the cumulative effect of radiation in the skin. The tolerability and effectiveness of Defend is tested under dermatological control.

Defend is a multifunctional product.

Due to the presence of several active ingredients Defend has a moisturizing, soothing and anti-age action.

ALOE VERA; COLLOIDAL OATMEAL; SYN®-AKE; HYALURONICACID.

ALOE VERA

The renose Aloe Vera or Aloe Barbadensis has been scientifically tested for all types of burn, radiant, heat, or solar. It has also been shown that it has a prophylactic effect if used before, during and after these skin damaging events.

Many of the benefits of the Aloe Vera can be attributed to the polysaccharides contained in the leaf gel.⁸ However, many other natural chemical elements of the Aloe Vera extract have been associated with its beneficial health effects: amino acids, anthraquinones, enzymes, organic and inorganic compounds, lipids, carbohydrates, lignin, salicylic acid, saponins, sterols and vitamins (B1, B2, B6, C, β-carotene, choline, folic acid and α-tocopherol).⁹

Several studies have shown that the protective effects of the Aloe Vera extract against photo damage are intrinsically related to the preventive action against the photo-oxidation of lipidic membranes and to the protection of the lysosome membrane.

The effect of the Aloe Vera extract on the lysosomes has the following results: a significant reduction of the lipofuscinogenesis (a granular accumulation of polymeric molecules not degradable by the lysosomal hydrolases, and not eliminated by exocytosis. These granules usually have a brown color and are mainly lipid compounds.) activated by UVA, maintenance of cellular homeostasis and increased cell survival. ^{10,11}

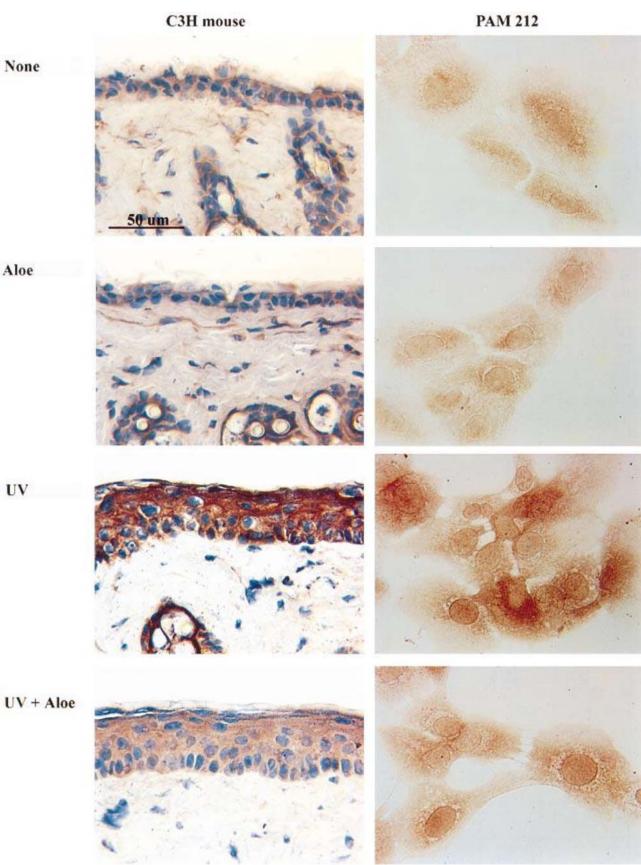


Figure 5. Aloe oligosaccharides decrease IL-10 production by UV irradiated murinekeratinocytes.

Shaved dorsal skin of C3H/HeN mice was Exposed to 15 kJ UVB radiation per m² and treated with PBS or 500 μg oligosaccharides per ml purified from lot ARF94K Aloe polysaccharide. Cryosections of dorsal skin were prepared 4 d later. The transformed keratinocyte cell line, Pam 212, was exposed in vitro to 300 J UVB radiation per m² and treated for 1 h with 10 μg Aloe oligosaccharides per ml in PBS. The cells were washed, fresh serum-free medium was added, and the Incubation continued at 37°C. Twenty-four hours later, the cells were washed, fixed, and stained for IL-10 using rat monoclonal anti-mouse IL-10 IgG, biotinylated anti-rat IgG, peroxidase labeled streptavidin, and diaminobenzidine substrate. The samples were counterstained with Gill's Hematoxylin dye and examined under light microscopy using an 320 objective.

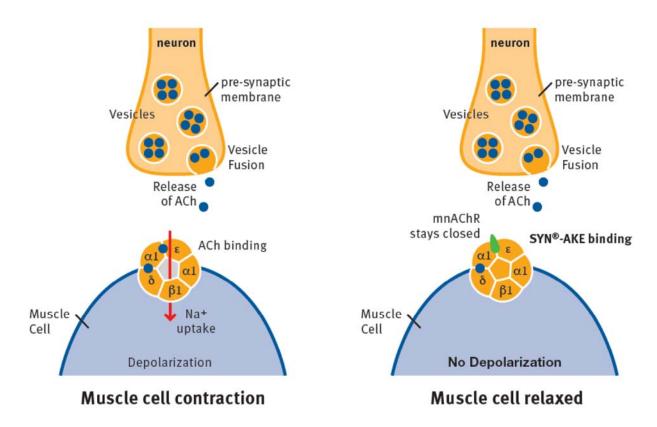
SYN®-AKE

Lines caused by facial expressions are always visible. We use about 60 muscles while we communicate. Frowning, raising eyebrows, laughing, are some examples of typical facial expressions we normally use to communicate. With the passing of time and with the frequent use of these facial movements, these fold persist and become permanent deep wrinkles on the forehead, smiling lines and crow's feet.

SYN®-AKE is a synthetic peptide with low molecular weight which smoothes expression wrinkles by topical application.

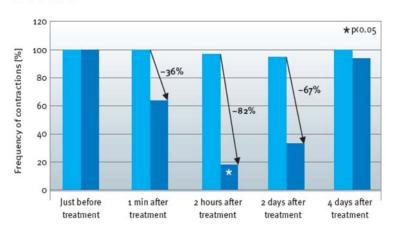
The mechanism of action is inspired by nature, as it mimics the activity of the Waglerin-1, a natural peptide present in the venom of the "Viper of the Temple" (*Tropidolaemus Wagleri*).

SYN®-AKE is based on a patented mechanism. It mimics the essential aminoacid sequence of the Waglerin-1 function. The safety and the activity of the SYN®-AKE have been thoroughly tested. The main effect is the immediate and long lasting wrinkle relaxation caused by the interruption of the neuronal transmission on the nicotinic acetylcholine receptor. The peptide is a reversible antagonist of the nicotinic acetylcholine membrane receptor present on the neuromuscolar junction (mnAChR). As the muscle nicotinic Ach receptors are blocked, the ion channel remains closed. It does not occur the Na+ absorption and the muscle cells remain relaxed. The transmission of nerve impulses to the mescles is inhibited and facial muscles are relaxed.



- IN VITRO AND IN VIVO STUDIES

In vitro

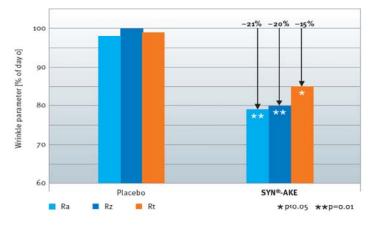


The efficacy of the SYN®-AKE tripeptide (0,5 mM) has been demonstrated in vitro by measuring the <u>frequency of the innervated muscle cells contraction</u> in function of the incubation time.

Results:

- •It significantly reduces muscle cells contraction
- Fast action
- Long lasting
- •Fully reversibile

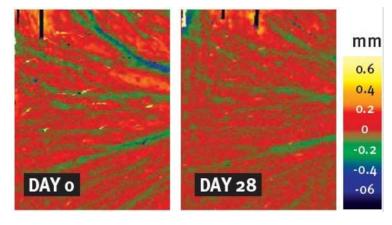
In vivo



The measurement of the **smoothing and anti-wrinkle effect of SYN®-AKE** has been compared to a placebo. A cream has been applied on the forehead twice a day for 28 days. The study included 15 volunteers per group (age 40-60).

Results:

- Wrinkle reduction up to 52% after 28 days
- Smoothing effect measurable on 80% of volunteers
- Measurable wrinkle reduction on 73% of volunteers



Measurement of the smoothing effect (Ra) and anti – wrinkle (Rz and Rt) of SYN®-AKE measured on the periocular "crow's feet" area after 28 days.

Results:

- The depth of the wrinkle is visibly reduced
- It is possible to observe less wrinkles and a smoother and more uniform skin surface

HYALURONIC ACID Low Molecular Weight (5-10 kDA)

Molecola di Acido laluronico.

Hyaluronic acid, and more generally the Mucopolysaccharides, are one of the main constituents of the connective tissue structures.

The very low molecular weight (5-10 kDA) of the Hyaluronic acid present in DEFEND improves the intradermal penetration, forming also a raw material for the formation of hyaluronic acid with medium molecular weight.

This type of Hyaluronic acid is especially suitable to retain water, both in the

connective tissue and in the fundamental layer of the dermis (and therefore responsible for a deep moisturizing), both in the upper layer of the skin, reducing the transdermal water loss (TEWL).

COLLOIDAL OAT



The colloidal oat flour has been used for thousand years in the treatment of dermatological deseases. Colloidal oat flour is appreciated for its moisturizing, purifying, antioxidant and anti-inflammatory properties, which are conferred by its chemical heterogeneity.

It has been shown that the oat flour extract inhibits the activity of the nuclear factor Kappa B (NF-kappa B) in the keratinocytes and the release of pro-inflammatory cytokine histamine.13 It modulates also arachidonic acid, cytosolic phospholipase A2 and tumor necrosis factor-alpha (TNF-alpha). Colloidal oat flour has proven to be a safe and effective ingredient in a variety of products for personal care.

It Contains a variety of active components including polysaccharides, proteins, lipids, saponins, enzymes, flavonoids, vitamins and avenantramides (polyphenols).¹⁶

A total of 47 subjects completed the study of the clinical efficacy of a body cream containing oat flour. This study showed that skin hydration was significantly higher at all times, even 2 weeks after the end of the application, compared to baseline.

The surface area of dead epithelial cells and the epithelial desquamation index on the forearm were significantly reduced at all assessment times compared to baseline.¹⁷

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Mesotech is innovative company, specialized in providing skin care and beauty solutions from the conception to the manufacturing of devices for aestetic medical field. Customer satisfation and quality are the main priorities for our staff. We develop our range relying on an ongoing dialogue with our customers.

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