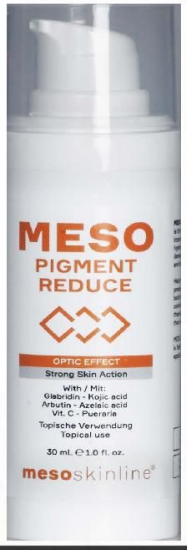


Strong Skin Action

Glabridina, Alfa-arbutina, Acido Kojico, Acido Azelaico, Pueraria (Kdzu), Vitamina C, Vitamina A, Semi di Colza

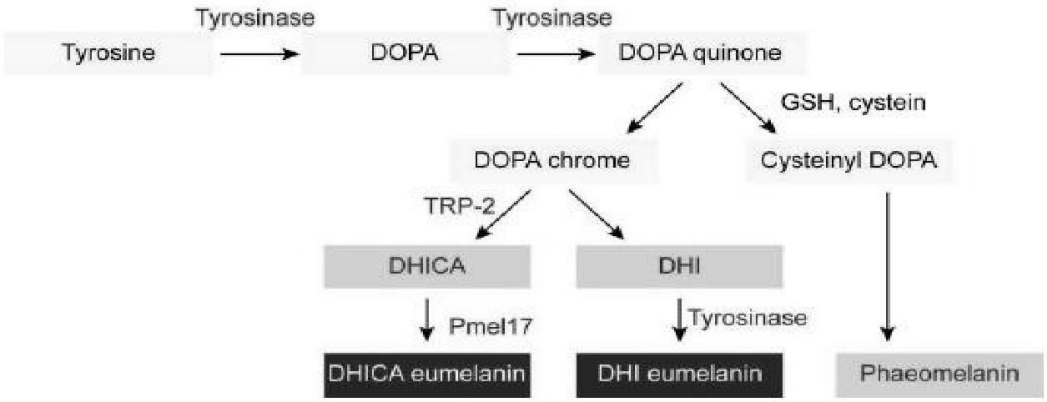
With immediate effect Soft Focus (cover spot)

Technical brochure

mesoskinline

1. MELANOGENESIS

The color of the skin is the result of the presence of various pigments. The contained hemoglobin in the red globules, the contained carotene mainly in the adipocitis.
The pigment that influences more than the others the color of the skin is the melanin that is produced by specialized cells situated in the epidermis called melanocytes. The melanin regulates, through a complex mechanism, the color of the skin.
The melanocytes are epidermal cells, situated in the deepest layer of the skin, the basal layer, provided of extended branchings (dendrites), extending among the keratinocytes wrapping them tightly. Every melanocyte can come into contact with more than thirty different keratinocytes.
The color of the skin is the result of the transfer of the melanosomes, organelles containing melanin, produced by the melanocytes, inside the keratinocytes in the epidermis and their following degradation.
The process of production of the melanin in the melanosomes is given by a series of oxidative reactions including the amino acid tyrosine and the enzyme tyrosinase.
The first phase is the more critical; it starts with the hydrosilylation of the tyrosine at 3,4–hydroxyphenylalanine (L-DOPA) thanks to the enzyme tyrosinase , that then oxidises the L– DOPA to O–Dopaquinone.



This o-quinone it is a very reactive mix and itcan self-oxydise spontaneously bringing to the formation of dopachrome and following of dihydroxy benzopyrrole or acid of dihydroxy benzopyrrole -2 - carboxylic (DHICA) up to constitute eumelanine, a polymer of brown-black color. In presence of cysteine or glutathione, the dopaquinone is converted in cystenil-DOPA or glutathione-DOPA. Later takes place the formation of feomelanine, a smaller molecule of yellow-red color.
The key enzyme ruling this process is the **tyrosinase**, a glycoprotein located on the membrane of the melanosomis. The activity of this enzyme is stimulated by UV radiations. The exposure to them, infact, gives place to fragments of Dna as dinucleotides of thymidine promoting the enzymatic activity.
There are several factors that can influence the activity of the tyrosinase: The transcription factor associate to teh microphthalmia (MITF); the hormone stimulating the alpha-melanocyte (alpha-MSH) and the adrenocorticotrope hormone (ACTH), produced by the keratinocites.
In case of inflammation, the prostaglandine E2 (PGE2) is able to stimulate the activity of the tyrosinase. Moreover , histamine can activate the synthesis of melanine in the common human melanocytes. In the same way, the nitrogen (No) monoxide can increase the synthesis of melanine, but only in association with the UV radiations, bringing to the production of cyclical (GMPc) guanosine-monophosphate that increases the expression of the enzyme tyrosinase.

2. DYSCHROMIAS

The cutaneous dyscromias are alterations of the skin color caused by an excess of melanine or, in some cases, to the deposit of pigments of other nature on the epidermis. This alteration can be located in a specific area of the body or in an extensive area. The dyscromias or skin spot are not all the same, each one has different origin and different depth.

2.1 Lentigo sunspot

They appear like spots of irregular shape and dimensions, whose coloration can go from the yellow to the brown one. They manifest usually on the areas more exposed to the sun radiations and they are caused by an excessive exposure to the sun without suitable protections. They affect mostly people over 45-50 years.

2.2 Age related Lentigo

Differently form the sunpot lentigo, they are due to the addition of the sun damages caused by the sun exposure during the time. They appear as brown macular lesions , usually of the diameter of 1 cm, and are more commons in the man that in the woman. The affected areas are more typically the face and the back of the hand.[1]

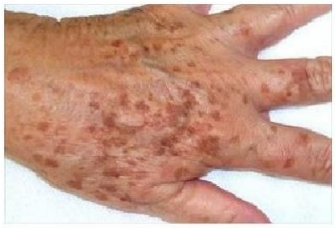


Fig.1 Lentigo Senili

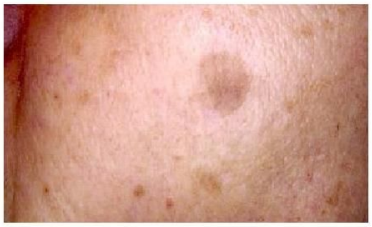


Fig. 2 Lentigo Solari

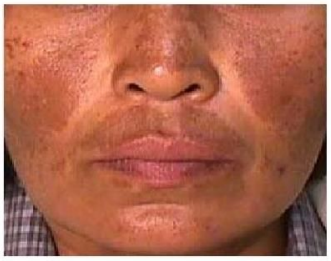


Fig.3 Melasma

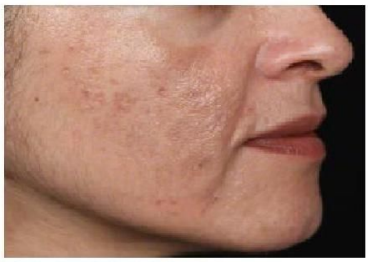


Fig. 4 Iperpigmentazione Post-Infiammatoria

2.3 Melasma

The melasma or cloasma gravidarium, is linked to an irregular and intense stack of melanine, not accompanied by a proliferation of the melanocytes, but by an hiperproduction of the same pigment.
The spots are often visible under the lips, the nose, the cheeks, the chin, the forehead and sometimes also on the neck.
Despite the etiology of the melasma is still in depth analisys, among the principal causes of its appearance we find the exposure to the UV radiations and the use of estrogens. The reason seems ascribable to the hormonal levels, in particolar way to 17-β-estradiol, that has shown to meaningfully increase the activity of the tyrosinase if added to cultures of melanocytes.

2.4 Post-inflammatory Hyperpigmentation

The post-inflammatory hyperpigmentation (Pipe) appears as a set of points of irregular shape and of dark pigmentation that surrounds a zone previously inflamed. It is common in people of darker phototypes and it can appear in any part of the body. Such pathology can be a consequence of different cutaneous events (acne, skin rash, hair follicle infection, burns, scars)or skin treatments as peeling or laser.[2]

2.5 Tanning bed lentigo

They have been often reported cases of uncommon melanocytics damages after the exposure to UV rays of tanning beds. They apparently seems solar lentigos but the histological analysis has revealed a melanocytic hyperplasia and therefore the patient with such manifestations seriously risks the appearance of a skin cancer. If the patient wants to continue the use of the tanning beds, it is suggested an annual check up for the examination of the skin status.6

2.6 Eyes' dark circles

The cause of eyes' dark circles is poorly still known even if they are very common, both in the men and in the women. Many believe that the thinning of the skin in that zone makes the underlying blood vessels more visible, giving the the unwanted coloration. Every inflammation or vasodilatation in this area could appear as a darkening. Although a lot of cosmetic firms promise an improvement of this condition, the use of clearing agents for this purpose still results of doubtful effectiveness.

DESCRIPTION PIGMENT REDUCE

Pigment Reduce is the result of the research of Mesotech laboratories . The company mission is always to develop highly effective products, to answer to the demands of careful customers searching more and more performing products, always keeping focussed to the toxicological profile of the raw materials used.

Pigment Reduce is the more effective and innovative intensive treatment for hyperpigmentations, melasma, sun damages , age related spots, dyscrhomias,dark circles. It helps to attenuate, to reduce and to prevent the cutaneous spots on face, body and hands.

The formulation of Pigment Reduce is rich in active principles, present in high concentrations and with strong depigmenting properties , able to contrast the biological and chemical-physical phenomenons , lying at the base of the appearance of these skin imperfections.

GLABRIDINE

Glabridine is an isoflavonoid extract and isolated by the root of Glycyrrhiza Glabra L. In vitro and In Vivo studies have shown that this Phytoestrogen has several properties: anti-oxidant, anti-inflammatory, neuroprotective, anti-teratogen, anti-bacterial and also depigmenting when applied on the skin.[3]
The depigmenting activity of Glabridine is due to a multifunctional action on the causes bringing to the appearance of cutaneous dyscrhomias.
It has been proved that the topical application of Glab at 0,5% on the skin of the test animals reduces the rash and the pigmentation induced by UVB (Figure 4).
The Glabridine acts through a mechanism that brings to the inhibition of the tyrosinase, active enzyme on the pathway that brings to the formation of melanin. Therefore, the inhibitors of the tyrosinase can be important for the treatement of the troubles of the abnormal pigmentation and to act as bleaching agents of the skin in cosmetics.[4]
It has been proved that glabridine inhibits the activity of the isoenzymes tyrosinase T1 and T3 implicated in the melanogenesys in the cells of murine melanoma B16 . 5
Several studies have shown the anti-oxidant activity of the glabridine. The production of supeoxide anion, powerful anti-oxidant agent, has been inhibited from glabridine. Other studies have underlined the inhibiting effect of glabridine on the activity of the cyclooxygenase.

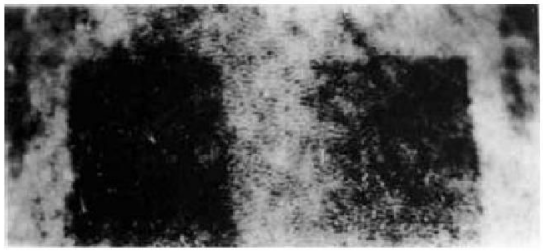


Figura 4. Effect of glabridin applications on UVB-induced pigmentation in the back of a brownish guinea pig. I b o pigmented square-shaped areas were exposed to UVB irradiation (250 mJ/cm2/day for four successive days), and then, 0.5% glabridin (or base solutions for the control) were topically applied for 3 weeks. Reduced pigmentation was seen in glabridin-treated skin. Similar results were obtained on all three guinea pigs tested.

VITAMIN C

Vitamin C or Ascorbic Acid, molecule almost ubiquitous in nature, present especially in the citrusis and in green leaf vegetables, reduces the production of melanin since it is able to reduce o-DOPAquinone to the previous mixture, DOPA, interrupting the process of oxidation that brings to the formation of melanin.7
In the formulation of Pigment Reduce has been inserted a more stable form of Vitamin C, Ascorbyl Glucoside. Indeed this last appears to be more stable to oxidation, increasing in this way the performance of the product.

ARBUTIN

Arbutin is a natural glycoside of Idroquinone, chemically known as hydroquinone -β-D-Glycopiranoside, that has fluently been employed for treating the disorders of the pigmentation in Japan.8 it is a compound available in Bearberry leaves, blueberries, raspberries and in many types of pears. As the Hydroquinone, also Arbutin is a good inhibitor of the tyrosinase. The mechanism of action nevertheless seems different, because in many studies on cultures of human melanocytes it has been suggested that it doesn't act neither on the synthesis neither on the expression of the enzyme. Clinical studies have verified that its applications don't give collateral effects,on the contrary of Hydroquinones.

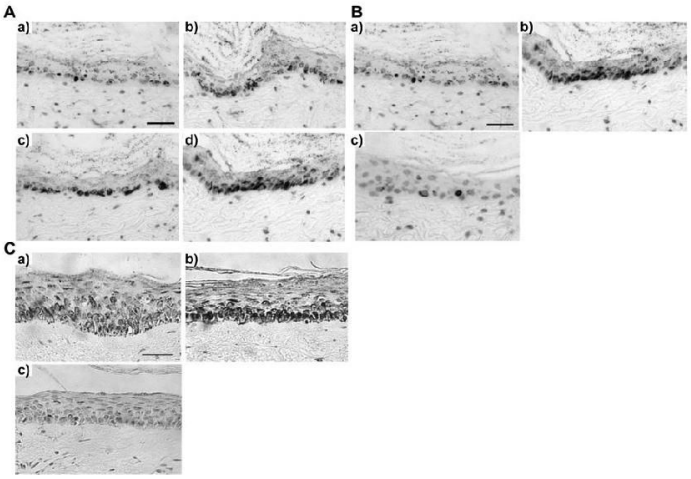


Figura 5. Melanin content visualized by Fontana-Masson staining of brownish guinea pig and human skin. A. The morphological distribution of melanin in brownish guinea pig skin as visualized using Fontana-Masson staining. Pigmented skin was treated for 24 h with 100, 200, or 500 nM of α-MSH. a) control; b) 100 nM α-MSH; c) 200 nM α- MSH; d) 500 nM α-MSH. Scale bar = 20 μm. B. The melanin content was visualized using Fontana-Masson staining of brownish guinea pig skin. The skin was treated with α-MSH for 24 h and then with arbutin for 72 h. a) control; b) 500 nM α-MSH treatment; c) 500 nM α-MSH and 1 mM arbutin treatment. Scale bar = 20 μm. C. The melanin content was visualized using Fontana-Masson staining of human skin. The skin was treated with α-MSH for 24 h and then with arbutin for 72 h. a) control; b) 500 nM α-MSH treatment; c) 500 nM α-MSH and 1 mM arbutin treatment. Scale bar = 20 μm.

KOJIC ACID

Kojic Acid is a metabolite of fungoid origin produced by numerous kinds of Aspergillus, Acetobacter and Penicillium.9 th Kojic Acid inhibits the enzyme tyrosinase, chelating copper in the active site. Clinical studies have shown that Kojic Acid and the its esters have depigmenting properties and they are considered sure and not toxic. The inhibiting effect on the formation of melanin is due and to the inhibiting activity on the trascription factor associated to microphtalmia (MITF), and to the inhibition of the activity of the hormone stimulating the alpha-melanocyte (alpha-MSH). Therefore can be suggested that these depigmentin compositum have the potential to be used in the cosmetic formulations to treat Hiperpigmentation.[10]

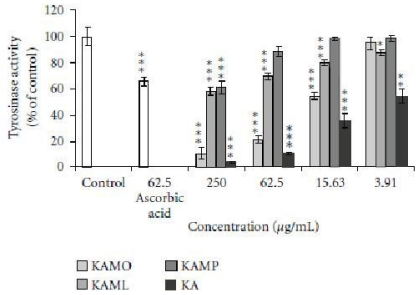


Figure 6. The results of the inhibition of mushroom tyrosinase activity by KAMO, KAML, KAMP, and KA. Denotes ∗P < 0.05, ∗∗P < 0.01, ∗∗∗P < 0.001 compared to α-MSH treated control. Data are presented as means±S.E.M, and expressed as%of control. 62.5 μg/mL ascorbic acid was used as reference. n ≥ 3.

AZELAIC ACID

Azelaic Acid is a dicarboxylic saturated acid present in nature in wheat, in barley, in rye. Many authors have confirmed the effectiveness of this acid in the reduction of the melasma, post-inflammatory hyperpigmentation or hyperpigmentation caused by phototoxic reactions.[11] The whitening properties of Azelaic Acid are due to the action of competitive inhibitor of the tyrosinase.

NIACINAMIDE

Niacinamide, also known as Nicotinamide or 3-Piridin-Carbossammide, it is biologically an active ammide of the vitamin B3. Niacinamide has underlined to be able to inhibit the transfer of the melanosomes to the keratinocytes. In vitro tests have shown that its ability to inhibit this transport system is of 68%.[12]

A clinical study carried out in October of 2002 (Kobe, Japan) submitted 79 Japanese women, aged between 28 and 54 years, with various disorders of cutaneous hyperpigmentation (age related lentigo, sunspots, melasma.) to a topical treatment with Niacinamide.(Fig.7) Therefore the treatment with Niacinamide has brought to meaningful improvements increasing the brightness of the skin and decreasing both the blush and the tones of the yellow, often unwanted .13 Clinical tests have shown that the association of Niacinamide with an opportune solar filter is able to give a great brightness in comparison to the only application of the sunscreen.

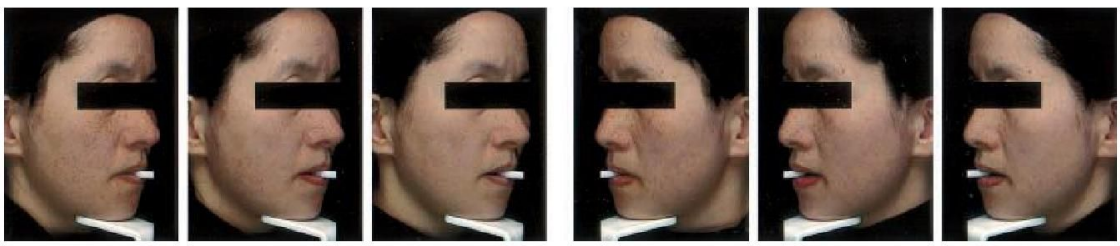


Figura 6. Facial images used for assessment of reduction of hyperpigmentation (human clinical study I). The subject used 5% niacinamide moisturizer on the right side of the face and vehicle moisturizer on the left side.

VITAMIN A

Retinoic Acid also acts as a depigmenting and it can produce a whitening effect if applied topically. The mechanism of action, also not being entirely clarified, is connected from one side to the increased cellular turnover of the keratinocytes, promoting in this way the loss of pigment of the epidermis[14], from the other side to a strengthening of indirect type of the cytotoxic effect on the melanocytes of some cutaneous depigmentant, through the inhibition of the detoxification ways (with relative increase of toxic species as for instance the quinones).[15]
In cosmetic field these molecules, having one well shown therapeutic action, cannot be used. It is possible to use only Vitamin A and its derivatives that can be biotransformed in Vivo into Retinoic Acid.

PUERARIA

The increasing interest for the natural based raw materials allowed that several studies have been made on new natural skin depigmentation actives.
Pueraria, known also as kudzu, is a climbing plant belonging to the Fabaceae family. Its root and flowers, used in the traditional medicine, have several medicinal properties.
Several studies have shown the activity of the extracts of this plant toward the melanogenesis. The activity of suppression of the melanogenesis has visually been confirmed by the coloration of Fontana-Masson (Fig. 8).

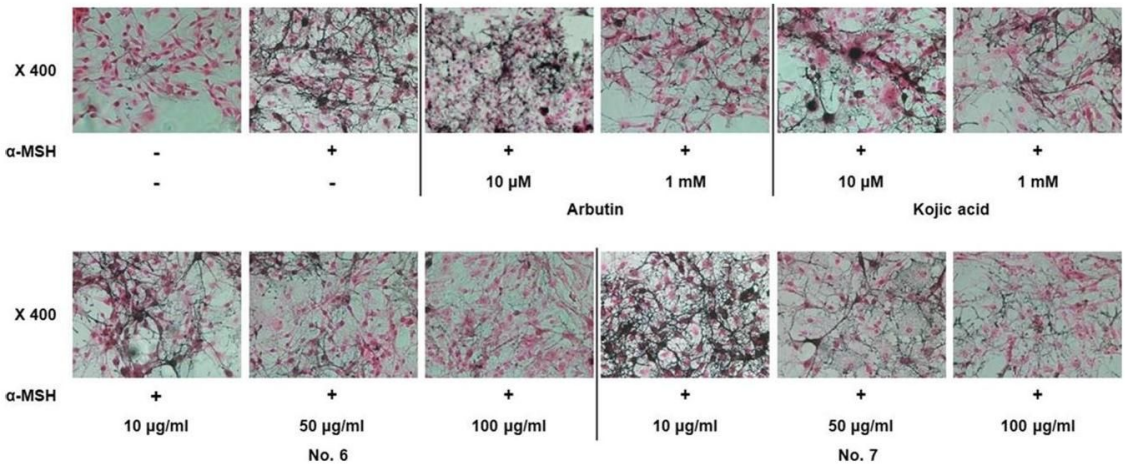


Figure 8. Optical images (magnification 9400) showing melanin content with Fontana–Masson staining in B16F10 cells. After 24 h of a- MSH pre-incubation, B16F10 cells were treated with a combination of a-MSH and extract No. 6 or 7, arbutin, or kojic acid for 48 h. Pigmentation observed upon Fontana–Masson staining (magnification x 400)

The process of melanogenesis is regulated by an intracellular enzymatic cascade . To determine if the aerial part of P. thunbergiana directly influences the tyrosinase, the key enzyme for the synthesis of melanine, in the study have been used the essays of the activity of the cellular and fungal tyosinase . It is interesting to notice that, the activity of the cellular tyrosinase has gone down to lower levels from those of the cells not treated (Fig. 9).
These results point out that the activity anti-melanogenesis of the aerial part of P. thunbergiana is involved in the regulation of the superior levels enzyme tyrosinase as transcription, translation and maturation.

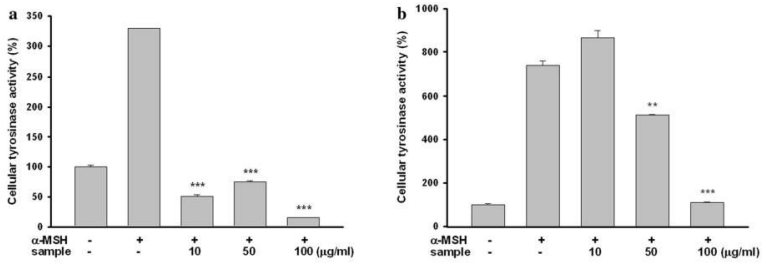


Figura 9. Optical images (magnification 9400) showing melanin content with Fontana–Masson staining in B16F10 cells. After 24 h of a-MSH pre-incubation, B16F10 cells were treated with a combination of a-MSH and extract No. 6 or 7, arbutin, or kojic acid for 48 h.

UV radiation is a strong inductor of oxidative stress, that contributes to the pigmentation of the skin. Therefore , antioxidants can reduce melanogenesis. In the above mentioned study it has been recorded that the antioxidant activity could be considered one of the reasons for which the aerial part of P. thunbergiana have antimelanogenesis activity. The results of our study suggest that the aerial part of P. thunbergiana can be used as a whitening agent of the skin (Fig.10) 16

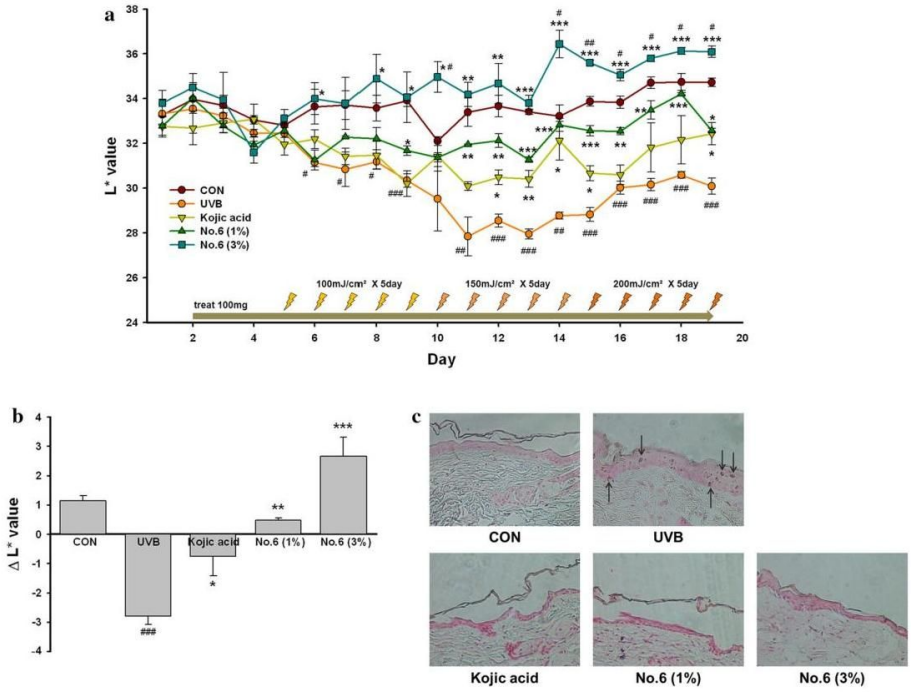
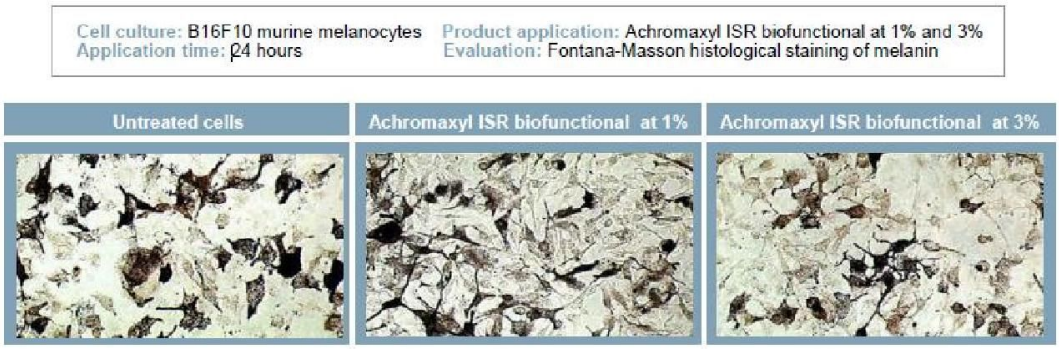


Figura 10. Effects of aerial part of P. thunbergiana on pigmentation in UV-irradiated animal. a Melanin possessing hairless mice were treated with 100 mg of cream base, kojic acid 1 % cream, No. 6 1 and 3 % cream on dorsal skins every day. UVB irradiation was performed according to the indicated schedules. The lightness (L* value) of skin was measured before applying cream on each day. b DL* values of each animal were calculated; values of days 17, 18, 19 minus values of days 2, 3, 4. Data represent mean ± SEM (n = 3). #p\0.05, ##p\0.01, and ###p\0.001 compared with CON. *p\0.05, **p\0.01, and ***p\0.001 compared with UVB group. c Microscopic images of skin sections. Melanogenesis of dorsal skin was highlighted by Fontana–Masson staining. Arrows indicate pigmentation)

BRASSICA NAPUS SEED EXTRACT

The Brassica Napus seed extract (Rape) is rich in antioxidants. In Vitro and in Vivo studies have shown that this functional ingredient is able to act against the signs of aging, reducing the cutaneous dyschromies and evenings the cutaneous complexion.(Fig.11 and Fig.12)



Pictures show a visible decrease in melanin staining intensity in melanocytes *in vitro*.

Fig 11

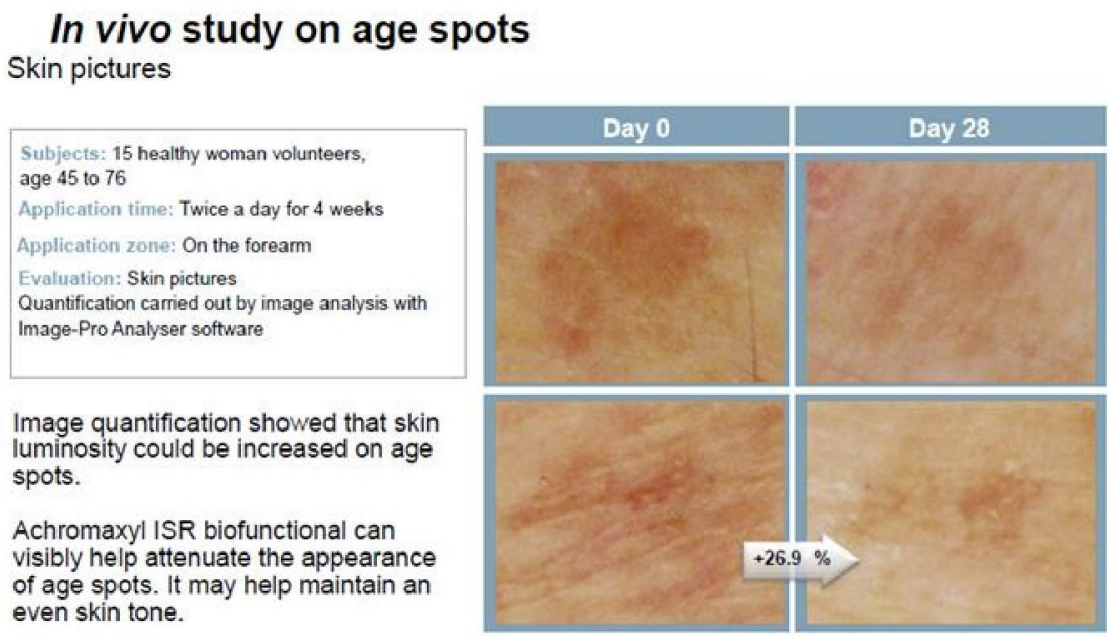


Figure 12

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Melanogenesis inhibitory effect of aerial part of Pueraria thunbergiana in vitro and in vivo

mesoskinline®

MILANO - HAMBURG - COPENHAGEN *By Aleksandra Kjaersfeldt*

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