

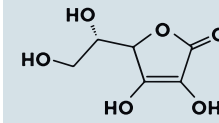
Hyperpigmentation AND ITS PATHOGENESIS

Dermaregen Lightening and anti-pigmentation protocol is based on three high-concentrate products specifically formulated to reduce the appearance of hyperpigmentation, such as photospots, light spots, and melasma. This protocol includes Tranexamic Acid Anti-Spot & Lightening Gel Cream, Vitamin C-Ferulic Gel Cream, and TXA Eye Contour Gel Cream. The application is suggested for one month before or after aesthetic procedures, depending on the physician's suggestion.

The main active ingredients include Tranexamic Acid (TXA), Niacinamide, Retinol, Vitamin C, and Arbutin. These ingredients are clinically proven to have synergistic actions, utilizing different mechanisms to achieve effective



Vitamin C



Vitamin C is also known to decrease skin pigmentation. We evaluated whether a mixture of nicotinamide, vitamin C decreased melanogenesis by modulating mitochondrial oxidative stress and NNT expression in UV-B-irradiated animals and in an in vitro model of melanocytes treated with conditioned media (CM) from UV-B-irradiated keratinocytes. The topical use of vitamin C and nicotinamide has also shown excellent safety, we thought that their combination (NVP-mix) could be used safely as a therapeutic for hyperpigmentation.²

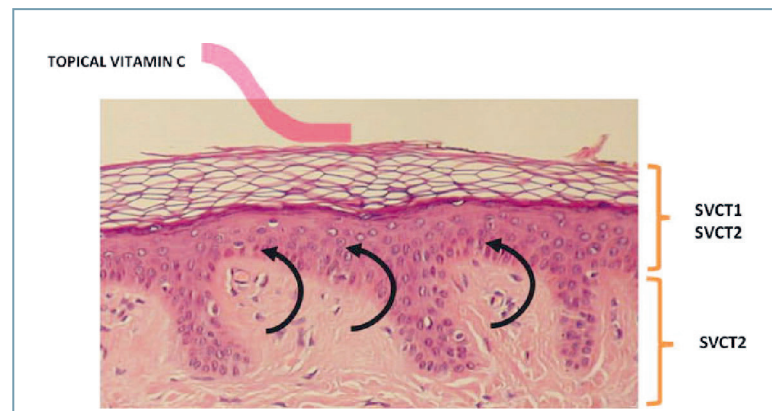
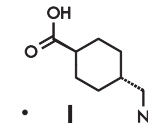


Figure 1. Distribution of vitamin C in the skin mediated by SVCT1 and SVCT2. The black arrows indicate the transport from the dermis to the epidermis (avascular layer).

Tranexamic acid



Tranexamic acid (TA) is an old drug used for a long time to treat or prevent excessive blood loss. The first mention of TA in dermatology was in 1979 in actinic prurigo, with good results. Later it was demonstrated in vitro that TA was able to block melanogenesis. During the 2010's more and more trials were published, assessing its efficacy in melasma, but also in erythrotelangiectatic rosacea. First, systemic TA was prescribed, but soon, because of the rare but severe complications susceptible of occurring, topical way was tested, giving similar results without risk of side effects. In this review we shall bring a summary of published clinical trials using systemic or topical TA in melasma and intend to compare the efficacy and safety of both regimens. Mechanism of action of TA will also be investigated.

MECHANISM OF ACTION OF TA IN HYPERPIGMENTATION The particular interest of TA in the management of melasma is due to that it displays an activity at various levels. First, TA was shown to downregulate the activity of mast cells and consequently the release of histamine. TA also directly inhibits melanogenesis through suppressing the expression of prohormone convertase (PC2) and α -melanocyte stimulating hormone (α -MSH). On the other hand, TA reduces the number of blood vessels in dermis, and inhibits neovascularization induced by basic fibroblast growth factor. Finally, TA reduces VEGF levels by downregulating the activity of mast cells. Figure summarizes the multifactorial mechanism of action of tranexamic acid on melasma.³

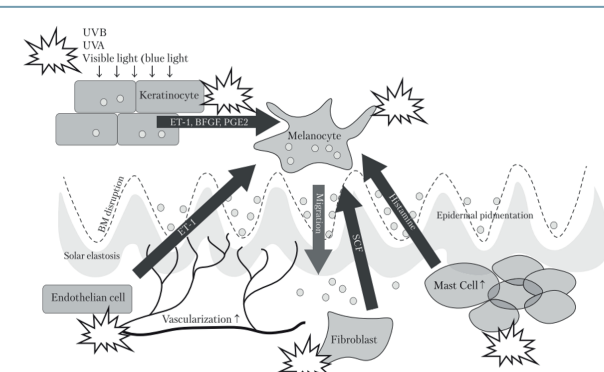
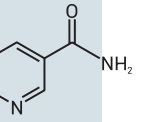


Figure 2. Mechanism of action of tranexamic acid on melasma

Niacinamide



Nicotinamide, also known as niacinamide, is another well-known depigmentary agent [9], which suppresses melanosome transfer from melanocytes to keratinocytes. Niacinamide, is the pyridine-3-carboxylic acid amide form of niacin, a component of the vitamin B complex. Niacinamide is beneficial because it results in the increased synthesis of proteins and keratin, stimulation of ceramide synthesis and acceleration of the differentiation of keratinocytes. These factors provide a stabilizing influence on epidermal barrier function and an improvement in the moisture content of the horny layer. On ageing skin, niacinamide improves the surface structure of the skin, shows a wrinkle-smoothing effect and has an inhibitory effect on photo carcinogenesis. There are reports of topical niacinamide providing beneficial effects on reduction in acne severity. Topical niacinamide has marked anti-inflammatory properties. Anti-inflammatory action affecting neutrophil chemotaxis has been reported for niacinamide. Niacinamide has been proved to inhibit histamine release and to suppress the lymphocyte transformation test. Additionally, niacinamide has been shown to suppress cytokine-mediated induction of nitric oxide synthase in a number of cells, resulting in decreased inflammation. Also, topical niacinamide is effective in lowering sebum excretion rate in skin.⁴

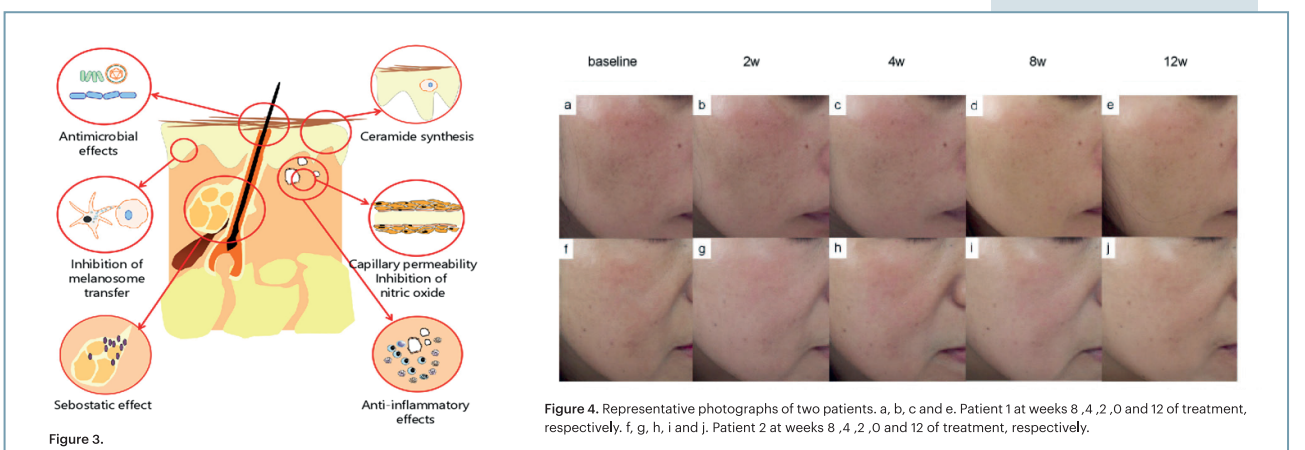


Figure 4. Representative photographs of two patients. a, b, c and e. Patient 1 at weeks 0, 2, 4, 8, and 12 of treatment, respectively. f, g, h, i and j. Patient 2 at weeks 0, 2, 4, 8, and 12 of treatment, respectively.

Retinol

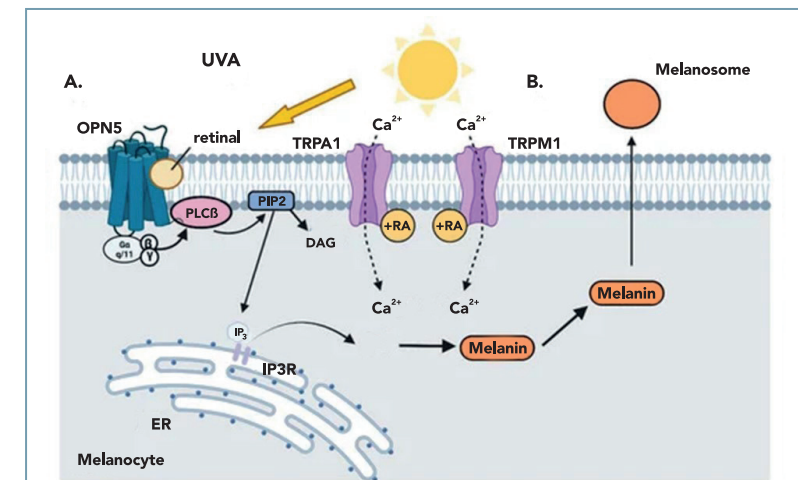
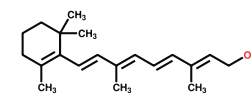


Figure 5.

Vitamin A is a fat-soluble micronutrient necessary for the growth of healthy skin and hair. However, both too little and too much vitamin A has deleterious effects. Retinoic acid and retinol are the main active metabolites of vitamin A. Retinoic acid dose-dependently regulating hair follicle stem cells, influencing the functioning of the hair cycle, wound healing, and melanocyte stem cells. Retinoic acid also influences melanocyte differentiation and proliferation in a dose-dependent and temporal manner. Levels of retinoids decline when exposed to ultraviolet irradiation in the skin. Retinol is necessary for the phototransduction cascade that initiates melanogenesis but the source of that retinol is currently unknown.⁵

CONCLUSION

In various studies that have formed the basis and main concept for developing the post-treatment lightening and brightening protocol in the Dermaregen brand, these ingredients have been proven to be highly effective on all skin pigmentation types. In a study conducted by Xing et al, Hyperpigmentation all patients were shown how to apply the solution containing %5-3 tranexamic acid, 10-5 % niacinamide, Retinol %0.5-0.2 covering the entire face twice a day. The duration of therapy was 12 weeks. Patients were also asked to apply a sunscreen cream. The final clinical outcome was evaluated by dermatologists at the end of the 12-week treatment using a 5-grade clinical assessment scale: "almost clear", >%75 improvement; "marked improvement", %75-51 improvement; "moderate improvement", %50-25 improvement; "minimal improvement", %25-0 improvement; "stable or worsening", no improvement or aggravation.⁶

In a study conducted by Hyun Jun Park et al, Nicotinamide, vitamin C, and PDRN are well-known antioxidants. Thus, we hypothesized that their combination (NVP-mix) could modulate redox levels by increasing NNT expression and decreasing mitochondrial oxidative stress to eventually decrease melanin synthesis mediated by the redox system. We therefore evaluated the ability of NVP-mix to decrease melanogenesis in UV-B-irradiated animal skin and in vitro in a human melanocyte model after treatment with CM from UV-B-irradiated keratinocyte cultures. For effective delivery of NVP-mix into the skin, a MTS was used in this study.¹

In a study conducted by Christine A et al, research demonstrably argues that retinoids perform important regulatory roles in the hair and skin. Recent studies suggest that RA regulates the induction of anagen by inhibiting HFSCs, maintaining them in refractory telogen. RA also regulates catagen induction by a different mechanism. In addition, RA synthesized in HFSCs in vivo has been shown to induce the differentiation of McSCs. Similar increased differentiation was also seen if RA was provided early in that process in vitro. However, addition of RA to a fully differentiated melanocyte stunts that growth and causes the loss of their dendrites. In epidermal phototransduction, retinol is critical for UV-induced melanin synthesis, yet ultraviolet irradiation depletes both retinoids and their nuclear receptors, yet increases RA synthesis enzymes in the epidermis. Retinoid metabolism in the keratinocyte is well characterized. However, future studies are needed to determine both the specific retinoid metabolon in the melanocyte and the source of the retinal needed for phototransduction.⁵

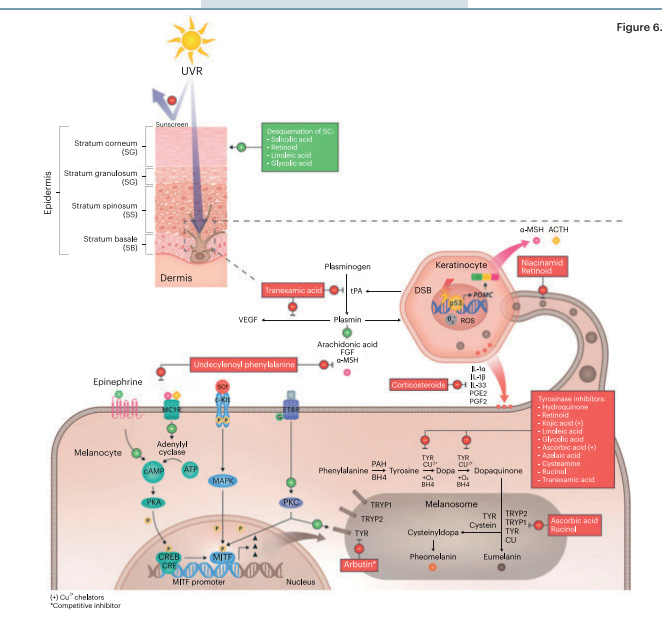


Figure 6.

REFERENCES:

- Hyun Jun Park 1,†, Kyung-A Byun 2,3,†, Seyeon Oh 3 , Hyoung Moon Kim 2 , Moon Suk Chung 4 , Kuk Hui Son 5,* and Kyunghye Byun 2,3,* The Combination of Niacinamide, Vitamin C, and PDRN Mitigates Melanogenesis by Modulating Nicotinamide Nucleotide Transhydrogenase
- M.D. Enrique Lorente Prieto, Cosmetic Topical Use of Vitamin C
- Dr. Christian Diehl, Department of Dermatology, Università Degli Studi Guglielmo Marconi Via Plinio, 00193 ,44, Rome, Italy, Use of tranexamic acid in melasma
- Yeşim Kaymak,1* MD, Meltem Önder, MD, An Investigation of Efficacy of Topical Niacinamide for the Treatment of Mild and Moderate Acne Vulgaris
- Christine A. VanBuren and Helen B. Everts, (2022) Vitamin A in Skin and Hair: An Update
- Xiaoxue Xing, Li Chen, Zhongyi Xu, Shanglin Jin, Chengfeng Zhang, and Leihong Xiang, (2021) Efficacy of a Topical Agent Containing Tranexamic Acid, Niacinamide in Melasma
- Valeria González-Molina, MD, Alicia Martí-Pineda, BS, and Noelani González, MD, Topical Treatments for Melasma and Their Mechanism of Action (Figure 6)

DERMAREGEN
PROFESSIONAL SKIN CARE
COSMECEUTICALS & CLINICEUTICALS
TO SUPPORT & IMPROVE THE RESULTS
OF AESTHETIC PROCEDURES

www.dermaregen.ir
+98 21 22044991-3 +98 21 22044991-3
Unit 1, 2nd Floor, 60 East Maryam St, Elahiye Ave, Tehran, 19649-66335, Iran



DERMAREGEN
PROFESSIONAL SKIN CARE
COSMECEUTICALS & CLINICEUTICALS
TO SUPPORT & IMPROVE THE RESULTS
OF AESTHETIC PROCEDURES

**POST TREATMENT
LIGHTENING &
BRIGHTENING
PROTOCOL**

Prevent
Vitamin C Complex
Niacinamide Triacetate
Hyaluronic Acid
Matrix B

Transform
Niacinamide Triacetate
Vitamin C
Matrix B

Eye Contour
Vitamin C
Niacinamide Triacetate
Matrix B