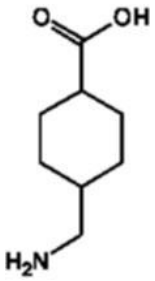
Approved skin lightener – tranexamic acid is effective against pigmented spots and redness

published in medical Beauty Forum 2015 (3), 12-14

In the medical field, tranexamic acid is a reliable haemostatic agent during surgery and in the case of accidental injuries. In medical cosmetics, tranexamic acid is used for skin treatments: already small amounts can bleach pigmented spots and reduce redness – also in combination with instrument-based techniques.

Tranexamic acid also is known as a pharmaceutical agent. Already in 2011[1] it has been entered on the "Model List of Essential Medicines" (EML) of the World Health Organisation (WHO) – in particular for the treatment of trauma after traffic accidents or in the case of haemorrhagic risks and even fatal haemorrhage. Tranexamic acid (= International Nonproprietary Name, INN), from the chemical viewpoint, is an amino acid, and more precisely, we are speaking of trans-4-(aminomethyl)cyclohexanecarboxylic acid.



Structure of tranexamic acid

The colourless crystalline compound belongs to the group of antifibrinolytics, or in other words, agents that prevent the breakdown of fibrin. Fibrin is a cross-linked protein which is formed during bleeding and which closes the wounds. Fibrinolysis, or in other words, the opposed process of dissolution of protein, starts shortly after fibrin formation. Antifibrinolytics are frequently used during surgical interventions and tooth extractions in order to reduce bleedings.

A chance discovery for dermatology

In dermatology the effects of tranexamic acid have been known for a long time, namely in the context of pigment disorders. The first report on the treatment of melasmas with tranexamic acid dates back to 1979[2] and comes from an accidental observation after the oral administration of tranexamic acid. In the particular case, the intensity of a melasma was significantly reduced within a period of two to three weeks.

Melasmas or hyperpigmentations form in a variety of ways[3]. They are triggered by miscellaneous endogenic and exogenous influences such as

- UV radiation of the sunlight
- photosensitization, or in other words, the reduced sensitivity threshold of the skin to light caused by essential oils for instance
- hormonal influences, as for example during pregnancy
- inflammation mediators such as prostaglandins and cytokines (post-inflammatory hyperpigmentation)
- AGE (Advanced Glycation Endproducts), or in other words, products that form in the body due to the reaction of proteins or lipids with carbohydrates; they are held responsible for a variety of health implications
- other deposits of endogenous metabolic products

A considerable number of studies on the effects

Pale or dark spots on the skin are annoying and can affect the mental health when the spots are clearly visible. Preparations against hyperpigmentations therefore have special aesthetic importance. This is the reason why first many clinical and later on also cosmetic studies on tranexamic acid have been pub-

[1] 18th Meeting of the WHO Expert Committee

[2] Sadako N, Treatment of melasma with tranexamic acid, The Clin Rep 1979; 13: 3129-31

[3] Lautenschläger H, Haut ohne Makel – Wirkstoffe und Wirksysteme, medical Beauty Forum 2014; 5: 32-35

lished after its effects had been observed for the first time[4].
The studies have shown the following results: tranexamic acid is effective after oral administration and after topical application. A variety of biochemical mechanisms have been discussed, among them the inhibition of tyrosinase and the preceding processes such as the reduction of free arachidonic acid and prostaglandin E_2. Main field of application of tranexamic acid however is the prevention. Tranexamic acid already is effective in low dosage; high dosage will not improve the effects but rather cause irritations.

Solo in creams and sera...

In cosmetics, the water-soluble acid is used in commercial creams and liposomal sera in a dosage of 2% at the maximum. The first liposomal formulation was developed in 2002.[5] The native phosphatidylcholine in liposomal sera improves the penetration. Other techniques to enhance the efficacy such as for instance the iontophoresis have not proved successful. There have been reports on intradermal microinjections.[6] Therefore it can be assumed that tranexamic acid can be successfully used in the context of dermal needling.

...and in combination with instrument-based techniques

The combination of fruit acid peelings, microdermabrasion, IPL and laser treatments with liposomal tranexamic acid preparations is widely spread in South East Asia and meanwhile also applied in Europe. Occasionally, additional tyrosinase inhibitors such as ascorbyl phosphate (vitamin C), herbal extracts and kojic acid, and in the medical context also hydroquinone (banned in the European Cosmetic Directive) are topically applied in order to remove existing hyperpigmentations or prevent the new formation. A simultaneous administration of vitamin C and E will not intensify the effects though. In the nineties, Shiseido, the Japanese cosmetic manufacturer, had applied for patents for tranexamic acid derivatives, among others esters of antioxidative polyphenols such as hydroquinone which altogether did not prevail and subsequently were withdrawn.

Among the numerous adjuvants used to optimize the depigmentation with tranexamic acid, niacinamide (vitamin B_3 alias nicotinic acid amide) should be mentioned particularly.[7] Niacinamide is not a tyrosinase inhibitor though but rather interferes with the melanosomes transport. The AGE inhibition of niacinamide is being discussed.
Besides the bleaching effect, tranexamic acid also reduces the translucent reddish colour of the superficial blood vessels. The result is an even complexion. Reduced redness also meets the desire of Asian women for a perfectly white skin tone.

Effective skin care adjuvant in the case of rosacea and acne

Tranexamic acid and niacinamide also complement each other in another indication, i.e. the skin care of the rosacea prone skin. While in this particular case tranexamic acid reduces the redness, vitamin B_3 has anti-inflammatory effects, which, by the way, also is observed in the case of acne.[8] The combination of tranexamic acid with azelaic acid and boswellic acids offers a very effective treatment option, since azelaic acid as alpha-reductase inhibitor controls the anaerobic bacterial flora (propionibacterium acnes and staphylococcus epidermidis) which is typical for acne and rosacea, and boswellic acids reduce the increased activity of the natural proteases.

Orally administered tranexamic acid that entered the circulatory system via gastro-intestinal tract is renal excreted within a few hours. The safety report required by the European Cosmetic Directive does not mention any health risks in the context of topically applied tranexamic acid for cosmetic purposes. Irrita-

[4] Tsz Wah Tse et al., Tranexamic acid: an important adjuvant in the treatment of melasma (Review Article), Journal of Cosmetic Dermatology 2013; 12: 57-66

[5] Manosroi A, Podjanasoonthon K, Manosroi J, Development of novel topical tranexamic acid liposome formulations, International Journal of Pharmaceutics 2002; 235: 61-70

[6] Lee JH, Park JG, Lim SH, Kim JY, Ahn KY, Kim MY, Park YM, Localized intradermal microinjection of tranexamic acid for treatment of melasma in Asian patients: a preliminary clinical trial. Dermatol Surg. 2006 May ;32 (5):626-31

[7] Lee do H, Oh IY, Koo KT, Suk JM, Jung SW, Park JO, Kim BJ, Choi YM, Reduction in facial hyperpigmentation after treatment with a combination of topical niacinamide and tranexamic acid: a randomized, double-blind, vehicle-controlled trial, Skin Res Technol. 2014;20(2):208-12

[8] Shalita AR, Smith JG, Parish LC, Sofman MS, Chalker DK, Topical nicotinamide compared with clindamycin gel in the treatment of anti-inflammatory acne vulgaris, International Journal of Dermatology 1995; 34 (6): 434-437

tions after application of liposomal preparations (with or without niacinamide) have not yet been observed.

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