Essential Calcium GABAergic Activation for Mature Skin

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Abstract

Mature skin suffers from essential nutrient deficiencies (minerals, vitamins, amino acids) causing skin slackening, skin thinning, dull complexion, irregular skin surface, dehydration and age spots. For these reasons, we have formulated a new ingredient to help people of sixty plus to fortify and restructure their thin and fragile skin. The new ingredient is a complementary source of calcium and essential amino acids and is especially designed to re-boost cell metabolism and protein synthesis, rebalance ion flow and recreate calcium gradient in order to regulate the barrier.

Introduction

Seniors of both genders want to "feel good for their age". However, hormonal deficiency (in the ladies) and environmental factors in both genders give rise to tissue sagging and dehydration in the skin: the neck wrinkles and the skin begins to look like "crepe paper". Tissue sagging begins gradually as the rate of replacement of macromolecules does not match their destruction by proteolytic enzymes. Calcium, which in young skin displays a concentration gradient across the epidermis and is highly present in the superior part of the stratum granulosum and almost absent from the stratum spinosum and stratum basale is, in the elderly population, more uniformly (and more sparsely) distributed throughout the thickness of the epidermis[1]. Thus, the epidermal "depolarisation" of the calcium gradient is reported to be one of the principal causes of skin atrophy.

To combat epidermal atrophy and tissue sagging, and to help restore the natural, youth related calcium gradient in the skin, we focused on the natural micronutrients essential to cell life, among which two amino acids play a particular role: methionine and taurine.

A natural analog of methionine, hydroxymethionine, is potentially endowed with the same activities while able, because of its hydroxy-acid function, to chelate calcium. It also contains sulphur, which has antioxidant properties, and is able to contribute to the methylation pool via SAM, like methionine itself, thus playing a proteogenic role.

Taurine is the quantitatively preponderant amino acid in the body's circulation. With age, taurine levels fall off[2]. The role of taurine in maintaining ion pumps and calcium homeostasis and in neuroprotection has been clearly described[3,4]. Homotaurine is a more stable analog with similar properties to taurine; it is also of further interest for its gamma-aminobutyric acid (GABA) mimetic properties. Denda's work[5] and Warskulat's studies[6] showed the importance of chloride-channel activation by Gaba in the maintenance of skin barrier homeostasis, osmolarity, calcium gradient and cell volume in keratinocytes, thus describing a new role of Gaba agonists at cutaneous level.

In order to help the skin restore enhanced cell function, particularly the mentioned calcium gradient, to relax and soothe the skin, we formulated a synergistic blend of Calcium-Hydroxymethionine and Homotaurine (trade name Essenskin™), the expected benefit of which combination is a decrease in epidermal atrophy, superior skin tone and a soothed and comfortable skin.

Efficacy Studies: *In vitro*

Gene expression profile by DNA array studies

Human keratinocytes, incubated with Calcium-Hydroxy-methionine were cultivated in monolayer protocol; RNA was extracted and the gene expression was compared to a control culture. PredictSearch® data- and textmining software allowed us to extract the following pathways of activity induced by the molecule:

i) marked activation of the genes involved in cell proliferation (gene HK2, 3-fold increase) and cell differentiation (endothelin 1, 10-fold increase)
ii) increased activity of the gene for RYR (ryanodine receptor, 3-fold increase) which regulates the variations in cytosolic calcium flux and CACNA1C (subunit $\alpha 1$ of the voltage-dependent calcium channel).

Differentiation activities are strongly expressed and illustrated, first by increased synthesis of polyamines via ornithine