

A challenge to abnormal melanogenesis evoked by Environmental Pollution, thanks to natural α - β and γ hydroxiacids, presenting decreasing Kas

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Sir,

Air pollution is being shown to play an overwhelming role in all the most common skin diseases as late acne, hyperpigmentation, atopic dermatitis and psoriasis have been manifesting to be almost always influenced by air pollution.

The attention is focused to melasmas and odd hyperpigmentation, always increasing in our modern outdoor lifestyle (typical dermal manifestations appearing in joggers, runners and footing lovers who like to run under the sun to grow slimmer and well trained) [1].

Melanogenesis starts from by inner stratum basale where the fundamental aminoacid tyrosine is the origin of a well coordinated enzymatic process, driving to the synthesis of eumelanin or pheomelanin in some mammals or reptiles [2].

Effectively tyrosine, a non essential aminoacid, is converted to dihydroxyphenylalanine (DOPA) via the enzyme tyrosinase and thenreafter DOPA is polymerized into melanin.

The copper-ion based enzyme-catalyzed oxidative transformation of catechol derivative dopa to light absorbing dopaquinone to indole-5,6-quinone gives access to the polymerization to melanin, and owing to the presence of melanoblasts that are allocated through all the layers of the epydermis from stratum spinosum, granulosum, lucidum and finally corneum, can reveal the skin colour from red to dark brown and bronze [2,3].

A gentle natural scrub (containing alpha, betha and gamma hydroxyacids deriving from vegetals) should display a range of chemical substances apt to penetrate the single layers thanks to their peculiar Ka and this phenomenon is explained by the concept that acids endowed by elevated ka are able to permeate and peel off the upper skin layers, idest hydroxyacid characterised by the major Ka (for instance salycilic acid that is a beta hydroxy acid) is to be reputed the culprit of the drastic peeling and revovating effect of the upper skin layers (corneum and lucidum), while milder alpha-hydroxyacids shall be fitted to scrub and permeate the other two skin layers (granulosum and spinosum) and finally the mildest gamma hydroxyacid (orthophenylmandelic, cfr ultra) is able do evoke its peeling action at niveau of the deepest layer (basale or germinativum) where tyrosine is converted to DOPA [4,5].

The creator of a revolutionary cosmetic formula includes four hydroxyacids characterised by increasing Ka that shall find the route to trespass the layers from outer to inner so that all the epydermis shall be treated and scrubbed, in order to attenuate the rigidity of the melanin polymer and disaggregate it, in cases of hyperpigmentations. keeping on account the complexity of organic substances that constitute all the skin layers and the melanines produced by melanosomes in the deeper layer that gradually polymerize raising to the upper layers till the stratum corneum [3,6].

The organic acids are the following, respecting the increasing Ka values at 298°K:

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Pyruvic Acid 2.5; Mandelic Acid 3.41; Malic Acid 5.2; Salicylic Acid 13.8.

And all this means that meanwhile Salicylic acid is to peel the outer layers (stratum corneum and lucidum), malic and pyruvic acids shall be apt to permeate the inner layer (stratum granulosum and spinosum), the latest (mandelic) will permeate and disaggregate the primeval monomers of eu and pheomelanins that will polymerize during the migration from basale to corneum [7].

Strata:

The stratum corneum, 20-30 cell layers, is the uppermost layer, made up of keratin and horny scales made up of dead keratinocytes, known as anucleate squamous cells. This is the layer which varies most in thickness, especially in callused skin. Within this layer, the dead keratinocytes secrete defensins which are part of our first immune defense.

It comprises several levels of flattened corneocytes that are divided into two layers: the *stratum disjunctum* and *stratum compactum*. The skin's protective acid mantle and lipid barrier sit on top of the stratum disjunctum. The stratum disjunctum is the uppermost and loosest layer of skin. The stratum compactum is the comparatively deeper, more compacted and more cohesive part of the stratum corneum. The corneocytes of the stratum disjunctum are larger, more rigid and more hydrophobic than that of the stratum compactum.

Stratum lucidum, 2-3 cell layers, present in thicker skin found in the palms and soles, is a thin clear layer consisting of eleidin which is a transformation product of keratohyalin.

Stratum granulosum, 3-5 cell layers, contains diamond shaped cells with keratohyalin granules and lamellar granules. Keratohyalin granules contain keratin precursors that eventually aggregate, crosslink, and form bundles. The lamellar granules contain the glycolipids that get secreted to the surface of the cells and function as a glue, keeping the cells stuck together.

Stratum spinosum, 8-10 cell layers, also known as the prickle cell layer contains irregular, polyhedral cells with cytoplasmic processes, sometimes called "spines", that extend outward and contact neighboring cells by desmosomes. Dendritic cells can be found in this layer.

moreover microfilaments between desmosomes may be retrieved although the actual keratinocytes begin in the stratum basale and are active in synthesizing fibrillar proteins, known as cytokeratin, which build up within the cells aggregating together forming tonofibrils. The tonofibrils go on to form the desmosomes, which allow for strong connections to form between adjacent keratinocytes. The stratum spinosum also contains Langerhans cells, that are not but tissue-resident macrophages of the skin once thought to be a resident dendritic cells but that do contain organelles called Birbeck granules, that reveals their the main function in the migration to the periphery of the Langerhans cells and release their contents into the extracellular matrix, and they are synthesised starting from langerin, that is a transmembrane protein.

Stratum basale, also known as stratum germinativum, is the deepest layer, separated from the dermis by the basement membrane (basal lamina) and attached to the basement membrane by hemidesmosomes. The cells found in this layer are cuboidal to columnar mitotically active stem cells that are constantly producing keratinocytes. This layer also contains melanocytes.

Summarising, stratum corneum offers its physical barrier owing to the presence of corneocytes, the stratum lucidum presents a large amount of eleidin, stratum granulosum contains keratohyalin, stratum spinosum is rich in Langerhans cells and Birbeck's organelles, and finally stratum basale where the prodromes of melanocytes are present in hemidesmosomes and melanosomes [8,9].

But, two are the chief argumentations to keep on account in order to understand the mechanism of exfoliating disclosed by the original formula containing this combination of organic acids:

The Odland bodies and the organic metastructure of the Lewis's formula of the mandelic acid, that when in an acidic milieu characterised by a strongest pH, as in case of the presence of salicylic acid, endowed by a high K_a , is a gamma hydroxyacid, with a weak K_a .

Effectively, as far the first concern is concerned,

Odland bodies are lamellar small sub-cellular structures of size 200-300 nm that are present in the upper spinous and granular cell layers of the epidermis. These act as processing and repository areas for lipids that

contribute to the epidermal permeability barrier. They also contain proteases, cathepsin D, kallikrein and other proteins including corneo-desmosins.

These substances represents a strong barrier to mild aggressors, so that a hydroxyacid characterised by a light Ka (as an alpha or gamma hydroxyacid, like pyruvic, malic or mandelic in its metamer structure, cfr ultra) cannot penetrate these two first layers rich of the aforesaid hydrophobic obstacles.

To exfoliate the upper layers of the epidermis salicylic acid is always the most recommended route, thanks to its strong Ka.

Besides, mandelic acid, that is an alpha hydroxyacid, when is dispersed in a stronger acidic milieu (salicylic acid at high concentrations) reveals its metamer structure defined “ortho-phenyl glycolic acid, or 2-phenolic mandelic acid”, that is definitively a gamma hydroxyacid, characterised by a lightest Ka and its molecule, being big and characterised by a long chain, must anyway be conveyed in the deeper layers of the skin and can so act gently and progressively.

The formula comprehends even allantoin, bisabolol, ceramides, hyaluronates, panthenol in order to restore the skin layers from the delicate chemical assaults and to relieve from eventual slight inflammations [10].

Melasma and odd hyperpigmentations were considered during the last millennium the effects of several physical, physiological, chemical or pathological causes like senescence, (UVA, UVB and UVC and IR burning), post partum conditions and others (hormonal disequilibrium, diabetes, irritations as acne ribelle or eczemas, wound healings or even medicaments side effects) [11].

Nowaday the risk of environmental pollution shall never be neglected: effectively when skin is exposed to pollutants in the air, it tries to fight it by producing melanin and antioxidants. These cause dark spots on skin, more than UV rays actually did or generally do and maculae appear in younger age individuals than d'antan and the number of brownish patches pro/sq-inch upon skin is doubled anyways.

Often the excessive epidermal dark spots may reveal the occurrence of Acanthosis nigricans, typical in Latins, Hispanic descent native to South America, caribbeans and all the dark skin obese and diabetic individuals

and AN is more accentuated in huge metropoleis exaggeratedly polluted, as Caracas and Mexico City.

Empirical tests on a panel group of 20 women (22-87 y.old) display a marvelous bleaching effect after three weeks of the application of this emulsion containing acids from fruits and salix alba bark.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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