

# HISTOPATHOLOGICAL ASPECTS OF CUTANEOUS PHOTOAGING AND PHENOL PEELING

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## ABSTRACT

The skin is regarded as the largest organ in our system and has the general purposes of physical, mechanical and immunological protection, sealing against the elements and thermoregulation and tactile perception of environmental stimuli. Skin aging is a complex biological event that affects all skin layers. The dermis, however, is particularly affected due to its histophysiology's characteristics. With the expansion of life expectancy, the dermatological questions among the older population has had an increasingly bigger importance, propelling the development and perfecting of rejuvenation techniques. The phenol peeling is a deep, chemical one, which offers intense clinical results. The application on small areas of the body, for example, around the eyes, is safe and does not lead to cardiovascular complications. This review aims to update the knowledge of skin histology, the alterations related to photoaging and phenol peeling.

## KEYWORDS

Skin. Photoaging. Histomorphology. Peeling. Phenol.

## 1 INTRODUCTION

The skin is regarded as the largest organ in our system, accounting to 15% of our body weight. Along with its annexes, the skin constitutes the tegumentary system. The general purposes of this system are physical, mechanical and immunological protection, sealing against the elements and thermoregulation and tactile perception of environmental stimuli (FARAGE et al., 2007b; SAMPAIO et al., 2008).

Skin aging is a complex biological event affecting all layers of the skin, especially the dermis, due to its histophysiology's properties. Such a complex aging process is induced by different mechanisms, both intrinsic and extrinsic in nature, which act simultaneously on the skin in spite of being clinically and biologically distinct. Intrinsic structural changes occur as a natural consequence of aging. While this factor is genetically determined, the intrinsic rate of skin aging is dramatically influenced by environmental factors, such as the amount of exposure to solar radiation, which leads to photodamage (BAUMANN, 2007; FARAGE et al., 2008; PAES et al., 2009).

Among various rejuvenation techniques, phenol offers desirable clinical results and, classically, it is recommended to be used as peeling in skin lightening, static facial wrinkles, cutaneous sagging, treatment of acne scarring and age spots, although recent studies highlight its use as an aid blepharoplasty (GATTI, 2008).

Phenol or carbolic acid is an aromatic organic compound, derived from benzene. Among its applications in dermatological therapy, it stands out its use as a facial peeling agent in medium and deep procedures, being considered a chemical agent that produces significant facial rejuvenation. However, its use results in limitations due to the great potential of related side effects (LUPI et al., 2010; SAMPAIO et al., 2008).

## 2 HISTOLOGICAL ASPECTS OF THE SKIN

The skin is composed of three layers: the epidermis, the outermost layer that is in direct contact with the environment; the dermis or corium, intermediate and adjacent to the epidermis; and the hypodermis or subcutaneous tissue, the deepest layer. The epidermis is formed by keratinized stratified squamous epithelium tissue, which is avascular like the other epithelia. The cellular element that composes its parenchyma is the keratinocyte, a labial cell with an average useful life of 26 days. It is also possible to find melanocytes, Merkel cells and Langerhans cells around the epidermis (FARAGE et al., 2007b; SAMPAIO et al., 2008).

The keratinocytes show their cytoarchitecture organized in layers: basal or germinative; spinous or Malpighian; granulous and

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corneous, thus placed, from the interface with the dermis towards the surface. From the basal layer, in which the keratinocytes undergo mitosis, the cells go toward the surface, presenting morphological modifications that represent their differentiation. Sequentially, always in the skin surface direction, the nucleus, previously round and intensely basophilic, becomes less colored and squamous as it takes on a more horizontally polarized orientation. On the outmost granulous layer, the fully differentiated keratinocytes go into apoptosis, liberating keratin, which constitutes the corneal layer, in the fragmentation process (AARESTRUP, 2012).

The melanocytes are cells of neuroectodermal origin, near the neural crest, which migrate, guided by the basal lamina into the deep of the epidermis. They constitute 10% of the basal layer and produce melanin, which is transferred to the keratinocyte cytoplasm through the melanosomes, giving coloring to the epidermis. Even though the melanocytes aren't identified in the Hematoxylin-Eosin (HE) coloring and through observation of its intensely colored nucleus, surrounded by weakly eosinophilic cytoplasmic halo among the keratinocytes of the basal layer, its ramified morphological plenitude is only identified in histochemical procedures (OVALE et al., 2008).

The Langerhans cells make up 2 to 8% of the total cell constitution of the epidermis. They are antigen-presenting (APC) dendritic cells responsible for the superficial immunological response (AARESTRUP, 2012; SAMPAIO et al., 2008).

The dermis, on the other hand, can be found subjacent to the epidermis and it's composed by proper conjunctive tissue, formed by extracellular material cells or extracellular matrix. The extracellular material or extracellular matrix of the dermis is formed by the fundamental amorphous substance and by fibers (AARESTRUP, 2012).

The nearest dermic portion to the basal lamina is composed by conjunctive tissue appropriately called lax. This portion, found between the epithelial crests, is named papilar dermis, and according to its own histological characteristics, is richly vascularized and innervated, full of cells and collagen fibers and delicately elastic fibers, abundantly involved by fundamental amorphous substance. Deeper into the papilar dermis, there is the reticular dermis, formed by conjunctive tissue appropriately called dense, with thicker collagen fibers when compared to the papilar dermis and paralleled to the epidermis. In this portion of the dermis, one can find most cutaneous annexes, such as sweat glands and the hair follicles associated to the sebaceous glands. In this part, there is a lower concentration of fibroblasts and fundamental amorphous substance (SAMPAIO et al., 2008).

The fundamental amorphous substance, also known as fundamental intercellular substance, has a gelatinous consistence and involves all the other elements of the dermis. It should be noted that the fundamental amorphous substance properties enhance the

general properties of the conjunctive tissues. The fluid that is present in the gel provides a medium for exchanges of gases between the cellular elements and the blood. Since the proteins that are present in the amorphous substance associate themselves to the adhesion molecules and growth factors, they allow the conjunctive system as a whole to fulfill immunological defense and healing functions (OVALE et al., 2008).

The fibery proteins of the extracellular material are called fibers, due to their elongated and cylindrical form. There are two protein families: the collagen system and the elastic system, both of which form various types of fibers, different from each other, according to the proteic precursor and the structural organization of each basic unit, giving them clinical and microscopical traits particular to each one (AARESTRUP, 2012).

The collagen system, which comprises 95% of the dermis volume, forms a series of collagen proteins that originate the collagen fibers – among which there are 16 structural variations – and the reticular fibers. Among those, we can highlight collagen Type I. It corresponds to 80% of the collagen, whose fibers are organized in beams, giving the skin high resistance to traction and tension forces (AARESTRUP, 2012; SAMPAIO et al., 2008).

The elastic system is composed by three types of fibers: the oxytalan fibers, the elaunin fibers and the elastic fibers synthesized on the dermis by the fibroblasts. These cells deposit elastin until the entire fibrillar structure is filled, and at the end of the process, we have the mature elastic fiber, organized in microfibrils that extend perpendicularly to the epidermis when in the papilar dermis and parallel to the reticular dermis, with thicker, more abundant structure (EL-DOMYATI et al., 2002).

The epidermis-dermis interface, constituted by the wrinkling that comes from the crests and the papillae, provide resistance to friction aside from augmenting the nutrient diffusion surface from the dermis to the epidermis (OVALE et al., 2008).

The dermis cells, as well as the other conjunctive tissues, are divided into two groups: the resident cells – fibroblasts, mastocytes, macrophages, monocytes and lymphocytes – and the occasional mobile cells – neutrophils, basophils and eosinophils. During the healing process, the proportion between these elements is modified, according to the evolution of the process, as well as the emergence of the myofibroblasts in the area (AARESTRUP, 2012).

### 3 SKIN AGING

Skin aging is a complex biological event that affects all skin layers, but the dermis is particularly affected due to its histophysiology's characteristics. The complexity of this aging has its cause in the fact that there are distinct and independent

aging mechanisms – intrinsic and extrinsic – which affect the skin simultaneously. The mechanisms involved in the intrinsic or innate aging processes (“biological clock”) evolve in agreement with the other tissues and involves the decrease of cellular metabolism, slowly and irreversibly. Such alterations are genetically determined, under the influence of ethnicity and anatomic and hormonal variations (EL-DOMYATI et al., 2002; FARAGE et al., 2007a; FARAGE et al., 2008; UITTO et al., 1998).

The main effect of ethnicity in aging is linked to skin pigmentation. High levels of pigmentation give protection against photodamage caused by ultraviolet radiation (UV), emitted by the Sun. We can base the skin’s sensibility to UV radiation on the Fitzpatrick’s Classification (FITZPATRICK, 1998; SAMUEL et al., 2005), that is:

- Type I – Very light skin; always burns, never tans;
- Type II – Light skin; usually burns and sometimes tans;
- Type III – Medium-light skin; sometimes mild burn and sometimes tans;
- Type IV – Light brown skin; rarely burns, tans with ease;
- Type V – Dark brown skin; rarely burns, always tans;
- Type VI – Black skin; never burns, always tans.

The anatomical variations have an important role in this analysis, and the analyzed location needs to be considered. The cutaneous thickness is important because the face bears one of the thinnest places on the skin, the eyelids, with the thickness of under 0,05 mm. Unexposed areas, protected by clothing, for example, lose less in terms of hydration, elasticity and susceptibility to irritation (FARAGE et al., 2007a; SAMPAIO et al., 2008).

Hormonal estrogenic alterations, which happen to the woman in the post-menopause period, carry great influence on the facial skin aging, contributing to the decrease in hair follicles, cutaneous thickness and dryness, also declining in collagen and water retention (FARAGE et al., 2007b).

These are characteristics of histopathological and physiological alterations of skin aging (EL-DOMYATI et al., 2002; FARAGE et al., 2007a; SAMPAIO et al., 2008):

- Decrease in cutaneous thickness due to decrease of number of cells;
- Decrease of microcirculation around the hair follicle bulb and other annexes;
- Lower capacity of inflammatory response. After 70 years of age, especially, the skin responds slowly and less intensely to exogenous agents. There is a significant decrease of around 50%, compared to a young adult, of the number of Langerhans cells, aside from the diminishing of the response capacity of lymphocytes;
- Lower healing capacity. As observed in all high synthetic capacity cells, the fibroblasts start showing a declining of cellular

proliferation, lower metabolic activity with lower collagen remodeling, producing altered elastic and collagen fibers resulting in more rigid and less elastic skin; such factors result in a general delay in the healing process.

The phenomena involved in intrinsic aging can be influenced by extrinsic factors, represented by social and environmental factors, with special attention to exposure to smoking and UV radiation, respectively (BAUMANN, 2007; FARAGE et al., 2008; SAMUEL et al., 2005).

Smoking is strongly linked to elastosis in both sexes. It causes decrease of capillary blood flow, leading to tissue hypoxia, with less nutrient input and lower catabolite removal from skin tissues. One can also see the diminishing number of elastic and collagen fibers, which makes the skin more rigid and less elastic (FARAGE et al., 2008).

UV radiation is subdivided into three types. UVC (100-290 nanometers) is mostly blocked by the ozone layer and thus exerts little impact on the skin. UVB radiation (290-320 nanometers) pierces through the epidermis and is responsible for erythema and sunburn. Finally, the UVA radiation (320-400 nanometers) hits the epidermis and the dermis and it’s responsible for most of the chronic alterations of photodamage. Among those is the activation of the metalloproteinase of the extracellular matrix that stimulates the production of collagenase, gelatinase and stromelysin-1 in the fibroblasts, resulting in the deterioration of collagen and elastic fibers (FARAGE et al., 2008).

Photodamage also strongly elevates the risk of cutaneous neoplasia by alteration of the genetic makeup through DNA (deoxyribonucleic acid) mutation, free radicals formation and inhibitory interference of immune system components – especially T lymphocytes and Langerhans cells (FARAGE et al., 2008).

It should be noted that the face is especially affected by these factors, because its skin is constantly exposed to the external environment. There is loss of volume with gravitational alterations with the loss of elasticity, atrophy of fat tissue, decrease and thinning of elastic and collagen fibers and bone resorption. There is the emergence of dynamic wrinkles caused by the action of muscles responsible for facial mimicry, as well as static wrinkles. The skin surface is intensely altered in its texture, by being thinner and drier, as well as in its pigmentation, with the formation of actinic keratosis, lentigines, leucoderma, telangiectasias, among other diseases (BEER et al., 2009).

Studies have demonstrated a significant correlation between reduction in length, thickness, number and total area of elastic fibers and the severity of wrinkles, also showing a positive correlation between the quantity of regenerated collagen fibers and attenuation of static and expression wrinkles (BUTLER et al., 2001; KLIGMAN et al., 1985; LEE et al., 2008).

#### 4 PHENOL PEELING

The first scientific reports of its use as a chemical peeling agent date back to 1927 by H. P. Bames. Subsequently, in 1946, Joseph C. Urkov, plastic surgeon, reported his 15-year experience in using phenol treating 2000 patients with scars, spots and wrinkles. The author concluded that the agent is safe and effective. In the early '60s, several publications promoted awareness and legitimization of phenol peeling (BAKER et al., 1961; BAKER, 1962; BAKER et al., 1966; LANDAU, 2005).

Phenol or carbolic acid (C<sub>6</sub>H<sub>5</sub>OH) derives from coal tar, has a distinctive odor, and its aspect ranges from colorless to rosy, becoming darker when exposed to light and air. When used in 88% concentration, it promotes destruction of the epidermis, the papillary dermis, reaching the surface of the reticular dermis. During this process, the phenol causes the denaturation of the skin proteins, producing a keratolytic action by the burst of the sulfur bridges of the keratin. Clinically, this action is shown as a whitening or frost in the places where the phenol was applied. The affected area evolves to the crust after 24 hours and falls after a few days (FISCHER et al., 2010).

When applied to extended areas, such as the whole face, it is important to take cautionary measures when using phenol peeling. Its application should be avoided on patients who have history of cardiac, renal and liver disease, recurring episodes of herpetic infection, continuous exposure to UV radiation, recurring use of isotretinoin, mental instability, predisposition to keloids and skin types IV, V and VI, according to the Fitzpatrick's Classification (FITZPATRICK, 1998).

When the phenol peeling is done on the whole face, the area must be divided into five parts, with applications every 15 minutes from one part to the other, so that the absorbed concentration can be eliminated in the urine without causing cardiac alterations (BROWN et al., 1960; KADUNK et al., 2009; LANDAU, 2005). The ideal population for this treatment should have light and thin skin, so, according to the Fitzpatrick's Classification, subjects with skin types I, II and III, with fine wrinkles. Male patients have thicker skin when compared to females, which decreases the phenol action in men, diminishing the efficiency of the treatment (GATTI, 2008; PAES et al., 2009).

In light of what was exposed, it is necessary to highlight that the application of phenol on small areas of the body, like around the eyes, is safe and doesn't lead to cardiovascular complications; in these cases, pigment alterations, secondary infections and prolonged erythema were reported (GATTI, 2008).

#### 5 CONCLUSION

The skin rejuvenation techniques have been perfected every day, be it due to technological advances or higher concern from people with things like health and physical appearance and longevity.

Although chemical peelings have been used for several years, nowadays they are still a very important therapeutic tool in skin rejuvenation, especially the phenol peeling, as it is considered a deep chemical peeling and offers intense clinical results.

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