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Review article

Use of apidermocosmetics in patients with some genodermatoses

Yordania Velázquez Avila [1*] https://orcid.org/0000-0002-2846-3432
Alejandro Bernardo Cervantes Palomino [2] https://orcid,org/0000-0003-0300-8596
Claudio TirabassoBier [2] https://orcid,org/0009-0004-4226-4140

[1] Mártires de Las Tunas Provincial Teaching Pediatric Hospital. Las Tunas, Cuba.
[2] Natural Integrative Medicine Center. Sosúa, Dominican Republic.

*Author for correspondence: email: yordaniacuba@gmail.com

ABSTRACT

Introduction: In some diseases as genodermatoses that present with blisters and keratinization disorders, the skin structure is permanently damaged. These patients need permanent cares to improve the physiologic functions of the skin. Apidermocosmetics is the branch of cosmetology that deals with the care and cleansing of skin with certain structural characteristics, through the use of bee products.

Objective: To explain the conceptual basis of apidermocosmetics as part of beekeeping and promote the use of integrative medicine in some genodermatoses.

Method: A review of the available literature was carried out in Medline, Ebsco, Hinari, Cochrane, Scopus, Clinicalkey, Elsevier, Lilacs, Scielo, Medigraphic. The descriptors used were: genetic dermatological diseases, cosmetics, dermocosmetics, beekeeping and apicosmetics. Five books were mentioned and thirty three published articles were cited, with 78.9% of update rate.

Results: The conceptualization of pharmaceutical, cosmetic, dermocosmetic, and apicosmetic was reviewed. Also, apidermocosmetics is conceptualized; and the benefits of apicultural products and their uses in some genodermatoses as part of integrative medicine are explored in depth.

Conclusions: It is important to know the benefits and uses of apidermocosmetics in some genodermatoses and how it promotes the improvement of the dermatological evolution of these patients.

Keywords: genodermatosis; cosmetics; dermocosmetics; beekeeping; apicosmetics; integrative medicine; naturopathy.

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Introduction

Genodermatoses constitute a group of very heterogeneous clinical conditions, where genetic anomalies play a predominant role in the origin of the disease, whose main manifestations lie in the skin.[1]

These diseases are difficult to diagnose, treat and monitor because there is great diversity in the types of inheritance, even within the same condition. The degree of impact on individuals within the same family will depend on the expressiveness and penetrance; socially, they are stigmatized individuals. [2]

One of the main functions of the epidermis is to form a barrier against the external environment, the mechanical, thermal and chemical stimuli, as well as radiations in general which are carried out through the keratinization and metallogenesis processes. [3]

In some conditions such as genodermatoses where patients present with blisters (epidermolysis bullosa), keratinization disorders (ichthyosis), Darier and Hailey-Haile diseases, *pityriais rubra pilaris*, porokeratosis of Mibelli, as well as palmoplantar keratoderma, the skin structure is permanently damaged and the protective, melanogenic, self-cleaning and thermoregulatory functions are affected. [4] It has not been possible to determine the prevalence and incidence in all. In the most studied cases, the results differ from country to country; nevertheless, the prevalence of epidermolysis bullosa (1 per 50 000 live births),[5] ichthyosis (1 per 300 000 births),[6] Hailey-Hailey disease (1 per 40 000 inhabitants) [7] and Unna-Thostes palmoplantar keratoderma (1 per 60 000 births) has been reported. [8]

The World Health Organization, since 1963, has urged members states to consider adopting measures for the control and prevention of genetic diseases. From 1980, the Cuban National Health System implemented the National Program of diagnosis, care and prevention of genetic diseases and congenital defects. [2]

In Cuba there are no records of these diseases in the national statistical yearbook; however, in the eastern province of Las Tunas, a population study was carried out in 2019, where prevalences of genodermatoses affecting the skin´s protective

function were found, such as ichthyosis vulgaris with 5 per 100 000 inhabitants, palmoplantar keratoderma with 1.3 per 100 000 inhabitants and epidermolysis bullosa simple with 1.1 per 100 000 inhabitants. [9]

Due to the need for ongoing care that these patients require to achieve better functional skin quality and avoid complications such as infections, it was decided to carry out this work with the objective of presenting the scientific basis of apidermocosmetics, as part of apiculture and promoting the use of integrative medicine in some genodermatoses.

Methods

The review of the literature available in databases as Medline, Ebsco, Hinari, Cochrane, Scopus, Clinicalkey, Elsevier, Lilacs, Scielo and Medigraphic was carried out, as well as search motors as PubMed and Google Scholar for whose localization the searchers of these databases were used. The descriptors used were: genetic dermatologic diseases, cosmetics, dermocosmetics, beekeeping, apicosmetics. During the review process, books and published articles were consulted, of which 38 were mentioned inside the bibliographical references, of them 5 books and 33 published articles, with 78.9% updating.

The investigation was approved by the ethics Committee of investigation and the scientific Council of Martires de Las Tunas Teaching Provincial Pediatric Hospital as implementing institution, according to the principles of the Helsinki Declaration and the World Medical Association. [10] All the images were taken by the team of investigators and obtained under informed consent.

Conceptual bases of apidermocosmetics

To be able to go into in the conceptual bases of the apidermocosmetics it is necessary to define some basic concepts.

Pharmacotherapy, according to Herrero,[11] is the branch of pharmacology responsible for the use and administration of medications in order to restore the health of individuals by curing disease."

On the other hand, Montes[12] refers that a drug is a substance that produces a therapeutic effect and has a pharmacological active principle in its formulation, with a certain legal regulation". Also, it outlines that in the topical drugs, percutaneous absorption takes place until arriving to the dermis capillary, what allows that a systemic absorption exists, as it happens with analgesic patches, antibiotic creams, sexual hormones, among others.

In such a sense, apitherapy deals with the maintenance and restoration of health through the use of beehive products: apitoxin (bee venom), beeswax, royal jelly, honey, pollen and propolis. Their use covers all the body tissues and is also in charge of the aesthetic part, having a great range of cosmetics products. [13]

According to the reasoning above, cosmetics are substances or formulations intended to be placed in contact with the superficial parts of the human body, such as the epidermis, the hair and scalp system, nails, lips, external genital organs, teeth and oral mucosa; with the exclusive or main purpose of cleaning them, perfume them, helping to modify their aspect, protecting them, keeping them in good condition, correcting body odors, mitigating or preventing deficiencies or alterations in the functioning of healthy skin. [14]

The term apicola cosmetics or apicosmetics, from the Latin Apis (bee), refers to cosmetics that contain products derived from the beehive in their formulation: wax, honey, royal jelly, propolis and pollen. [15]

It should be added that dermocosmetics is a discipline that lies between cosmetics and dermatology; that is, dermocosmetics products are not considered medications, but their benefits for the skin go beyond the action of cosmetics. [16] Therefore, these products are indicated in situations that is necessary to reinforce or rebuild the skin barrier function, reduce transepidermal water loss, stimulate epidermal cell renewal, keep the natural PH of the skin, and achieve a soothing or decongestant effect. [12,16]

Indeed, these products are formulated to keep the health and beauty of the skin and hair; they are backed by specialists, mainly dermatologists, and their development is based on specialized clinical studies that are indicated, after evaluation by the dermatologist. [16]

Natural dermocosmetics uses products of natural origin in 95% of its composition (including water), and do not use chemicals such as synthetic antioxidants (butylhydroxyanisole, butylhydroxytoluene), sodium lauryl sulfate, triclosan, formaldehyde, parabenzenes, polyethylene glycol compounds, amines (monoethanolamine, diethanolamine, triethanolamine), dibutyl phthalate, siloxane, silicones (dimethicone, cyclomethicone), perfume, ethynol derivatives, petroleum derivatives (paraffin, synthetic vaseline, petrolatum); being ecological, if for its preparation the care of the environment has been taken into account. [17]

As maximum, the remaining 5% can be synthetic ingredients that are part of a short restrictive list, which includes some preservatives and auxiliary substances as the benzoic, sorbic acids and its salts, bencilic alcohol, mineral artificial colors and some indispensable artificial ingredients still not available, of natural origin. [18]

It can be stated that bee products, when used for dermocosmetics ends, have a greater reach than their use as apicosmetics. Apidermocosmetics can be defined as the branch of cosmetology that deals with the care and cleaning of skin with certain structural characteristics that do not allow it to function properly, through the use of natural products derived from the hive as honey, propolis, wax, jelly and bee venom.

Cervantes,[19] affirms that integrative medicine, combines technology and science, with the benefits offered by nature and self-defense and self-healing

capabilities of the human body, based on health, and offers a qualitatively and quantitatively superior approach."

Apidermocosmetics, as part of integrative medicine, is very important as an adjunct to conventional pharmacological or specialized treatments to protect the skin, prevent complications and in turn accelerate the healing process of different dermatoses.

Beekeeping products and its properties

"Beehive products are generated starting from the interaction between bees and their environment (environment), through the pollination of flowers and extraction of nectar and/or perspired vegetables". [20] Almost all beehive products are photosensitive, thermosensitive and hygroscopic (they absorb moisture that alters them). [13]

The venom of the honeybee or apitoxin is produced through 2 glands located in its abdomen; the venom glands and "dufor " glands also called acid and alkaline glands, respectively. Only females A. mellifera (worker and queen) have the ability to produce venom and possess a stinger, which is located in the last abdominal segment and is associated with the acid and alkaline glands. It is used as a means of defense against predators and for combat among themselves. [21]

Now, the poison is a transparent liquid, with pH of 4.5 to 5.5; composed mainly of water (80%) and a mixture of peptides, enzymes, biologically active amines, amino acids, carbohydrates, volatile compounds, phospholipids, pheromones and minerals as the calcium, magnesium and phosphorus. Its main biological action is due to the melittin peptide that induces mild allergic reactions. Studies conducted with cell cultures and animal models have shown that this component has anticancer activity, since it inhibits the angiogenesis process, what slows tumor growth, in addition to altering the cell membrane and causing necrosis in the cell. It has also demonstrated *in vitro* antibacterial activity against strains of that includes methicillin – resistant *Staphylococcus aureus*. [21]

Others components include apamin, a peptide with neuroprotective and anti-inflammatory activity, as well as the mast cell degranulation peptide, which in low doses produces degranulation of mast cells; however, it has been shown that at high doses it inhibits this degranulation and acts as a potent anti-inflammatory agent. The phospholipase enzyme 2, with immunogenic and allergenic activity lowers blood pressure and inhibits blood clotting. [21]

Bee venom should be kept refrigerated and covered to prevent light and moisture. While it is true that bee venom can withstand up to 100º C, it is not advisable to expose it to high temperatures, especially if it is not going to be used relatively quick. [13]

With respect to wax, it is the material with which the bees build the structure of the honeycombs. This is produced by the wax glands in the abdomen of young

bees, and its secretion is directly related to the ambient temperature. This production decreases with low temperatures. [13]

For example, wax is made up of a complex mixture of around 300 compounds. Constituted by hydro-carbons, free fatty acids, fatty acids esters, fatty alcohols, diesters and exogenous substances, the latter being mainly made up of propolis residues, pollen and small pieces of floral components. [22]

Wax is a fatty substance par excellence; one of the big properties of the wax is to soften the skin, hence its main use is as a vehicle for other preparations (creams, ointments) mainly in cosmetic application. White wax figure in the composition of creams, astringent, of cleaning, whitener, as well as of masks for the face. It acts as natural barrier against agents of the environment and ultraviolet radiations. [20] The vitamin A content of the wax is very high; 100 grams contain 4.096 IU. However, Vitamin A and many volatile substances that it contains, get lost with its heating. [13]

With regard to the real jelly it is a product of internal secretion of the bees. This is produced by the hypopharyngeal glands and mandibular glands of the young bees. It depends directly on the quantity of honey, pollen and water in the beehive; as well as the temperature and the quantity of breedings. It has gammaglobulin that is not antigenically related to the gammaglobulin of the human plasm (as happens with the animal origin). It Contains 20 amino acids it possesses a high quantity of micro elements, important for the human health: Iron, Gold, Calcium, Cobalt, Silicon, Magnesium, Manganese, Nickel, Silver, Sulfur, Chromium and Zinc. [20]

It has been demonstrated in animal models that royal jelly has vasodilatory and hypotensive activity, disinfectant, antitumoral and antibacterial action this activity being attributed to the fatty acids that it contains. [22] It is regenerating and epithelizing; what gets normalization and scaring. However, the jelly itself is unable to penetrate the skin to produce its effects. In creams or ointments honey, pollen and propolis should be included in their formulation, so that they can penetrate the skin. [20]

The real jelly should be conserved to less than 4º C, avoiding light, moisture and air that oxidizes it making him lose its effect. It can also be stabilized with honey, being in this case very difficult of degrading. For its high acidity, it attacks the metals, reason why plastic materials or glass should be used for packing. [13]

Honey is the natural sweet substance produced by bees *Apis mellifera* from the nectar of plants, or from its living secretions, or from secretions of plant-sucking insects that remain on its living parts, and that the bees collect, transform and combine with specific substances of their own: deposit, dehydrate, store and leave in the honeycomb so that it matures and ages. [23]

Basically honey has 75% of sugars, up to 20% of humidity, a small quantity of proteins, acids, fatty and minerals.[23] The bioactive properties of honey are due to its high content of polyphenolic compounds, flavonoids and phenolic acids; these

compounds are associated with the antioxidant, antibacterian, antiviral, anti-inflammatory and healing capacity. [20]

In relation to the antibiotic effect, honey, for the action of the present enzymes, is permanently elaborating peroxide of hydrogen and possesses natural components, as the inhibin, so that it is indicated in extensive traumatisms of skin, ulcers of any origin, burns, etc. It can be alone or combined with propolis. [20] The organic acids are responsible for its acid PH between 3.5-4.5, which allows its expholiative and keratolitic effect in the keratosis. [23]

Honey nourishes epithelial tissues and subcutaneous nervous ramifications and has calming, demulcent (local protector), epithelizing, emollient, moisturizing, refreshing and toning properties. It can be used in soaps, gels, emulsions, lotions, creams, ointments, stick and topical pastes. Due to its hygroscopic properties, it absorbs skin secretions and acts as a disinfectant. It provides elasticity and smoothness to the skin, eliminating wrinkles and roughness. Due to its nutrients and astringent and antioxidant properties, it protects hair from dryness, gives it shine, helps its growth and keratin production, resulting in strong, less brittle hair and its antioxidant properties prevent the appearance of gray hair. [22]

In cosmetic preparations, honey is attributed with several benefits, including nourishing epithelial tissues and activating superficial capillary circulation, as well as combating dryness and skin imperfections. Because of all these benefits, it is commonly found in shampoos, conditioners, creams, masks (both for hair and skin), bath gels, exfoliating products, lotions, serums, soaps, facial cleansers, among others. [24]

In wounds, it adheres to the surface, and each of its components works together participating synergistically to achieve total wound healing. On the other hand, the physical properties of honey create a barrier and a moist local environment, allowing for surgical cleansing by removing necrotic tissue and scabs, thus promoting wound healing. [20]

Also, light, humidity and high temperatures cause honey to lose many of its properties. Light causes it to crystallize more quickly. Increasing its moisture content to over 20% allows it to ferment by yeasts. [13]

It is worth noting that the term pollen derives from the Latin *polleninis* that means very fine powder or flour flower. It corresponds to the male fertilizing element of the flowers, the bee uses it mainly as a source of proteins for larval food. [20]

Likewise, bee pollen is a mixture of pollen pellets of different colors. Pollen contains a high amount of minerals, amino acids, vitamins, very few carbohydrates (sugars) and very few fats. [13]

It possesses different antioxidant, antifungal, anticariogenic properties. It contains vitamin A, important at skin level, either as healing agent, to keep it well nourished or to recover it in cases of chronic skin diseases, where it will be a good aid; for example in psoriasis, vitiligo. When used preventively, it slows down hair loss, or

stops it when it is due to a lack of nutrients, weakness of the hair bulb or surrounding skins. [20]

As has been demonstrated, pollen is such a nutrient-rich element that humidity above 8% at the appropriate temperature inactivates it by fermentation in a matter of hours. It should be conserved refrigerated or at least well covered to prevent it from absorbing moisture from the air and protected from ultraviolet rays. It should be stored in the dark or away from direct light. [13]

Propolis is a hive product made from the resin of certain species of plants, flowers and leaf buds, which are mixed with saliva, enzymes and other secretions characteristic of the bees. [25]

Now, geopropolis is a natural product characterized by being a mixture of plant resins, tree exudates, salivary secretions, wax, clay or soil, which bees of the gender *Melipona* use in its hives to seal small cracks, prevent the entry of air, parasites or small animals, as well as to prevent the growth of microorganisms of bacterial and fungal origin. [26]

In some studies carried out in Mexico and South America (Brazil), more than 600 bioactive compounds have been identified in the geopropolis of many species of the genus *Melipona*, mainly terpenoids, cinnamic acid and phenolic compounds, among the latter phenols and total flavonoids stand out, that possess antimicrobial activity against pathogens such as *Staphylococcusaureus, Streptococcuspyogenes, Streptococcusmutans Pseudomona aureginosa, Escherichiacoli*. [25,26]

Antifungal property, would be well mediated by benzoic acid, bisabolol, pinocembrin, sacranetin, perostibene and stalibdenes. All of them has proven antifungal action, fundamentally against *Cándida albicans*. [12] The advantage of propolis in superficial mycoses, is that, as in most cases these infections are accompanied by itching and excoriations; propolis provides quick relief both through its anti-allergic action and the appearance of the scar, in addition to its antifungal effect. [20]

Propolis is attributed with properties including anti-irritant, anti-pruriginous and anti-microbial actions; what allows it to be used in a cosmetic form. It can be found in shampoos, creams, soaps, body lotions, mouth sprays, bath gels, among other preparations. [22]

It should be noted that t direct light inactivates propolis, humidity causes it to ferment and temperature also inactivates it. In general, when it is processed and packaged there are no problems with light and humidity. Propolis begins to lose its properties at temperatures above 52º C. [13]

The authors found some evidences of the use of apidermocosmetics such as the research by You et al., who published a study carried out on 136 patients with atopic dermatitis, using a moisturizing emollient that contained apitoxin among its ingredients, reporting a decrease in the area where the eczema is present and a decrease in pain according to the visual analog scale; the improvements in the

patients were mainly attributed to the anti-inflammatory activity of the bee poison used, which corresponds to a glycerinated extract. [27]

Guamán et al, in their design of a honey and propolis soap, found that the pattern that contained honey 3%; propolis 3.0%; glycerine 3.0% and citric acid 1.5%), contributed to the best results in relation to organoleptic and physiochemical parameters. [28]

Anyone allergic to bee stings should refrain from consuming or using bee products. It is inevitable that all hive products will be "contaminated" to a greater or lesser degree with pollen and bee venom. [13]

Apidermocosmetics in genodermatosis as part of integrative medicine.

It would be very complex to try to address all the genodermatoses that present affectation of the skin tegument and barrier function. This work will address the three most frequent ones described in Las Tunas.

Epidermolysis Bullosa

Epidermolysis bullosa corresponds to a heterogeneous group of hereditary disorders characterized by increased mucocutaneous fragility, with the appearance of blisters spontaneously or in response to minimal mechanical trauma. It is caused by mutations in genes that codify proteins responsible for the integrity and mechanical stability of the tegument. So far, more than 1.000 mutations have been documented in 21 structural genes that result in defective skin adhesion and consequent skin fragility, leading to various forms of cutaneous and extracutaneous involvement. [29]

It is clinically characterized by the formation of blisters due to mechanical trauma (Figure1) that can be superficial or deep depending on their cleavage plane. The lesions can occur on the skin as well as on the tracheal, genitourinary, oral, esophageal and ocular mucous membranes, and manifest as erosions, ulcers and scars. Complications can include contractures, stenosis, mutilations, microstomia, among others, which leads to significant morbidity for patients. [30]

Fig. 1. Blisters produced by friction in a patient with generalized simple epidermolysis bullosa.

For the time being, daily treatment revolves around preventing mechanical trauma, wounds care avoiding the infections. (31)

Taking into account the described properties of bee products, honey and propolis soaps can be used for cleaning lesions; propolis tincture for erosive lesions and in a scaly state of the skin, creams or ointments containing royal jelly, honey, pollen and propolis can be used.

Ichthyosis

The term ichthyosis derives from the Greek ichthlys that means skin that takes the appearance of fish scales, making reference to xeroderma (dry skin); it refers to a group of predominantly cutaneous conditions that have in common the development of alterations in cornification. (32) It is characterized by hyperkeratosis, scaling and fissures in the skin. (33)

Also in the year 2009 a group of experts developed a new consent classification based mainly on the clinical characteristics, in the pathophysiological and molecular aspects found by the time. Non syndromic ichthyosis are divided in: vulgar ichthyosis; chromosome X bound ichthyosis; recessive congenital ichthyosis, which in turn are subdivided in: laminar ichthyosis and non-bullous congenital ichthyosiform erythroderma. The two first are the most frequent types. (34)

In the same way ichthyosis vulgaris is an autosomal dominant genodermatosis, it can be congenital or begin in the first months of life, with fine and adherent scales

that respect the flexural folds. [8] It is the most frequent form. It affects both sexes equally, with a tendency to improve at puberty. A family history of dry skin is common. The fine and white scaly lesions are located fundamentally in the trunk and limbs, with predilection for the lower limbs, where the scales are large, very dry and rough. (Figure 2A)

The soles and palms are thickened and dry, the palmar groove are accentuated (Figure 2B), and hyperkeratosis simulates a wrinkled skin. The flexural surfaces are always respected. These symptoms worsen in cold and dry weather; cracks may appear in the fingertips. [9]


A


B

Fig. 2. Patient with vulgar ichthyosis. A: Scales in lower limbs.
B: Pronounced palmar groove.

Recessive congenital ichthyosis manifests at birth as a membrane covering them (collodion) that detaches within 10 to 14 days after birth. Later on large rhomboid, hyperpigmented, dark, thick scales with fissures are observed, with a generalized distribution and mosaic pattern, with minimal or no erythroderma, generalized hyperkeratosis and blockage of the sweat ducts, induce decreased sweating and

hyperthermia, likewise there are alterations in the sweating glands that favor dry and inflexible skin, with decreased range of joint mobility with flexural contractures; palmoplantar keratoderma is common, the nails may present with onychogryphosis, lateral deviation, subungual hyperkeratosis, grooves and longitudinal fissures, hair shaft abnormalities are not frequent, it usually presents with ectropion, eclabion and hypoplasia of nasal and atrial cartilages. [35]

The symptomatic treatment should be individualized, since effectiveness and tolerance of each patient is different, it is important to consider the age, type and severity of the ichthyosis, the extent and/or localization of the lesions and the response to previous therapies. Topical emollients and keratolytic agents are usually the first line of treatment, as they improve the barrier function and facilitate desquamation when applied at least twice a day. To moisturize the skin, preparations containing urea, glycerol or petrolatum are used. In patients with thick scales and marked hyperkeratosis, one or more keratolytic agents such as high concentrations of urea, lactic acid, salicylic acid and propylene glycol may be added. [32]

The authors suggest the use of creams formulated with wax and honey as emollients and moisturizers in scaly lesions and in presence of erythroderma or eczema the use of creams that contain apitoxin in their formulation.

Hereditary Palmoplantar Keratodermas

They are a group of skin conditions clinically characterized by thickening of the stratum corneum (hyperkeratosis) on the palms and soles. (Figure 3) According to their distribution, they can be diffuse, focal (nummular or linear) or papular. [36]

Fig. 3: Hyperkeratosis with fissures in patient with palmoplantar keratoderma

In most cases, hereditary forms are caused by mutations in the genes of these areas that code for the production of keratins, connexins and desmosomal components. Regardless of heredity, the keratinocyte is affected by mutations in the genes that encode proteins essential for the mechanical integrity of the skin, as the keratin intermediate filaments, desmosomal and junctional proteins, resulting in an increment in keratin formation. [36]

Some palmoplantar keratodermas only affect the skin of the palms and soles of the feet and others have associated syndromic characteristics that include changes in the hair, teeth, nails, hearing loss or cardiomyopathy. It may be accompanied by hyperhidrosis with bacterial and fungal proliferation that causes superinfection of hands and feet with malodorous maceration and reduced mobility. [37]

The treatment of PPK is not very successful, the improvement is transitory, so it must be applied in a continuous way and throughout life. Repetitive trauma should be avoided, since hyperkeratosis is a consequence of an exaggerated response to the alteration of the mechanical integrity of the skin. The basis of local treatment consists of the application of preparations with keratolytic and moisturizing substances. [38]

Based on the described properties of honey and propolis, the authors suggest using propolis tincture to heal fissures and combat or prevent bacterial and fungal infections, and in keratoderma lesions, the use of honey emulsion, in which the acidic PH will have a keratolytic action, providing softness to palms and soles.

Conclusions

In some genodermatosis that pressent with blisters and keratinization disorders, the structure of the skin is damaged in a permanent way and the protection function is affected. To know the benefits of apidermocosmetic and its uses in some genodermatoses, favors the improvement of the dermatologic evolution of these patients.

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Conflict of interest

The authors declare that they have no conflict of interest in carrying out this study. This article can be found on the website of the International Congress of Dermatology 2024.

Authors´ contribution

Yordania Velázquez Avila: conceptualization, formal analysis, research, methodologies, writing-draft original, writing-review and editing. 60%

Alejandro Bernardo Cervantes Palomino: conceptualization, formal analysis, research, writing-review and editing. 20 %

Claudio Tirabasso Bier: formal analysis, research, writing-review and editing. 20 %

Traductor: Lic Enma Luisa Caballero Mustelier