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Review Article

A Minireview on Hyperpigmentation its Mechanism and Remedies

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Abstract

Beauty is everyday priority and million-dollar dream. Fair skin is appreciated by large population worldwide. So, in this review various problems associated with causation of hyperpigmentation is defined and various herbal remedies and their mechanism of action is discussed for development of efficient anti-hyperpigmentation product.

Keywords: fair skin; hyperpigmentation; herbal remedies

Introduction

In this review we have evaluated various research and review papers appeared in the last 15 years and we have collected the most significant data. Several databases, such as Scifinder, Pubmed, Google Scholar, ISI-Web of Science and Scopus, were used as literature sources.The main stress of research is based on scientifically approved herbs which were claimed in traditional and folklore medicine to cure hyperpigmentation.

Hyper pigmentation of the skin is a common problem among patients as exposed by dermatologists. Most of the world's population is brown-skinned, and an enormous amount of interest worldwide is focused on restoring hyperpigmented skin to its natural or fairer color by skin care specialists. Treatment of hyperpigmentation disorders, however, is often tough and prolonged, required patience and knowledge of a variety of treatments to achieve success. Over the past decade, a new therapies are developed for disorders of hyperpigmentation.Although these therapies are expensive and out of reach of general people.[1]

Hyperpigmentary symptoms, including post-inflammatory hyperpigmentation, solar lentigos, and melasma, occur in the human population and are thus this is problem of concern. On the basis of genomic and proteomic studies of the melanocyte and melanogenesis, there are potentially hundreds of proteins and other effectors involved in pigmentation. These hyperpigmentary symptoms,are complex phenomenon. There are new laboratory screening methods and skin color measurement tools are available that are increasing the pace at which materials can be screened and evaluated clinically for their effectiveness .[2]

Fluorescence photography for identifying mottled and diffuse hyperpigmentation

Fluorescence photography is a noninvasive method that is sensitive in the evaluation and quantification of distribution and changes of mottled and diffuse hyperpigmentation.[3]

Allied symtoms such as Dyschromia

Dyschromia is a common dermatological concern in patients with darker skin. Disorders of hyperpigmentation and facial hyperpigmentation, are the most frequently treated dyschromias and they have considerable psychosocial impact. Due to high occurance of hyperpigmentation and the considerable demand for even and fair complexion, newer treatment options for hyperpigmentation are of growing interest among consumers, manufacturers, and dermatologists. Blinded, controlled studies demonstrating skin lightening effects in soy, niacinamide, n-acetylglucosamine, licorice extract, arbutin, vitamin c, kojic acid, embolic extract, lignin peroxidase, and glutathione have led to the development of a growing list of over the counter skin care products that can be incorporated (mostly as adjuncts) in the management of hyperpigmentation.[4]

By midcentury, the U.S.A. will be more ethnically and racially diverse. Due to population from different countries skin conditions and color is diverse. Structural and functional differences in the skin, as well as the influence of cultural practices, produce variances in skin disease and presentation based on skin type. In the skin of color population, dyschromia is a growing concern, and a top chief complaint when patients present to the physician. A thorough understanding of the etiology and

management strategies of facial hyperpigmentation is of importance in caring for those afflicted and also in the development of new therapies.[5]

The subtype of hyperpigmentation is important for treatment prognosis, with dermal hyperpigmentation less responsive to treatment. Botanical extracts and standard therapies may play an integrative role in the abolition of hyperpigmentation.[6]

Causes of hypigmentation

Hyperpigmentation of skin is caused by several factors. UV exposure, in addition to oxidative stress, elevates inflammatory mediators stimulating melanogenesis. Herbal-derived compounds for improving skin lightness are gaining interest as they are perceived to be milder, safer, and healthier than fully synthetic products. This review briefly discusses the causes of skin hyperpigmentation and extensively summarizes the status of herbs currently used in skin-lightening cosmetics. The properties of active compounds and their dose rate information are summarized where available, along with human or animal relevant models for activity testing.[7]

Mycosis fungoides

Pigmentary changes in mycosis fungoides usually occur in association with poikiloderma atrophicans vascular or following therapy and regression of lesions. Several cases of hypopigmented mycosis fungoides have also been reported. In various studies Giant melanin granules were found in the tumor cells, as well as in keratinocytes and Langerhans cells. Cutaneous hyperpigmentation is single presenting sign of mycosis fungoides.[8]

Azidothymidine

Hyperpigmentation developed in six patients while they were receiving azidothymidine. All demonstrated hyperpigmentation of the nails; hyperpigmentation of the skin (two patients) and oral mucosa (two patients) also developed. The degree of nail pigmentation was related to the intrinsic skin color of the patient. Mucosal hyperpigmentation developed only in dark-skinned blacks. The pigmentation occur due to increased **melanin** in the epidermis and dermis.[9]

Mechanism of action

Human skin grafted on to athymic nude mice (BALB/C-nu/nu) spontaneously hyper pigments. We wished to identify the morphological and molecular bases for the hyperpigmentation for this phenomenon. Biopsies were taken at preset times post-graft and studied by histological and immunohistochemical methods. DOPA-positive melanocytes first became visible 120 h post-graft and melanin deposition became visible along the basal cell layer 2 weeks post-graft and increased in quantify with time. By immunochemical stains the quantity of three melanocyte specific enzymes, i.e., tyrosinase, tyrosinase-related protein-1 (TRP-1) and DOPA-chrome tautomerase (TRP-2), was markedly enhanced 1 week after grafting and persisted until 4 weeks post-graft. α-Melanocyte-stimulating hormone and adrenocorticotrophic hormone were clearly detected in the epidermis soon after grafting. They were still strongly detected in the epidermis and in the dermis 2–4 weeks post-graft. It is concluded that that hyperpigmentation in the grafted skin accompanies a marked increase in the quantity of melanogenic enzymes and melanogenic peptides.[10]

Tyrosinase inhibitory properties

The antioxidant and tyrosinase inhibitory properties of extracts of mango seed kernel (*Mangifera indica* L.), were studied. Extracts contained phenolic components by a high antioxidant activity, which was assessed in homogeneous solution by the 2,2-diphenyl-1-picrylhydrazyl radical and 2,2′-azinobis (3-ethylbenzothialozinesulfonic acid) radical cation-scavenging assays and in an emulsion with the ferric thiocyanate test. The extracts also possessed tyrosinase inhibitory activity. Drying conditions and extraction solvent were varied, and optimum conditions for preparation of mango seed kernel extract were found to be sun-drying with ethanol extraction at room temperature. Refluxing in acidified ethanol gave an increase in yield and the obtained extract had the highest content of total phenolics, and also was the most effective antioxidant with the highest radical-scavenging, metal-chelating and tyrosinase inhibitory activity. The extracts did not cause acute irritation of rabbit skins; This study for the first time reveals the high total phenol content, radical-scavenging, metal-chelating and tyrosinase inhibitory activities of the extract from mango seed kernel.[11]

Remedies for Hyperpigmentation

Vit B12 supplement

A 49-year-old man presented with neurosis, hyperpigmentation of the skin, and depigmentation of the hair. On examination, hyperpigmentation was observed on the oral mucosa and the skin of the forearms, elbows, palmar creases and periunguinal area, knees, and feet. He had megaloblastic anemia with a low serum level of vitamin B12 due to malabsorption resulting from a gastrectomy 10 years previously. His hyperpigmentation was resolved with vitamin B12 supplementation. Histology showed an increase of melanin in the basal layer. In electron microscopic study, many melanosomes were observed in melanocytes and surrounding keratinocytes. We consider that the dominant mechanism of hyperpigmentation due to vitamin B12 deficiency is not a defect in melanin transport but is rather an increase in melanin synthesis.[12]

Hydroquinones

Facial hyperpigmented disorders are a common complaint in the adult population of all races. First-line topical treatments are usually hydroquinone or topical retinoids, which can cause irritant reactions. The need for better tolerated, yet effective, skin lightening agents that could be utilized by a wider population has led to the investigation of several potential botanical/natural compounds. There are currently many topical cosmetic formulations claiming skin depigmenting effects. A few of the ingredients (e.g., soy) are supported not only by *in vitro* results but also by a body of controlled clinical efficacy studies; other ingredients, instead, are backed mostly by *in vitro* data and a few small uncontrolled clinical studies. In this review, we describe the most common natural ingredients used for skin depigmentation and their major published studies: soy, licorice extracts, kojic acid, arbutin, niacinamide, N-acetylglucosamine, Coffee and green tea.[13]

Tretinoin

The fluorescence photographs were evaluated blindly and yielded macule counts that decreased significantly from baseline in tretinoin-treated subjects compared with vehicle-treated subjects (31% vs 11% decrease; $p = 0.02$). Diffuse hyperpigmentation, as evaluated from the fluorescence photographs, decreased 16% from baseline for tretinoin-treated subjects and increased 5% for vehicle-treated subjects ($p < 0.01$). No significant differences in mottled or diffuse hyperpigmentation were observed between groups through clinical evaluation.

Salicylic acid

Here are no randomized split-face model studies investigating treatments for postinflammatory hyperpigmentation in dark skin. Ten subjects with Fitzpatrick skin phototypes IV to VI were randomized to receive two 20% salicylic acid peels followed by three 30% salicylic acid peels to half of the face. The contralateral half remained untreated. Response was evaluated by photography reviewed by three blinded dermatologists. The Visual Analog Scale, Dermatology Life Quality Index (DLQI), and treatment quality questionnaire were administered.Quality of life measured according to the DLQI improved after treatment but not statistically significantly so (p=.13). Treatment had no significant adverse effects.Salicylic acid peels are safe in this population. Although patients rated them as clinically effective, blinded raters found a brief series of peels to have less efficacy. Measured quality of life improved nominally.[14]

Flavonol

A common flavonol, kaempferol, isolated from the fresh flower petals of *Crocus sativus* L. (Iridaceae) was found to inhibit the oxidation of L-3,4-dihydroxyphenylalanine (L-DOPA) catalyzed by mushroom tyrosinase with an ID_{50} of 67 μg/mL (0.23 mM). Interestingly, its 3-*O*-glycoside derivatives did not inhibit this oxidation. The inhibition kinetics analyzed by a Lineweaver−Burk plot found kaempferol to be a competitive inhibitor, and this inhibitory activity presumably comes from its ability to chelate copper in the enzyme. This copper chelation mechanism can be applicable for all of the flavonols as long as their 3-hydroxyl group is free. However, quercetin, kaempferol, and galangin each affect the oxidation of L-tyrosine in somewhat different ways.[15]

Sunscreen

Besides the unquestionable positive effects of solar exposure for human health, UV rays have been widely investigated for toxicology aspects related to excessive UVB and UVA doses, which involve sunburns, skin aging, DNA skin damage and tumorigenesis. Although a large number of herbal extracts and plant origin molecules can deserve potential applications, most of the study reported utilizes different method and different strategies of investigation, making thus difficult to understand the real versus claimed potential. This may be the reasons why, beside the large body of literature there are no officially approved natural commercial sun-filter but a consistent number of commercially available solar products (sunscreen) on the market that contain herbal derivatives. New formulation, new skin delivery systems, skin penetration enhancers and boosters are most likely the next frontier of investigation in order to better understand the role of whole herbal extracts in exerting their photo protective activity.[16]

Turmeric

The extract (at 300 or 1000 mg/kg, twice daily) prevented an increase in skin thickness and a reduction in skin elasticity induced by chronic UVB exposure. It also prevented the formation of wrinkles and melanin (at 1000 mg/kg, twice daily)[17]

Pharbitis nil, Sophora japonica, Spatholobus suberectus,* and *Morus alba,

Because tyrosinase catalyzes melanin synthesis, tyrosinase inhibitors are important in cosmetic skin-whitening. Oxidative stress contributes to skin aging and can adversely affect skin health, which means antioxidants active in skin cells may support skin health. Twenty-five traditional Chinese herbal medicines extracts (100 μg/mL) were tested for cytotoxicity on human epidermal melanocytes (HEMn); 12 exhibited low cytotoxicity. Their effects on tyrosinase and melanin inhibitory activities and free radical scavenging activities were further assessed. Phenolic contents were evaluated using Folin–Ciocalteu reagent. Four herbs, *Pharbitis nil*, *Sophora japonica*, *Spatholobus suberectus*, and *Morus alba*, exhibited potent inhibitory effects on tyrosinase (IC_{50} values 24.9, 95.6, 83.9, and 78.3 μg/mL, respectively). Melanin inhibition was not dose-dependent. *Sophora japonica* (IC_{50}: 14.46 μg/mL, 1,1-diphenyl-2-picrylhydrazyl (DPPH); 1.95 μg/mL, hydroxyl radical) and *Spatholobus suberectus* (IC_{50}: 10.51 μg/mL, DPPH; 4.36 μg/mL, hydroxyl radical) showed good antioxidative activities and high phenolic contents (255 and 189 mg of gallic acid/g extract, respectively). Among active anti-tyrosinase extracts, *Sophora japonica* and *Spatholobus suberectus* were especially potent in HEMn cells in terms of free radical scavenging effects and high phenolic contents, making them the strongest candidates for cosmetic application found in the current study.[18]

Conclusion

This article give insights about hyperpigmentation, dischromia,mechanism of hyperpigmentation and its remedies such as trintoin,flavonol ,Curcuma longa and other herbs.

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