A COMPREHENSIVE REVIEW ON METAL NANOPARTICLES

ABSTRACT:

Natural products offer promising solutions for treating skin pigmentation disorders due to their non-toxic properties and effective mechanisms of action. Studies highlight their safety and efficacy through methods such as cytotoxicity tests, tyrosinase activity assays, and melanogenesis inhibition evaluations. Advanced delivery systems like liposomes and nanoparticles further enhance their performance by improving solubility and skin penetration. Skin pigmentation disorders, influenced by factors such as UV radiation, hormonal changes, and inflammation, result in melanin overproduction and uneven skin tone. Eumelanin and pheomelanin, the two primary pigments, play distinct roles in skin protection and temperature regulation. Historically, pigmentation has been unjustly linked to racial biases, reflecting societal discrimination. Modern treatment options, including hydroquinone and tranexamic acid, provide targeted therapies, though the misuse of corticosteroids remains a concern. The development and application of natural products in pigmentation treatment combine efficacy, safety, and economic benefits, offering a sustainable approach to managing these conditions.

Keywords: Skin pigmentation, tyrosinase inhibitors, hypopigmentation, hyperpigmentation, vitiligo, skin lightening, depigmenatation

INTRODUCTION:

In this review, we examine the pathophysiology and therapeutic approaches of disorders while concentrating on the application and mechanism of natural products in the treatment of skin pigmentation. Additionally, a summary of the innovative natural product compositions used to treat skin pigmentation is provided. In conclusion, the traditional pharmacodynamic assessment techniques for researching pigmentation disorders are emphasized as a resource for creating novel formulations of natural products. Natural remedies that have whitening and spot-lightening effects have become more and more popular in recent years because of their great biocompatibility, natural nature, and lack of toxicity.[1] Furthermore, numerous studies have verified the safety and effectiveness of these products based on their cytotoxicity, tyrosinase activity[2], antioxidant levels[3], suppression of melanogenesis[4], as well as the well-established animal pigmentation models.[5,6] In the meanwhile, innovative delivery techniques such liposomes,[7] nanoparticles,[8] Nano emulsions,[9] and mironeedls,[10] have been applied to enhance therapeutic benefits by increasing skin permeability, decreasing skin irritation, or improving drug solubility.[11] Without a doubt, research into natural items as treatments for pigmentation offers great promise and value in terms of producing positive social and economic effects.Uneven brown to dark brown dots on the skin are a sign of skin pigmentation.[12,13] Skin injury, acne, cellular inflammation, UV radiation, hormonal changes, and medication effects are all related to the beginning of skin pigmentation.[14,15] Melanocytes experience excessive proliferation, aggregation, and pigment release under the influence of many stimuli, which culminates in the creation of freckles and pigmentation.[12]

The dark brown pigment eumelanin, which absorbs UV radiation from the sun, shields the skin from sunburn. Higher amounts of epimelanin are linked to darker skin tones, whilst lower levels are linked to lighter skin tones. One of the extra advantages of eumelanin is that it can prevent skin cancer. According to studies, those with higher eumelanin levels were less likely than those with lower levels to acquire skin cancer. In addition to helping to control body temperature, eumelanin absorbs solar heat and keeps the body cool.[16,17] The pigment, phenomelanin, has a lighter yellow-red color. Pheomelanin has a lesser absorption of UV light than eumelanin, which is why people with higher levels have lighter skin tones and are more vulnerable to sunburns and skin damage. There are, nevertheless, certain advantages to phenolelanin. By reflecting heat away from the body, it aids in controlling body temperature

and helps keep the body cool in heated environments. Additionally helpful in preventing melanoma and other forms of skin cancer is phenolomelanin.[18,19]

The earliest distinguishable and changeable characteristic of humans is their skin color. The idea of pigmentation variation has grown over time and has frequently been applied to the creation of "racial classifications." The belief of the primacy of whiteness and the legalization of a lifelong and inherited state of slavery for races deemed inferior marked the beginning of the distinction of people based on "races" in the 17th and 18th centuries.The term "Negroes" was used to refer to those with very pigmented complexion as a distinct race, suggesting that Europeans, who were thought to have fair skin, were the master race.[20] According to Agassiz, the distinctions between "Whites" and "Blacks" are constant and intrinsic, resulting from the distinct creations of the two races.[21] Racism thus has multiple aspects. Italian immigration to the United States of America in the 19th and 20th centuries—mostly darker-skinned individuals from southern Italy represented a specific example. Italians were mockingly referred to as "kinky-haired" or "swarthy" and called epithets like "guinea" and "dago," which were used to refer to Africans who were held in slavery and their descendants.[22]

People typically explore a variety of home cures and potential treatment options without consulting a dermatologist. Topical treatments typically contain ingredients that lighten the skin, like vitamin C, azelaic acid, hydroquinone, kojic acid, and retinoids like tretinoin.In research done over the past ten years, 5 TC has been listed as the medicine for hyperpigmentation that is most frequently misused.[23] The main goal of starting a steroid cream is to have skin that is excellent, fairer, and more gorgeous. On the skin, TC shows anti-inflammatory and pigment-lightening properties. TC quickly relieves uncomfortable indications and symptoms of inflammatory skin changes. Sadly, if TCs are used incorrectly or for an extended period of time, the initial condition may worsen, making this "improvement" transient. Steroids interfere with the formation of melanin by smaller melanocytes, leading to patchy patches of hypopigmentation which are reversible following withdrawal of steroids.[24]

There are numerous therapies available for hyperpigmentation at the moment, depending on the cause and course of the condition. Hydroquinone is the gold standard treatment for targeted hyperpigmentation, and topical therapies are commonly utilized for this condition.[25] In particular, hydroquinone works to reduce epidermal hyperpigmentation by blocking tyrosinase, which stops melanin from being produced and, in turn, stops L-DOPA from being converted to melanin.[26] The most used oral medication for treating hyperpigmentation is tranexamic

acid, which is regarded as a second-line treatment. Tranexamic acid acts by lowering Sufficient amounts of vitamins and proper growth and efficiency of metabolic processes depend on a human diet that is balanced in terms of macro- and micronutrients.Globally, inadequate food quality or quantity, higher dietary needs, higher metabolic losses, or less gastrointestinal absorption are the main causes of vitamin deficiencies. Micronutrients, particularly sufficient vitamin levels, are necessary for the efficient and ideal development of metabolic processes.Globally, inadequate food quality or quantity, higher dietary needs, higher metabolic losses, or less gastrointestinal absorption are the main causes of vitamin deficiencies.[27]

TYPES OF SKIN PIGMENTATION:

To be pigmented is to be colored. Skin color is impacted by illnesses related to skin pigmentation. Melanin is the pigment that gives your skin its color. Melanin is produced in the skin by certain cells. Melanin production is impacted by the health or injury of these cells. Certain pigmentation abnormalities only impact specific skin areas. People impact your body as a whole. An excess of melanin produced by the body results in darker skin. Your skin can become darker as a result of sun exposure, Addison's disease, and pregnancy. A deficiency of melanin in the body causes skin lightening. Light-colored patches of skin are a symptom of the vitiligo illness. A hereditary disorder affecting the skin is called albinism. A person with albinism may be completely colorless, have skin that is paler than usual, or have patches of missing color. Lighter skin can also result from burns, blisters, and infections.

- There are some common types of skin pigmentation:
- Melasma
- Albinism
- Vitiligo
- Addison’s Disease

1. Melasma:

Melasma is a gradual, nonclinging, macular hyper-melanosis of the skin that mostly affects the face and dorsal forearms when exposed to sunlight. It may be idiopathic or commonly linked to pregnancy, oral contraceptives, or anticonvulsants (such phenytoin [Dilantin]). There are three different kinds of melasma: mixed, dermal, and epidermal. Light brown in color, epidermal melasma becomes more prominent when examined under a wood lamp. The typical

color of dermal melasma is greyish with no enhancement. Dark brown with varying enhancement, mixed types. Some degree of effectiveness can be achieved with topical treatment with hydroquinone 3% or 4%, glycolic acid 10% peel, azelaic acid 20% cream, and retinoid (e.g., tretinoin 0.05% or 0.1% cream; apalene 0.1% or 0.3% gel [Differin]). Combination products that contain topical steroids, glycolic acid, and retinoids along with hydroquinone appear to be slightly more effective.For treatment to remain effective, it is usually necessary to continue it permanently.7–15 In one study funded by a pharmaceutical company, a triple-combination treatment (TriLuma) consisting of 0.01% fluocinonide, 4% hydroquinone, and 0.05% tretinoin cream demonstrated significantly better efficacy in improving dyspigmentation than treatment with any two of these ingredients combined, with only mild side effects.[28,29]

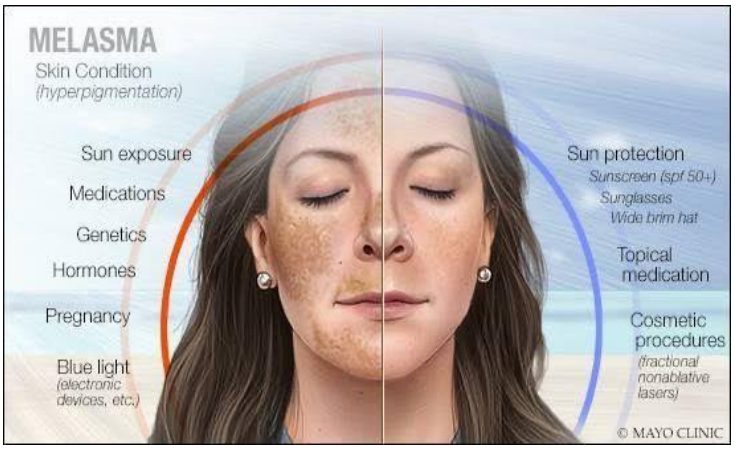

Fig :Melasma

However, a number of modest studies indicate that laser therapy or a combination of intense pulsed light therapy and hydroquinone with sunscreen may be an effective treatment for cutaneous or refractory/mixed-type Melasma.[30,31]

2. Albinism:

A genetic disorder called albinism causes the generation of less melanin, which leaves a person with a fair skin tone, light eyes and hair, and an increased susceptibility to certain skin and eye disorders. The pigment called melanin is what gives your skin and hair their color. It is present in the hair, the eyes, and the epidermis, the skin's outermost layer.Melanin supports in the prevention of skin damage and skin cancer by protecting your body from ultraviolet (UV) rays from the sun. The proportional proportions of the two primary forms of melanin—eumelanin and pheomelanin depend on an individual's genetic composition, which is inherited from their parents. There are two main forms of albinism: ocular albinism (OA), which is more rare and

affects mainly the eyes, and oculocutaneous albinism (OCA), which affects the eyes, hair, and skin.[32]

Fig :Albinism

Albinism can impact people of any ethnicity. According to estimates, 1 in 20,000 Americans and 1 in 17,000 Australians suffer from this illness. Certain regions of the world have higher prevalence rates of albinism, such as Zimbabwe, Africa, where the frequency is approximately 1 in 1,000.[32,33]

3. Vitiligo:

A disfiguring skin condition that causes pigmentation loss is vitiligo. One percent of the general population has vitiligo, which equally affects men and women. About 25–30% of patients have a documented family history of vitiligo. Although onset is frequently subtle, it is usually connected to a recent ailment, trauma, or stressor (such as sunburn). 50% of cases occur before the age of 20, with peak onset happening in the second and third decades of life.[34] Vitiligo lesions are composed of distinct, unpigmented macules that vary in size from 5 to 50 mm. A rim of erythema or hyperpigmentation will appear on some. The face, neck, dorsal hands, genitalia, body folds, and axillae are common locations of involvement.

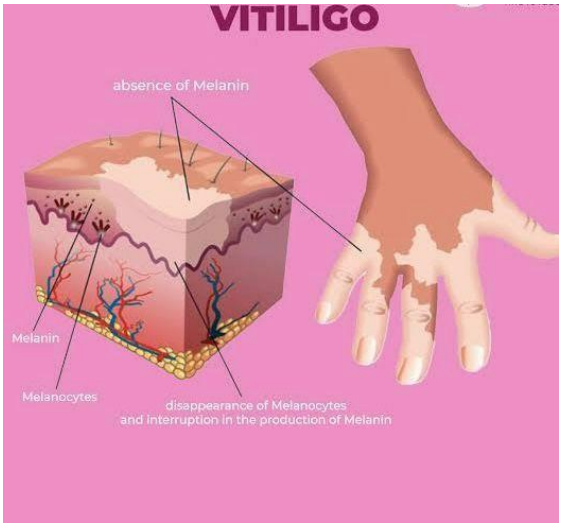

Fig :Vitiligo

Lesions of the perianal, perioral, periorbital, and periumbilical regions can also arise. There are four different kinds of vitiligo: segmental, acral/orofacial, localized, and generalized. More than 10% of the body's surface is affected by generalized vitiligo. Usually affecting the face and distal extremities, acral/orofacial vitiligo is referred to as the "tip/lip" pattern. Localized vitiligo is typically steady in nature and affects a limited area of the body. Treatment prognosis is worse for segmental vitiligo, which affects a single dermatome or extremities and is more common in youngsters.

4. Addison's disease :

A rare endocrine illness that affects one in 100,000 persons is Addison's disease. It affects both men and women equally and is present in all age groups. This illness bears the name of Thomas Addison, who published the first account of patients with this disorder in the book "On the Constitutional and Local Effects of the Disease of Supra Renal Cap" in 1855.[35,36] Because Addison's disease is often misdiagnosed in its early stages, it might present as a potentially fatal situation. Since its first description, the underlying cause of Addison's disease has shifted radically from an infectious source to an autoimmune pathology. Still, the most common cause of Addison's disease in poorer nations is tuberculosis.[37]

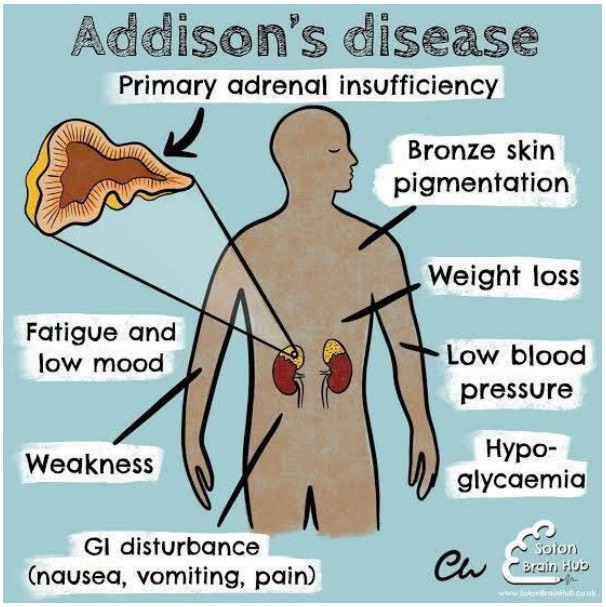

Fig :Addison's disease

CAUSES OF HYPERPIGMENTATION:

There are multiple causes of hyperpigmentation. These include endocrinologic factors such as Addison's disease, Cushing's syndrome, Nelson syndrome, phaeochromocytoma, carcinoid, acromegaly, hyperthyroidism, acanthosis Nigerians, and diabetes, as well as external factors such as these. Factors related to nutrition include tryptophan deficiency, vitamin A deficiency,[38,39] folic acid deficiency, niacin deficit, and Yum Kwashiorkor. An unwanted side effect of hormonal contraceptive usage is melisma.[40]

Low melanin concentration is a genetic defect that causes albinism at birth. Prior skin trauma, including skin lesions like blisters, infections, burns, exposure, white complexion, dark blue eyes, and white hair, are among the common physical characteristics of albinos.[41,42]

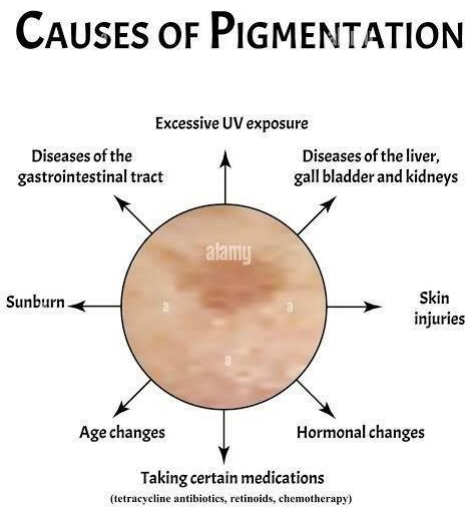

Fig :Causes of Pigmentation

A person's arms or face can get dark or blue-grey spots due to insufficient melanin level, which is most commonly caused by the inherited Melasma syndrome, chemicals, and other wounds. hormones (fake skin tone). The skin will be paler than it was before an injury healed, or it may be triggered by contraceptive prescription.[43,44] Chloasma and melasma are two instances of hyperpigmentation caused by hormonal causes. This condition, which is common in women, has been linked to the female sex hormones progesterone and estrogen, which increase the body's production of melanin when exposed to sunlight. Hyperpigmentation is a side effect of hormone replacement treatment.[45] These physiological changes demonstrate how aging manifests itself more visibly in humans. Melanocyte counts decrease with age, but those that remain increase beyond 40.[46] Pigmentation is influenced by genetics. Melanocyte development is specialized. These physiological changes demonstrate how aging becomes more noticeable and how specific genes are needed to affect skin color. As per the phrase in individuals over 40.[47]

REGULATION OF SKIN PIGMENTATION :

Depending on their racial or ethnic heritage, humans might have skin that is exceptionally fair or light or excessively dark, yet all skin types have about the same density of melanocytes in certain areas, including the arms or back.[48] In contrast to dark skin, where the highly pigmented melanosomes are dispersed independently inside keratinocytes to maximize light absorption, fair skin keratinocytes have a tendency to cluster their poorly colored melanosomes

above the nucleus. The melanocyte density varies greatly within an individual in different parts of the body, such as the skin. Because of their strong expression of Bcl2, epidermal melanocytes are very resistant to apoptosis and multiply slowly, if at all, in normal conditions. [49] UV light and substances released by nearby keratinocytes and fibroblasts have an impact on melanocyte density and differentiation. For instance, it has recently been demonstrated that fibroblasts in the dermis of the palms and soles express large amounts of DKK1, which inhibits the Want/-catenin signaling pathway to limit melanocyte development and function.[50,51] Want signaling in melanocytes is inhibited by DKK1, which has a profound effect on the melanogenic pathway. This effect extends to downstream melanogenic proteins as well as transcriptional regulators like MITF. DKK1 also has an impact on keratinocytes in the epidermis that covers them, which decreases their melanin uptake and results in a thicker, less pigmented skin phenotype.4 In adult skin, the expression patterns of HOX genes are preserved in the dermis.[52] Which, in the tanning response, are known to control patterning in primary and most evident of them are UV.[53,54] The intricate dynamics of the skin's reactions to UV light, which cause tanning over a few weeks, have been described in recent research.[55] The main factor affecting the pigmentation of human skin is UV light. Immediate pigment darkening, which happens within minutes and lasts for several hours, is a direct result of UV radiation, particularly UVA. Persistent pigment darkening, which happens within hours and lasts for several days, follows immediate pigment darkening.[56]

Additionally, in response to UV exposure, epidermal melanocytes and keratinocytes express more MSH and ACTH, which in turn upregulates the expression and function of MC1R and, as a result, intensifies melanocyte responses to those melanocortins. Weakly functioning variants of MC1R are prevalent in people with fair skin and red hair, who mostly contain pheomelanin and are relatively unable to become tan. UV also increases the expression of endothelin 1 by keratinocytes, which in turn amplifies the expression of MC1R. However, endothelin 1 acts through the receptor EDNRB on melanocytes. UV also induces keratinocytes to secrete interleukin-1, which in turn stimulates the release of ACTH, MSH, Endothelin 1, and bFGF. NGF and SCF are additional melanogenic factors that are generated by keratinocytes in reaction to UV light. The tanning reaction also depends on keratinocytes being stimulated to secrete NGF, which stops melanocytes from killing after being exposed to UV light.[57] Regulating the pigmentation of human skin has long been an aim in cosmetic and pharmacological purposes. It affects one's social status, physical look, and, of course, the skin's ability to fend off cancer and photoaging. Activation of the MC1R by agonists and bioactive

derivatives, topical application of factors that circumvent the MC1R, factors that stimulate TYR function, factors that improve melanosome transfer, etc. are some of the ways that have been tried to stimulate pigmentation. Due in part to the difficulty of crossing the skin barrier and in part to the desire for specificity—that is, to activate melanocyte function without impacting other types of skin cells—the majority of those tests have been met with little to no success.[58]

REGULATION FUNCTION OF SKIN:

Depending on their racial or ethnic history, humans might have skin that is highly pale or light or excessively dark, yet all skin types have almost the same density of melanocytes in certain areas, including the arms or back.[59] Dark skinned keratinocytes have individually distributed intensely colored melanosomes that maximize light absorption, while fair skinned keratinocytes tend to cluster their less pigmented melanosomes above the nuclei. The melanocyte density varies greatly within an individual in different parts of the body, such as the skin on the palms and soles versus other parts of the body. The environment can have an impact on the skin's constitutive melanocyte density. For example, prolonged exposure to UV light can triple or quadruple melanocyte density, and hydroquinone, a poisonous substance, can destroy melanocytes in the skin permanently.Increased melanocyte density, such as freckles, or decreased melanocyte density, such as vitiligo, can also be the outcome of inherited pigmentary illnesses.

Because of their high expression of Bcl2, epidermal melanocytes are highly resistant to apoptosis and multiply slowly, if at all, under normal conditions.[60] UV light and substances released by nearby keratinocytes and fibroblasts can have an impact on melanocyte density and differentiation. For instance, it has recently been demonstrated that fibroblasts in the dermis of the palms and soles release large amounts of DKK1, which inhibits the Want/-catenin signaling pathway and hence reduces melanocyte proliferation and function.[61] Fruit is the most essential and nutritious part of a well-balanced diet. Fruits are low in calories, salt, fat, and cholesterol, but they are also an excellent source of vitamins, minerals, and enzymes. Kiwi fruits are the most important fruit of all.[62]

Significantly suppresses the melanogenic pathway, with effects on downstream melanogenic proteins as well as transcriptional regulators such MITF. DKK1 also has an impact on keratinocytes in the epidermis that covers them, which decreases their melanin uptake and

results in a phenotype of thicker, less pigmented skin.The expression patterns of HOX genes are preserved in the dermis of adult skin.[63] Evident that they were exposed to UV in what is known as the tanning reaction.[64,65] The intricate dynamics of the skin's reactions to UV radiation, which cause tanning over a few weeks, have been described in recent studies.[66] The main factor affecting the pigmentation of human skin is UV light. Immediate pigment darkening, which happens within minutes and lasts for many hours, is a direct result of UV radiation, particularly UVA. This is followed by persistent pigment darkening, which happens within hours and lasts for several days.[67] The oxidation and polymerization of existing melanin as well as the redistribution of melanosomes are what cause these sudden increases in pigmentation rather than acute melanin creation. Although it takes longer, delayed tanning happens several days after UV exposure because it activates melanocyte function. The major transcriptional regulator of pigmentation, MITF, and its downstream melanogenic proteins, such as Pmel17, MART-1, TYR, TRP1, and DCT, are expressed more when exposed to UV light,[68] ultimately resulting in an increase in the amount of melanin. Exposure to UV light also causes keratinocytes to produce higher amounts of PAR2, which in turn promotes keratinocyte uptake and dispersion of melanosomes in the epidermis.[69] Additionally, in response to UV exposure, epidermal melanocytes and keratinocytes express more MSH and ACTH, which upregulates the expression and function of MC1R and, as a result, increases melanocyte responses to those melanocortins. Weakly functioning variants of MC1R are prevalent in people with fair skin and red hair, who mostly contain pheomelanin and are relatively incapable of getting tan. Even though it acts through its own receptor (EDNRB) on melanocytes, UV also increases the expression of endothelin 1 by keratinocytes and improves the expression of MC1R. UV also causes keratinocytes to secrete interleukin-1, which in turn induces the release of ACTH, MSH, Endothelin 1, and bFGF. NGF and SCF are additional melanogenic factors that are generated by keratinocytes in reaction to UV light. The tanning reaction also depends on keratinocytes being stimulated to secrete NGF, which stops melanocytes from dying after being exposed to UV light.[70]

FOOD THAT INFLUENCE SKIN PIGMENTATION:

- Melons
- Tamatoes
- Oranges

- Passion Fruit
- Coffee
- Green Tea

1. Melons :

Melons (Cucumismelo L) are a good source of beta carotene and vitamin C; cantaloupes have higher levels of these nutrients than honeydews.[71] Dried melon pulp juice concentrate (MPJC) consumption was linked to a reduction in UVR-induced damage in 44 White patients with FSPT II or III, who were between the ages of 18 and 50. For thirty days, participants took either the MPJC or a color-matched control capsule once a day in addition to a control topical cream.[72] The buttocks of the participants were exposed to radiation both at baseline and during supplementation. The MPJC group showed a statistically significant increase in the minimal erythema dose (MED) when compared to the controls. The minimum UVR necessary to cause a moderate sunburn or redness is represented by the MED. It is believed that a greater MED corresponds to a lower vulnerability to UVR injury.[73] In a another trial, which looked at women with FSPT II to IV between the ages of 40 and 70, participants took a capsule containing the MPJC for eight weeks in addition to grape seed extract, vitamin C, and zinc. Notable improvements were observed in the areas of skin color, brightness, irritation, dark circles beneath the eyes, and overall subjective satisfaction.[74]

2. Tomatoes:

The carotenoid lycopene, which has strong antioxidative defense properties, is abundant in tomatoes (Lycopersiconesculentum).[75,76] Among all body tissues, human skin and plasma have the highest concentrations of lycopene.[77] After 10 weeks of daily consumption of 40 g of tomato paste, which provides approximately 16 mg of lycopene, men and women with FSPT II aged 26 to 67 showed a substantial reduction in UV-induced erythema and an increase in blood lycopene levels in comparison to the olive oil control group.[78] When women with FSPT I or II, ages 21 to 74, received 55 g of tomato paste with 16 mg of lycopene every day for 12 weeks, their erythemal threshold rose noticeably in comparison to when they only consumed olive oil.[79] Furthermore, in response to UVR-induced tissue damage, those who consumed the tomato paste demonstrated a significant decrease in fibrillin-1, mitochondrial DNA damage, and an increase in procollagen I and suppression of collagenase metalloproteinase-1 production. When compared to a control containing medium-chain triglycerides, twelve weeks

of supplementation with a carotenoid-rich tomato nutritional complex incorporating rosemary extract significantly reduced UV-induced erythema in persons with FSPT I or II who were between the ages of 20 and 50.[80]

3. Oranges:

It is commonly known that oranges (Citrus sinensis) are high in vitamin C. Depending on the variety and environmental conditions during the growth season, different nutritional and polyphenolic profiles are present.[81] Citrus fruits are a good source of flavonoids, especially hesperidin, quercetin, and narrating. Blood oranges also contain another subclass of flavonoids called anthocyanins, which are responsible for the crimson color of the pulp and juice. After supplementing with 100 mg/d of a powdered extract made from a combination of blood orange varieties containing 2.8% to 3.2% anthocyanins, 1.8% to 2.2% hydrodynamic acids, 8.5% to 9.5% flavone glycosides, and 5.5% to 6.5% VitC, all on a weight-to-weight basis, 20 White participants, ages 26 to 47, with FSPT II and III, showed inhibition of UV-induced erythema.[82] In 25 individuals with FSPT II and IV, ranging in age from 40 to 70, the same study discovered a substantial reduction of UV-induced melanogenesis. Melanogenesis was measured in one lentigo-free area and three areas with solarlentigos on each hand. Melanin is a crucial molecule that helps shield the skin from UV ray damage by absorbing a wide spectrum of UV radiation and releasing energy as heat.[83]

4. Passion Fruits:

Beneficial seeds from passion fruits (Passifloraedulis) contain polyphenols that are good for the skin.[84] Only the seeds contain piceatannol, and the seeds contain more polyphenols than the pulp or rind.[85] 32 Japanese women with dry skin complaints, ages 35 to 55, who took passion fruit seed extract containing 5 mg piceatannol for 8 weeks showed improved skin barrier function as measured by a significantly higher moisture content and a significantly lower TEWL as opposed to controls.[86] After eight weeks of consuming beverages high in piceatannol, adults also showed increased levels of water content and viscoelasticity on their faces.[87] Piceatannol, a polyphenolic compound, has been demonstrated to improve oxidative defense in rats by reducing the amount of hydrogen peroxide produced by amines following a six-week daily treatment period.One passion fruit can provide 5 mg (2.2 mg/g) piceatannol63, which is equal to about 2.3 g of raw passion fruit seeds.[88]

5. Coffee:

Chlorophyll is one of the several polyphenols found in coffee (Coffea L).[89,90] An observational study that evaluated the amount of chlorogenic acid that 131 Japanese women between the ages

of 30 and 60 drank from coffee found a significant correlation between decreased hyperpigmentation and higher coffee consumption (450 mL/d) or coffee polyphenol (900 mg/d).[91] When Japanese women aged 25 to 35 drank a decaffeinated beverage containing 297 mg of coffee polyphenols daily for four weeks, their scaly face and mouth skin improved dramatically in comparison to the control drink.[92]

6. Green Tea:

Several flavanols are found in green tea (GT; Camelliasinensis), especially epigallocatechin gallant (EGCG).[93,94] Studies on tea flavanols have revealed anti-allergenic and UVR-protective qualities that may be good for skin health.[95] For a period of 12 weeks, 60 women with FSPT II, ages 40 to 60, who consumed 1 liter of a GT drink containing 1402 mg of total tea flavanols (980 mg EGCG), saw a significant reduction in UV-induced erythema, roughness, TEWL, and viscoelasticity (resistance to an applied vacuum), when compared to a beverage control that contained no polyphenols.[96] Moreover, higher levels of skin density, biological elasticity (the capacity to revert to one's initial posture), and serum flavanols were noted.

HERBS AND DRUGS USE IN SKIN PIGMENTATION:

Drugs for skin pigmentation have been known for a long time, although they have only recently been more readily accessible. The primary treatments for skin pigmentation are topical creams and oral medicines. To choose which medication is most advantageous, it is best to weigh the benefits and drawbacks of each.[97,98]

- **Oral medications**
- **Topical creams**

- **Oral medication :**

Treatment for skin conditions and skin tone modification may be accomplished without the use of oral medications. These medications are advantageous since they are more effective than topical creams and don't require as much application or disposal. On the other hand, using oral drugs has some disadvantages. Compared to topical treatments, they can be more costly and have more serious side effects.[99] Additionally, it has been used to treat a number of ailments. Tranexamic acid, a plasmin inhibitor, reversibly blocks lysine binding sites on plasminogen molecules to stop the plasminogen activator from turning plasminogen into plasmin. By doing so, blood loss is avoided and abnormal fibrinolysis is decreased. Recent research indicates that

tranexamic acid facilitates the untangling of tangles via tyrosinase. By lowering the synthesis of melanin, it may prevent and reverse hyperpigmentation. It is a popular pharmacological method that works well against pigment spots and is readily available. It reduces cutaneous vascularity and lowers melanin production while blocking tyrosinase's actions and altering the interaction between keratinocytes and melanocytes.[100,101]

- **Topical creams:**

The most popular kind of medication used to treat skin pigmentation is topical cream. They can lighten or darken the skin and are administered directly to the affected area. Topical creams provide the primary benefit of being applied at home without the need for a doctor's visit. Furthermore, their cost is usually lower than that of oral drugs. Applying cream topically, however, has a number of disadvantages. They may not always be as effective as oral drugs, and their application can be messy and time-consuming.[102] In dermatology, topical steroids are the medication that is most frequently advised. Their immunosuppressive, anti-mitogenic, and anti-inflammatory properties make them prescribed for a number of disorders, such as eczema, psoriasis, atopic dermatitis, lichen simplex chronicus, and intertrigo. One to three times a day is the range of dosages. Topical steroids include betamethasone 0.05% (Betnovate-N®, chemical) and clobetasol 0.05% (Dermovate®, compound). Betamethasone and clobetasol are glucocorticoids that suppress NF-Kappa B, which stops neutrophils from dying and shrinking.[103]

CONCLUSION:

In conclusion, natural products have shown considerable promise in treating skin pigmentation disorders due to their natural, non-toxic properties and effective mechanisms. Their use is supported by various studies demonstrating their safety and efficacy through methods such as cytotoxicity tests, tyrosinase activity assays, and melanogenesis inhibition evaluations.

Innovative delivery systems like liposomes and nanoparticles further enhance their effectiveness by improving drug solubility and skin penetration.

Skin pigmentation disorders are influenced by factors such as UV radiation, hormonal changes, and cellular inflammation, leading to the overproduction of melanin and uneven skin coloration. Eumelanin and pheomelanin, the two primary types of skin pigments, play different roles in skin protection and temperature regulation.

Historically, skin pigmentation has been unjustly associated with racial classifications and discrimination, reflecting broader societal biases. Today, various treatment options, including topical agents like hydroquinone and oral medications like tranexamic acid, offer targeted solutions for hyperpigmentation. However, the misuse of potent corticosteroids remains a concern, potentially exacerbating the condition if not used properly.Overall, the exploration and application of natural products for pigmentation treatment hold significant potential, combining efficacy with safety, and advancing both therapeutic and economic benefits.

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