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Lovely Glowing Skin Fair Forever

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If one reads through the matrimonial columns in a newspaper, one would invariably find a majority of the advertisement, seeking brides of the following requirements. “Well settled boy, seeks very fair beautiful girl...”. Similarly brides too solicit their prince charming with the following lines, “Well placed, highly qualified match for a fair attractive girl...”. The one common requirement that remains very influential, subconsciously even in the 21st century individual’s mind is to look fair skinned. Is this desire for fair skin, primarily because of our traditional belief that a person possessing a fair skin denotes a lineage of nobility and aristocracy?

The requirement of becoming fair skinned is fulfilled by the cosmetic industry with a wide range of products specifically offering skin lightening properties. Fairness creams and lotions, in general, have had been a euphemism for sun block products for long. In reality, fairness creams should actually lighten darker skin and so should be named as whitening creams. Thus, one can say that these products should fulfil the primary purpose of making the user’s skin whiter, lighter and brighter. Surprisingly, of the total Indian skin cream/lotion market that is valued around Rs. 1,200 crore, the fairness cream market itself is about Rs. 800 crore.

SKIN COLOUR

Products generally developed for skin care as a part of a brand or range hold a very significant market share. Predictably the largest sales of these products come from India, Southeast Asia, and Africa. Products offered in this category mainly comprise of massage, cleansing and emollient creams, hydrating lotions, and soaps. Whiteners belonging to the normal skin care variety have to be used on a daily basis for light skin feel. They sometimes also have sunscreen benefits, in addition to whitening effect. Speciality type of whiteners not falling in the general category contains high concen-

trations of actives and is used with an aim to prevent or treat problem areas like melanoma and freckles.

The colour of a person basically depends on the race of origin, climatic environment and sex. No individual has the same colour throughout all parts of the body. Some parts of the body are lighter and some parts darker. Skin thickness, haemoglobin content in blood, availability of minor, but important pigments, in our skin are all responsible. Thus, colour of human skin depends on the chemical and physical properties of the skin structure. All humans have some melanin pigments in their skin. Persons not having them are known as “albinos”, and suffer from a condition called “albinism”.

SKIN STRUCTURE

Skin is composed of two main layers, the “Epidermis”, and the “Dermis”. The Epidermis is the most superficial layer, composed of stratified squamous epithelium. From the outside inward, the stratified epithelium is divided into five layers as described below.

“Stratum Corneum” is the most superficially placed cells without nuclei that are keratinised, with indistinct cell outlines. This layer is thickest at the soles and the palms and very thin at the lips. Hairs’ nails, etc., are outgrowths of this layer.

“Stratum Lucidum” is a thin, slightly transparent layer 3 to 5 cells deep and placed below the “Stratum Corneum” very similar to it with indistinct cell outline without nuclei.

“Stratum Granulosum” consisting of 3 to 5 layers of flattened polyhedral cells is followed by “Stratum Spinosum” that is also made up of polyhedral cells of variable thickness. The surface of these cells is covered with minute spines, that interdigitate with similar spines of adjacent cells. These cytoplasmic

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protrusions are also called as the "Prickle Cells". The branches of two cells do not have cytoplasmic continuity, but are attached to by well-developed cytoplasmic nodes or desmosomes. These cells are basophilic supported by a network of cytoplasmic fibrils. Star shaped branched cells capable of DNA synthesis, also called as "cells of Langerhans" are scattered irregularly throughout this skin layer.

"Stratum Germinativum" (Stratum Malpighii), composed of a single layer, of columnar epithelium, having transverse, thin, short, cytoplasmic process on its basal lamina, anchors the epithelium to the lower dermis. These cells with oblong nuclei, with cuboidal to columnar cell's structure are placed perpendicular to the basement membrane, and produce newer cells to replace those above by the process of "mitosis."

"Dermis" or the "true skin" consisting of connective tissue, lies below the epidermal layer which it supports and binds to the underlying tissues. Chiefly made up of collagen and elastic fibre, it provides tensile strength. Structurally the superficial part of the dermis is compact and forms the papillary layer resembling innumerable finger-like projections into the prickle cell layer of the epidermis. The inner part of the dermis is made up of loose connective tissue containing fat. This layer constitutes the reticular layer of the dermis merging into the subcutaneous layer of fat. Fibroblasts cells from which the fibrous tissue of the dermis develops melanophores containing melanin pigments and cell belonging to the reticulo-endothelial system protecting the body from invading bacteria is also present in the dermis.

Unlike the epidermis, the dermis has an well-organised lymphatic system and a luxuriant capillary blood vessel network supplying blood to the tip of the dermal papillae that play an important role in regulating temperature. Besides bundles of involuntary muscles and vasomotor nerves, dermis has sensory nerve endings of different types that keep an individual informed about the surroundings. Pear shaped sebaceous glands located in the dermis open into the root of the hair follicles and secretes an oily material called as sebum. In places that are in-

dependent of hairs (sebaceous glands are not present at the palms and soles), the duct of the sebaceous glands opens directly to the surface of the skin. Sweat glands are distributed throughout most of the skin.

There are about 3 million active sweat glands in the body. The lower ends of the sweat glands reach deep part of the dermis and act as islands for regrowth of epidermis in cases of injury and burns. Modified smooth muscle cells, known as the myoepithelial cells present at the base of the sweat glands surround their ducts in a manner that their contraction help in elimination of sweat.

PIGMENTS THAT IMPART SKIN COLOUR

Melanin is a yellow to black pigment found in the Stratum Malpighii of skin structure. The amount of Melanin that is produced by the melanocytes is largely responsible to give one their skin colour. "Stratum Germinativum" (Stratum Malpighii), is composed of a single layer of columnar epithelium, having transverse, thin, short, cytoplasmic process on its basal lamina. It anchors the epithelium to the lower dermis. These cells with oblong nuclei, with cuboidal to columnar cell's structure are placed perpendicular to the basement membrane, and produce newer cells to replace those above by the process of "mitosis."

At the junction of the epidermis and dermis are present "melanocytes" or "melanin" containing branched cells. "Malpighain cells" and the "melanin" present in the deeper cells of the "Stratum Germinativum" are produced by these melanocytes. Melanin contributes colour to the skin and moreover protects one from the ultra-violet rays of solar radiation. Cytochrome secretion converts the fully formed melanin granules from melanocytes to the Malpighain cells. The ration of melanocytes to basal epidermal cells varies between 1 to 4 to 1 to 10. Although melanosomes are uniformly elongated, in red haired persons they are spherical. It is formed on a specific cell particle, the melanosome within the melanocytes. The stability of melanosomes after their incorporation into the cytoplasm of Malpighian cells and their increase in numbers is the main cause of the differences observed in skin colour between whites and blacks.

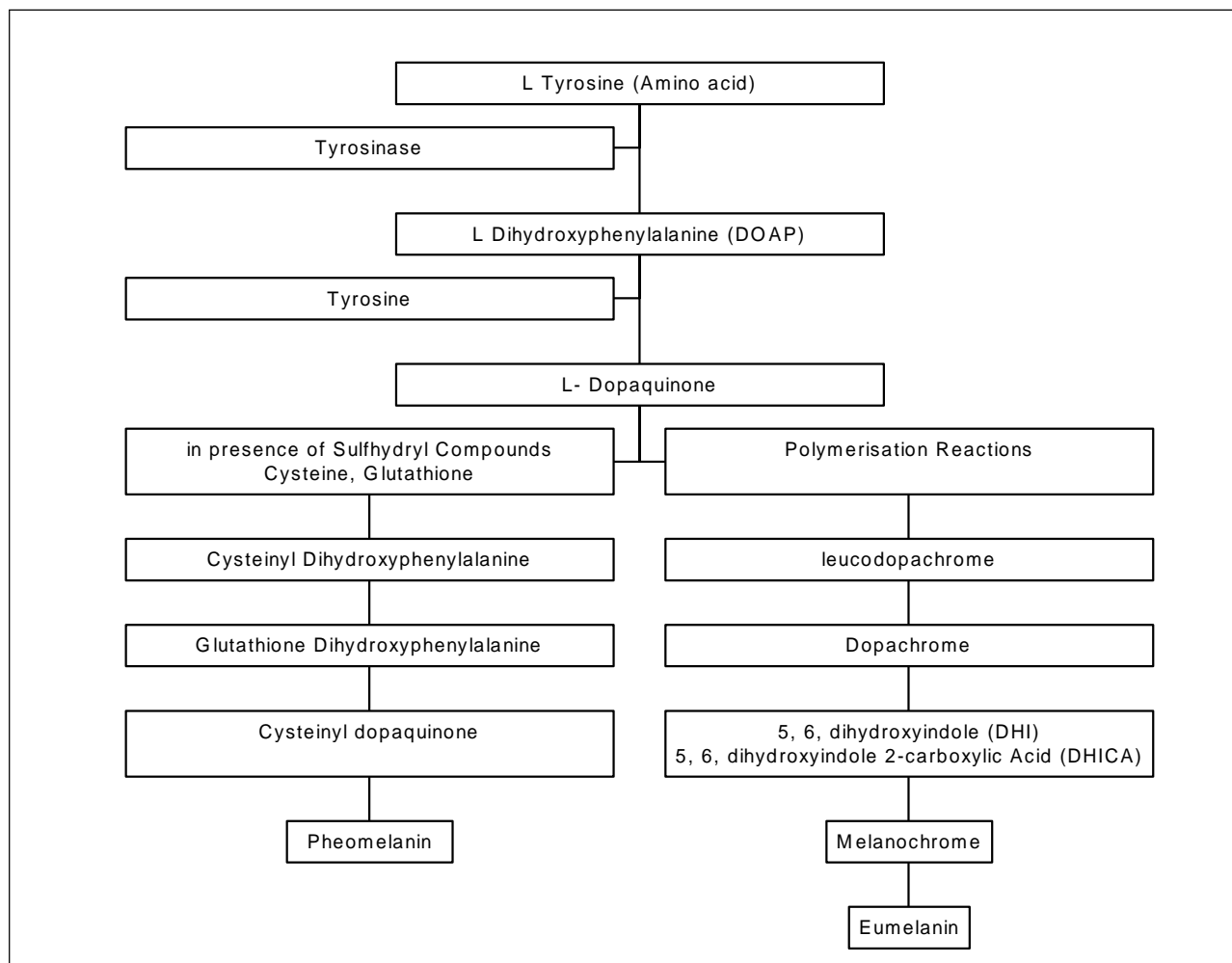
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Melanin supposedly gets degraded to melonoid that further gets diffused through the epidermis. Melanoid has a different absorption band of visible light. Carotene, a yellow-orange pigment, is present in lipid-rich areas like the stratum corneum and the fat of the corneum and subcutaneous tissue. Carotene is present in greater amounts in women than men and is responsible to the strong yellow colour component of skin.

Oxyhaemoglobin imparts a reddish hue to skin colour. It is present largely in areas where there is a rich supply of arterial blood. The main areas they are present are face, neck, palms, sole and nipples. Reduced haemoglobin imparts a bluish or purplish colour to skin. It is evident in the lower areas of the trunk. Concentration of melanin and skin thickness tends to suppress the haemoglobin pigment colour component effects.

The concentration of the various pigments and the pattern of distribution in the skin structure influence the colour of skin to a very large extent. However, skin thickness can also modify the skin colour considerably. Persons having a thin epidermis have a ruddier colour complexion and those having thicker epidermal skin look yellowed. This is due to the fact that a thicker epidermis is opaque than a thin epidermis. A thinner epidermis allows the colour of the blood pigments to express their colour characteristics unlike a thicker epidermal skin structure.

Human skin has light scattering qualities that vary with every individual and is a major factor modifying skin colour. A transparent "Stratum Corneum" scatters light slightly, and the deeper layer appears bluer because of the scattering light effect in the overlaying coarser tissue layer where the dark pig-



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ment granules are usually found. Greater the pigmentation of skin, greater the protection it renders to the underlying tissues against harmful solar radiation.

MELANIN METABOLISM

Although many biochemist researchers, have studied and intensively investigated the metabolism of melanin by the melanocytes, their mechanism is not yet completely understood. It is however partly established that two types of melanin are synthesised from the amino acid, tyrosine. The melanocytes synthesise melanin using tyrosine, to hydroxylate tyrosine into dihydroxy phenylalanine (DOPA). DOPA becomes the melanin polymer through a complex chain of oxidative reactions.

Tyrosine also helps in oxidising DOPA to Dopaquinone. Dopaquinone then splits to produce either Pheomelanin or Eumelanin. Some studies have also claimed that enzyme TRP-2 and Dihydroxyindole carboxylic acid (DHICA) also participate in the process through Dihydroxyindole carboxylic acid-oxidase. It can be safely concluded that tyrosinase, DCT and DHICA-oxidase all play important in the process. The entire process in the form of a flow chart is shown here.

As discussed earlier Melanin, pigment is responsible for skin colour. The colour of the skin will depend on the type of melanin — whether Pheomelanin or Eumelanin — and the quantity of melanin produced. Dark coloured people or Blacks have a large amount of Eumelanin pigmentation and light coloured Asians have less intense Eumelanin pigmentation. Blacks thus have maximum photo protection that varies largely among non blacks. Red haired or blondes have pheomelanin pigmentation that practically offers no photo protection. Genetic factors and external factors like hormonal secretion, ultraviolet light, food habits, etc., largely influence melanin biosynthesis. Although Tyrosinase is a key factor in melanin biosynthesis, other influencing factors include enzymes, dopachrome, tautomerase, oxidase, catalase, glutathione reductase, metallic ions like Cu^{+2} , Zn^{+2} , Iron, and hormone histamine are also equally responsible in determining skin colour.

BASIC REQUIREMENTS FOR SKIN LIGHTENING ACTIVE INGREDIENTS

The popularity of skin lightening product and its formulation development depends on the successful use of effective depigmenting ingredients. Any product or active ingredient that is capable to reduce melanin production in the melanocytes can function as a skin -lightening agent. Successful use of effective depigmenting ingredient is usually achieved by combining the various available ingredient actives to formulate a product giving optimum effect. The first and foremost step in screening a depigmenting ingredient is by estimating the inhibitory effect of the active on tyrosinase activity and for any effect on melanin synthesis in a melanocyte cell culture system. Actives found effective in vitro assay is tested in black mice and guinea pigs. In a clinical trial the depigmenting materials are applied to human skin and changes in skin colour monitored under ultraviolet radiation. Skin irritation allergenicity of actives both individually and in a cosmetic formulation are tested. All tests are analysed on the basis of relative efficacy testing so that inter-individual variations do not obscure real colour changes. Deep understanding and study of the various ingredient actives in the finished product formulation is required to confirm stability. Product safety on skin, optimal pH requirement, delivery system, skin penetration effect, compatibility, etc., are all without doubt very important.

ACTIVE INGREDIENTS IN SKIN LIGHTENING PRODUCTS

Skin lightening products prevalent in the first half of the twentieth century contained Mercury compounds, namely ammoniated mercuric chloride as depigmenting active. The use of mercuric compounds caused the top layer of skin to peel off on mechanical abrasion and thus exposing the lighter second layer of skin. Placental protein, hormones like estrogen, stimulating melanin elimination through the keratinocytes, followed mercury compounds as depigmenters. Use of mercury is now not permitted as its repeated use can lead to mercury poisoning. Placental protein, hormones, etc are also not popular now-a-days. Ascorbic acid derivatives, like ascorbyl palmitate, ascorbyl stearate, are

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also used in concentration ranges of 2 to 3% in skin lightening products as primary pigmenters. Ascorbic acid derivatives have incompatibility and stability problems. They are now being replaced in many formulations by magnesium ascorbyl phosphate that has comparatively better stability and compatibility.

Hydroquinone

Hydroquinone (1, 4, Benzenediol, p-dihydroxy benzene hydroquinol, $C_6H_6O_2$) has a crystalline structure with a melting point of 170 to 171°C. It is soluble in water, alcohol, ether and is a very popular chemical used as photographic reducer and developer. It is also a very good depigmenter when used at concentration levels of less than 2%. At higher concentrations, hydroquinone caused dermatitis and serious damage to human skin. Hydroquinone is relatively safe under normal condition of use and at low concentration levels without any serious hazard. Although at 2% concentration, hydroquinone is safe and effective only a partial change or about 50% lightening of dark skins is observed. The skin lightening effect is more pronounced on relatively lighter spots than on darker spots. The effect of a hydroquinone based cosmetic product largely depends on the product formulation and skin type of the user and seen only after about three weeks to three months regular usage.

The cytotoxic effect (i.e., the inhibition of melanin producing skin cells by injuring the melanin granules present in cells) on melanocytes of Hydroquinone is believed to be responsible in reducing skin darkening. Hydroquinone at higher concentrations of 2% is used in the treatment of melanoma and freckles and is considered as a pharmaceutical product to be used under strict medical supervision.

Kojic acid

Kojic acid; 5 Hydroxy-2-(hydroxymethyl)-4-pyrone; 2-hydroxymethyl-5-hydroxy-g-pyrone; 5-hydroxy-2-(hydroxymethyl)-4H-pyran-4-one, having a molecular formula $C_6H_6O_4$ is another popular antibiotic skin whitening substance produced in an aerobic process by a variety of micro-organisms, and isolated from *Aspergillus oryzae*.

Kojic acid has a prismatic needle like structure having a melting point of 153 to 154°C. It is freely soluble in water, alcohol, acetone, and sparingly soluble in ether and ethyl acetate. Kojic acid is converted to maltol and ethyl maltol that are used as flavour enhancing additive in food and pharmaceutical industry. Kojic acid and its palmitate and dipalmitate derivatives are used in various skin lightening cosmetic product formulations to inhibit the tyrosinase activity in the melanocytes and thereby reducing melanin formation. Copper ions are an essential metal of the active tyrosinase site of melanin synthesis.

Gluconic acid

Gluconic acid ($HOOC-CHO-CHOH-CHOH-CHOH-CH_2OH$) chelates copper thereby inhibiting oxidation reaction slowing down the enzyme activity. Gluconic acid along with other liposome actives like glucosamine and calcium-D-pantetheine-S-sulfonate effectively inhibit melanogenesis to prevent skin discoloration and improve skin complexion.

Others

Vitamin A stimulates the melanocyte activity. β Carotene that binds the cell receptors of Vitamin A and stops melanogenesis is also used as an active for skin lightening. Dithiooctanediol ($OH-CH_2-CH_2-S-CH_2-CH_2-S-CH_2-CH_2-OH$) is another molecule that inhibits the effect of tyrosinase glycosylation.

Researchers around the world have for several decades now have been looking for depigmenting materials in many natural herbs. Turmeric and sandal powder, gram flour and milk cream, tomato paste, butter milk, extracts of plants like watercress, honeysuckle, Iris, pimpernel, butterbur, sweet chestnut, silverweed, papaya, bamboo, mulberry, paper mulberry, mushroom, etc. have been used in traditional folk remedies to restore the natural skin fairness gradually reducing skin pigmentation.

Liquorice

Liquorice (*glycyrrhiza glabra*) extract obtained from the dried peeled or unpeeled root and stolon of a variety of species of *glycyrrhiza* is a drug having a sweet taste. *Glycyrrhiza glabra* is a tall

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erect perennial herb widely distributed over southern Europe. The unpeeled liquorice yields about 25% of water-soluble extract. The glycyrrhetic acid in liquorice extract is also believed to have skin smoothening and anti-irritant property and is normally used along with Kojic acid in skin whitening cosmetic formulations. In an unpeeled liquorice extract, glycyrrhizin is also largely found. It is slightly bitter in nature. However in a peeled liquorice extract this is absent, as it is not extracted being present in the outer peel tissue.

Liquorice contains approximately 7% of glycyrrhizin. It is a sweet white coloured crystalline powder consisting of calcium and potassium salts of glycyrrhizic acid. It has a melting point of 222 degree centigrade. Liquorice also contains glucose, sucrose, starch, other triterpenoid acids and numerous glycosides. Powdered liquorice is a brownish yellow powder with a faint characteristic odour and taste. Predominantly used in pharma preparations as a demulcent and a mild expectorant it is also a very good flavouring agent in compounded powder and liquid, and used largely in disguising the taste of bitter and nauseating medicines.

Paper Mulberry that contains an active ingredient called Kazionol F, [5 -(3-2,4, -dihydroxy phenyl) propyl] - 3,4, -bis (3 methyl - 2 butenyl) 1-2, benzenediol is found to be good depigmenting agent.

Bamboo Gradually lightens the skin. The phenolic compounds in Bamboo stem were reported to inhibit the melanin biosynthesis. They are also believed to have moisturizing properties.

Papaya extract gradually and gently lightens the skin, enhances cell regeneration has skin firming properties and vitamin A and vitamin C.

Concentrated purified extract of an ethnic African plant *Mitracarpa* (*Mitracarpus Scaber* extract) belonging to the genus *spermacoceae* is used in the treatment of dark spots and in skin fading. The active ingredient exhibits a strong tyrosinase activity to reduce pigmentary spots and cutaneous discoloration.

Japanese Mandarin (*Citrus Unshiu*) peel extract triturated to 0.3% in tyramine decreases melanin synthesis and acts on tyrosinase activity promoting skin lightening and reducing age spot pigmentation.

We all know very little about mushroom except being served as a delicacy in restaurants and buffet parties. Mushrooms are unique fungi belonging to the plant kingdom, even though they possess no chlorophyll. They cannot metabolise their own food, like normal plants, by the process of photosynthesis, but resort to symbiotic or parasitic relationship with other plants for survival. Some mushrooms derive nutrients growing freely in dead and decaying matter. Although mushrooms belong to the plant kingdom, unlike plants they consume Oxygen from the atmosphere and give out carbon dioxide, very similar to animal respiration.

Mushroom apart from their culinary attributes have also medicinal and cosmetic properties. Matsutake (*Tricholoma matsutake*) the Korean Pine mushroom, is popularly known as Song-Yi mushroom is traditionally used as a decoction, steeped overnight in water and used as a facial wash to remove summer sun tanned facial spots and for lightening of facial wrinkles. Matsutake mushroom that grows in a symbiotic relationship with pine trees is a very popular edible fungus in Korea, Japan and other East Asian states. It has a unique sweet pine like odour with earthy mushroom base notes. It is normally used as a natural flavouring and fragranting agent in certain festival delicacies.

Traditional and ethnic uses have led scientists to undertake investigations on the chemical constituents on Matsutake and finally develop extracts having functional properties. Chemically the mushroom extract contains α -pinene and β -pinene, cembrene, and S - Matsutake alcohol. It also contains amino acids, methyl cis methyl cinnamate that aid moisture retention, and 2- octen-1-ol that stimulates peripheral circulation. An ethanolic high steam distillation extraction of Matsutake mushroom produces a fraction rich in Songyic acid that is a unique skin whitener. Song-Yi mushroom liquid concentrate is said to possess better whitening power than Kojic acid and is non-irritating and stable in most skin

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whitening formulations. In case of Song-Yi mushroom extract, the skin whitening mechanism takes place on the skin surface without penetrating the deeper layers of skin.

Songyic acid is effective in lightening skin without actually inhibiting tyrosinase function or suppressing the melanogenesis by the total prevention of tyrosinase formation. The mechanism involves the formation of a leuco-melanin a reduced form of melanin on the skin surface cells, which becomes semi-permanent during the subsequent natural process of keratanisation of the epidermis.

In addition to giving skin a naturally lighter look unlike the bleached look obtained by use of Hydroquinone or Kojic acid, the presence of leuco-melanin is also said to give effective UV protection from sunlight. Song-Yi also provides a physical UV blocking effect preventing melanin re-oxidation and subsequent re-darkening of the skin that can occur in case of hydroquinone or kojic acid usage. Songyic acid is not easily absorbed through intact skin and claimed to show no signs of photosensitization or phototoxic properties.

DISADVANTAGES OF SKIN LIGHTENING

Most conventional skin whitening agents inhibit the formation of tyrosine in the melanogenesis stage of skin cell pigment formation. The chemical inhibitions of normal human biological processes in deeper skin layers may damage dermal physiology and elicits undesirable side effects such as denaturation of cells. This can lead to contact skin dermatitis; skin irritation and pigment disorders, which may later manifest as skin cancers and pigment cell death.

The loss of cell pigments opens up the possibility of UV A and UV B skin afflictions, that would normally be offered some amount of protection from melanin present on skin which in case of Hydroquinone or Kojic acid treatment is absent or its concentration substantially reduced. Some instances of skin melanoma have also been reported in sensitive skin whitened by use of Hydroquinone or Kojic acid. It is found that fair skinned people are more likely to develop malignant melanoma,

the most dangerous form of skin cancer. People with brown skin have a skin cancer rate of 0.8% whereas in case of white skinned people it is about 40%.

CONCLUSION

Skin lightening does not last forever. The lightened areas become darkened when exposed to light. That is the reason skin lightening and sunscreen agents are normally combined together in a product formulation to get optimum benefits of skin lightening and skin protection from sunlight.

Formulators are also combining various active ingredients capable of lightening skin in products and the synergistic effects investigated to take advantage. The search for new, safe, and effective actives both synthetic and from natural sources are being developed by various companies. Nevertheless in all these efforts product stability and its safety in use that is of paramount importance cannot be ignored.

Research and development on depigmentation and the inhibition of melanin biosynthesis have helped in the development of newer depigmenting materials. Hydrolyzable tannins from *Phyllanthus Embilica*, *Waltheria Indica* extracts and Ferulic acid, Exfocellia-Protease, Perflorocarbon, etc., are some ingredients where scientists are conducting researches. Well-known depigmenting materials are now-a-days also used as bases to synthesise better and more effective alternatives. The expanded knowledge of melanin biosynthesis and its mechanism gathered by researchers will continue to play a prominent role in product development, evaluation, stability, efficacy and safety during regular usage of skin lightening products.

Almost 89% of women consider skin complexion and fairness as an important need and concern. Indian woman is no different. She has also always felt a deep-seated psychological need to be fair and beautiful. As long as dark complexion is perceived a social disadvantage, skin lightening products promising long lasting lovely glowing fair skin will continue to charm them. Skin whitening creams that constitute more than two thirds of the skin cream market in India will only grow in times to come.