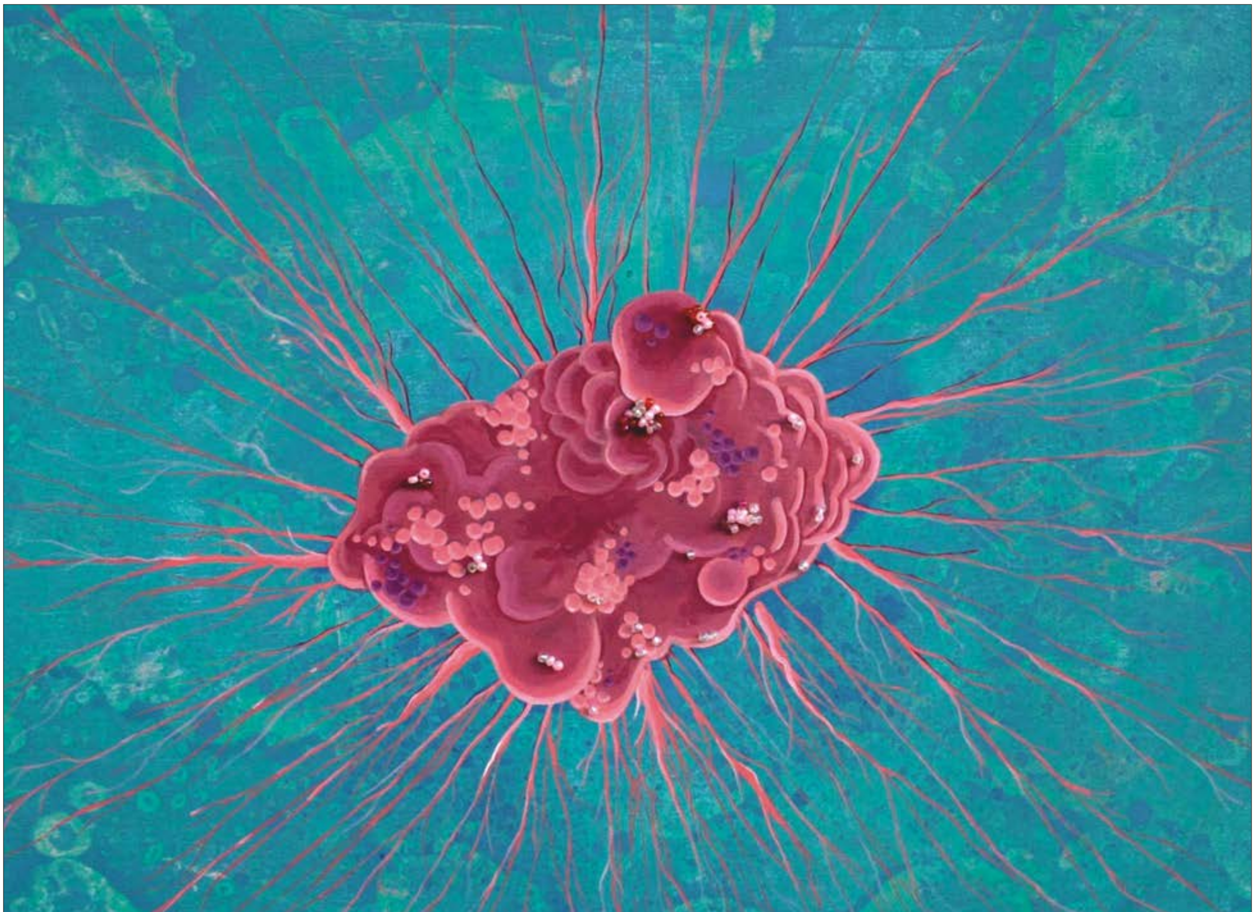

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Role of Highly Specific and Complex Molecules in Skin Care

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Abstract: Because of increased leisure time, the growing popularity of staying outdoors, it has become more and more imperative to study the molecular photobiological effects due to ultraviolet (UV) radiation on human skin. Information obtained from several studies is being used to constantly improve the quality of sunscreen preparations containing organic and inorganic filters. It also fostering the development of antioxidants and active agents that can be used in combination with or in addition to UV filters to provide better photoprotection for human skin. In this review, the examples are specified to illustrate the role and mechanism of highly specific and complex molecules obtained from natural sources; recognized as enzymes and examples are given to the development in skin care products: the use of topically applied DNA repair enzymes to prevent UVB radiation induced damage and the protective mechanism of superoxide dismutase and peroxidase to reduce UV-induced erythema, which can also be thought of as free radical scavenging ability.

Key words: Photolase, DNA repair enzyme, UV protection, superoxide dismutase, peroxidase

INTRODUCTION

Ultraviolet (UV) radiation is well known to exert a variety of deleterious effects on human skin. Chronic and possibly acute exposure to UV radiation increases the risk of skin cancer including basal cell and squamous cell carcinoma as well as malignant melanoma. Physicists classify ultraviolet light into three types, by its wavelengths: UVA, UVB and UVC. The dimensions of their wavelengths are roughly 400 to 320 nm for UVA, 320 to 290 nm for UVB and 290 to 200 nm for UVC. Although the UVC is less exposed to human, but direct exposure to UVC for a length of time may destroy the skin (Mahmoud, 2005). Fortunately UVC from sun is completely absorbed by gases in the atmosphere before it reaches the earth. The longer wavelengths of UVB and UVA causes skin aging, which is characterized by generalized wrinkling, dry and thin appearance and seborrheic keratosis. There are also many specific diseases like phototoxic or photoallergic reactions, autoimmune diseases including lupus erythematous, idiopathic photodermatosis and varieties of skin cancers which are triggered or exacerbated by UV radiation exposure (Berneburg *et al*., 1999). Excessive exposure of UV radiation especially in the western population, have resulted in an ever increasing demand to protect the human skin against cancers with these detrimental effects (Berneburg *et al*., 2000). In recent years highly advanced synthetic sunscreens have been developed which contains physical and chemical UV filters. These sunscreens have proven to be quite effective, in particular when used for the prevention of the erythema reaction to human skin (Kambayashi *et al*., 2005).

There is an ongoing debate whether UV filters also protect other harmful effects besides the sunburn reaction. The increasing evidences proved that sunscreen agents protects from sunburn but not other harmful effects (Glogau, 2000).

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There was regular use of sunscreen containing UV filter for protection, despite the fact that these were not perfect (Mahmoud, 2005). There are so many synthetic sunscreen agents (Octabenzone, Octyl methoxycinnamate, Benzophenone-3, Provatene, 2-Ethoxy Ethyl P-Methoxycinnamate, Sulisobenzone, Mexenone, Avobenzone, Dioxybenzone, 4-Dimethyl Amino Benzoic acid etc.) are available in form of photoprotectives with certain limitation, which restrict their use at cellular level.

These developments have been made possibly by recent photobiological and photodermatological research, which has greatly helped to biological effects on human skin. The active synthetic molecules are being used since years, but the research shows that these active molecules are adversely affects on human skin via self inducing reactive oxygen species. Thus, to overcome such serious side effects of synthetic molecules, the research is now diverted towards natural biomaterials (Ashawat *et al*., 2005). Naturally occurring antioxidants like alpha carotene, ascorbic acids, flavones, flavanone, have ability to donate electrons and stops free radical chain reactions and also showed broad spectrum UV absorption (Bajpai *et al*., 2005; Ashawat *et al*., 2006).

The herbs as biological additives in form of extracts are utilizing since long period of time in the cosmetic formulation and now scientific evidences proven that many plant extracts showed their photo protective activity with significant improvement in enzymes like superoxidedismutase, catalase and total protein and ascorbic acid level (Ashawat *et al*., 2007a). Extracts of many plants, citrus fruits and leafy vegetables as source of ascorbic acid, vitamin E and phenolics compounds and enzymes possess the ability to reduce the oxidative damage. These oxidative damages ultimately reduce the protective enzyme level and imbalances the level of total protein and ascorbic acid and other antioxidants level in cells. The creams comprises such extracts could be utilized for the protection of photo induced intrinsic oxidative stress as well as structural alteration in skin (Ashawat *et al*., 2007b).

In the series of natural photoprotective agents, enzymes like sodium dismutase (SOD), peroxidase and proteolytic enzymes have opened up new avenues to photoprotective reaction occurring within the cell.

These chemical entities were first discovered in 19th century, where as use of enzymes in cosmetics has been advocated for many years (Cleaver, 1968). Proteolytic enzymes like bromelaine, papain etc. has been used for skin peeling and smoothing (Yarosh *et al*., 2001). In the present review condensed studies regarding topically applied DNA repair enzymes are discussed with reference to UVB radiation-induced skin damage and the protective mechanism of superoxide dismutase and peroxidase, which were extracted from yeast. These are utilized as efficient tool to reduce UV-induced erythema, which can also be thought of as free radical scavenging ability (Lods *et al*., 2000).

UVB Photoprotection with Topically Delivery of DNA Repair Enzymes

The compel of photoproducts within the DNA of upper protective layer (epidermal cells) of skin is deleterious to human health. Among the DNA lesions induced by UVB radiation, cyclobutane pyrimidine dimmers predominate, dimer formation, which is thought to be crucial for the initiation of skin cancer, because it was found to be closely linked to the generation of mutations in tumor suppressor genes expressed in UV induced skin cancer (Fig. 1). There is also growing evidence that dimmers contribute to photocarcinogenesis by the suppression of the skins immune system, allowing transformed cells to grow unimpeded. Strategies directed at the removal of dimmers from UVB-irradiated human skin are thus of paramount concern for photo protection (Cleaver, 1968; Ames *et al*., 1995).

Research community find out the solution of such photo induced dimmer formation by using DNA repair enzyme photolase, which used specifically for the conversion of cyclobutane dimmers into their original DNA structure after exposure to photo reactivating light. The dimer specific to photolase is absent in human skin but can be obtained in active nature from numerous prokaryotes and certain eukaryotes animals including fish and marsupials. Photolase was incorporated into liposomes which were formed from the lipids egg phosphotidylcholine, oleic acid and membrane stabilizer cholesterol. These photolase containing liposomes were found to be reduced 40-45% of photo induced dimmers formation. The ability of topically applied DNA repair enzymes also lowers the rate of new skin cancers in patients with xerodermapigmentosum.

UV Induced Erythema Protection by Superoxide Dismutase and Peroxidase

The cells act as multitude of protective mechanisms to defend themselves against oxidative stress during the ageing process. All the cellular components are susceptible to damage by free radicals, which diminish their stress and efficient functioning. One of the most widely studied protective system is that of the free radical scavenging enzymes-super oxide dismutase (SOD) and perxidase e.g. catalase, glutathione peroxidase, lectoperoxidase etc. These enzymes have ability to reduce UV-induced erythema, when applied to the skin surface (Declercq *et al*., 2004; Belaiche, 1985).

Superoxidedismutase (SOD) is the most ubiquitous protective enzyme, first discovered as blue green protein, in 1938 (Fig. 2). However, its function as an enzyme, it is able to remove catalytically the superoxide radical specially copper-zinc containing SODs. They are found in all eukarytic cell such as yeast, plants and animals. All the copper-zinc SODs from eukaryotic cells contain two protein sub-units and have molecular weights of around 32,000, each subunit is composed primarily of eight anti parallel strands of β-pleated sheet structure that forms a flattened surface.

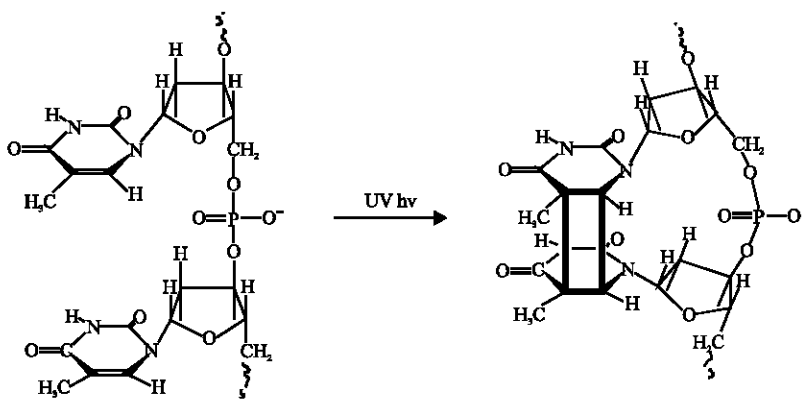

Fig. 1: Photocatalytic thymine-thymine dimerization in DNA

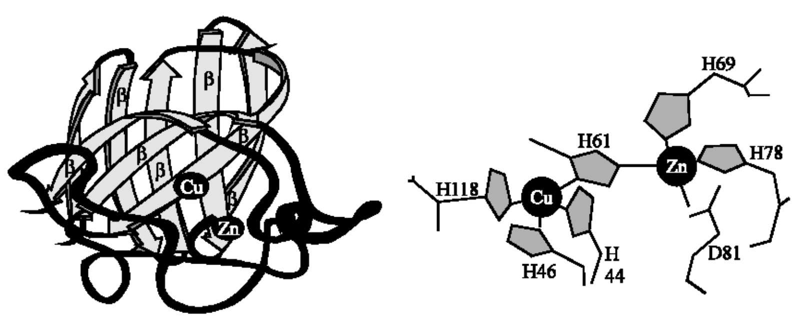

Fig. 2: Structure of copper-zinc SODs

The protein bonded SOD has excellent efficiency and stability at 45°C in aqueous solution, when compared to pure forms of SOD, which showed very poor stability. Extensive safety testing on yeast copper-zinc SOD indicated that it is non-irritating and non-sensitizing in both the powdered form and as a 1% active yeast copper-zinc SOD liposome. There have been reports of irritation using the pure form of SOD. It is believed that the yeast matrix proteins help to stabilize the enzymes under typical cosmetic use conditions and play a critical protective role in reducing irritation. Copper-zinc SOD (Fig. 2) in a liposomal form has excellent *in vitro* antioxidant activity than other popular cosmetic antioxidants, such as tocopherol and the polyphenols from green tea (Bassett *et al*., 1990).

Peroxidase

Hydrogen peroxide is formed in many aerobic cells as a result of the dismutation of free radical oxygen. In addition, there also several enzymes that produce hydrogen peroxide directly (e.g., Glycollate oxidase, D amino acid oxidase, etc.). Hydrogen peroxide is a weak oxidizing agent and can inhibit glycolysis. It can cross cell membranes and ones inside the cell it can react with ferrous ions to form the highly dangerous hydroxyl radical, which is probably the origin of many of the toxic effects attributed to it. The enzyme peroxidase and catalyses are very helpful to remove hydrogen peroxide from the cell and may prevent early aging of the skin cell also. The nonspecific peroxidase from horse radish plant (Amoracia) and fennel are used as excellent cosmetic material as skin protective against the ravages of the environment.

CONCLUSIONS

These days a lot of research is being conducted to analyze the use of natural biomaterials in cosmetic photoprotective formulations specifically for photo induced skin carcinomas. In this review, as far as research is concerned, the isolated or extracted active component could be utilize for the purpose of cosmetic values, but this is time to reach or deliver the active component at the specific site of the deformities in the body. It can be conclude that traditional and herbal crude extractives may not be acting like magic bullets, but these do produce beneficial affects with no or lesser undesirable side effects.

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