EXTENDED ABSTRACT

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Phyto-formulations for matrix metalloproteinases (mmps): novel targets in uv radiation induced skin carcinoma

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Abstract:

The continuous skin exposure to ultraviolet radiation creates reactive oxygen species leading to photoaging that causes dermal collagen deterioration and elastic fibre degeneration. Such fibers give the skin mechanical energy. In order to maintain the appearance of the skin, a complete understanding of the mechanism behind skin cellular degradation is desired, so that a better cosmetic formulation can be formulated. The studies have been shown that macrophages are crucially involved in skin Carcinoma and express significantly higher levels of M1 (CD40, CD127) and M2 (arginase I) markers as well as higher levels of MMP-9, a pivotal enzyme in cancerous matrix remodeling and cancerous invasion, than macrophages from the basal cell carcinomas. These macrophages represent different receptors like folic acid receptors which was exploited to know the extent of efficacy for delivery of phyto-formulations containing nanoparticles, transferosomes, liposomes etc. to cure carcinoma. The flavanoidal rich natural bioactives have been extensively integrated into a suitable base and have proved their ability as topical photoprotectants but their operation has remained constrained due to low solubility profile. Now researchers are working to develop the Novel Targeted formulations to distribute these natural flavanoidal drugs to enhance their potency and eventually skin properties. In current years, the focus area of work is on some traditionally used bioactive moieties as natural matrix metalloproteinases inhibitors (MMPIs) and emphasized on more extensive and specific studies, so that a good combination of natural as well as synthetic MMPIs with the conventional drugs can be used for treating UV radiations induced ailments.

A standard MMP consists of a propeptide of approximately 80 amino acids, a catalytic metalloproteinase domain of approximately 170 amino acids, a variable-length linker peptide (also known as the 'hinge region'), and a hemopexin (Hpx) domain of about 200 amino acids. Exceptions to this are MMP-7 (matrilysin 1), MMP-26 (matrilysin 2) and MMP-23; they lack the linker peptide and the Hpx domain, and after the metalloproteinase domain MMP-23 has a special cysteine-rich domain and an immunoglobulin-like one. In the metalloproteinase domain, two gelatinases, gelatinase A (MMP-2) and gelatinase B (MMP-9), have three repeats of a type II fibronectin motif. Matrix metalloproteinases (MMPs) is a class of extracellular proteinases characterized by two preserved patterns. One motif is a prodomain containing cysteine, which partially acts to inhibit catalytic activity. The other conserved motif is a catalytic domain rich in histine, responsible for endopeptidase action. Many MMPs have other domains, which are assumed to function in the recognition of substrates. In the lung, MMPs are produced essentially by all types of cells, including epithelial, interstitial, vascular and inflammatory cells; however, the pattern and rates of MMPs expressed differ across cell types and circumstances. Matrix metalloproteinases is a family of zinc-dependent endopeptidases which degrade different extracellular matrix (ECM) proteins. MMPs usually have a propeptide set, a catalytic metalloproteinase domain with catalytic zinc, a hinge region or peptide linker, and a domain of hemopexin. MMPs are generally categorized into collagenases, gelatinases, stromelysins, matrilysins, membrane-type (MT)-MMPs, and other MMPs based on their substrates and arrangement of their structural domains. Multiple cells like fibroblast, vascular smooth muscle (VSM), and leukocytes secrete MMPs. While long thought to be responsible for the extracellular matrix 's turnover and degradation, degradation of matrix per se is neither the primary nor the prevailing feature of these proteinases. Recent studies suggest that MMPs function on a number of extracellular proteins, such as cytokines , chemokines, antimicrobial peptides, and other proteins, controlling varying inflammation and immunity aspects. UV-radiation is part of the sun's available energy. Hidden radiation has shorter wavelengths than natural light in the electromagnetic spectrum and your eyes don't detect It but your skin don sense it. Even the tanning beds emit UV radiation. Two types of UV light have been found to lead to skin cancer risk: Ultraviolet A (UVA) has a longer wavelength, which is associated with skin ageing. Ultraviolet B (UVB) has a shorter duration, consistent with burning of the skin. While UVA and UVB rays have variations in how they affect the skin, both do damage. Unprotected UVA and UVB penetration affects the DNA in skin cells , causing genetic abnormalities or mutations that can lead to skin cancer (as well as premature aging) as well as causing eye damage, including cataracts and eyelid cancers. Non-melanoma skin cancers are most often found on areas of the body that are typically exposed to the light, such as head, nose, neck and forearms. This means that long-term, prolonged exposure to UV radiation is a significant causal factor. There is a strong association among certain countries between increasing occurrence of non-melanoma skin cancers and decreased latitude, i.e. higher rates of UV radiation. Face tumors that are not melanoma include basal cell carcinomas and squamous cell carcinomas. Which are never fatal but are debilitating and sometimes disfiguring surgical procedures. It is difficult to establish the temporal changes in the occurrence of non-melanoma skin cancers as accurate monitoring of these cancers has not been accomplished. Though much less common than non-melanoma skin cancers, malignant melanoma is the main cause of death from skin cancer and is more likely to be identified and treated correctly than non-melanoma skin cancers. The occurrence of malignant melanoma has grown dramatically since the early 1970s. A significant number of studies demonstrate that the risk of malignant melanoma is associated with genetic and personal characteristics, and the history of UV exposure of a individual. The role of accumulated sun exposure in malignant melanoma growth is an equivocal one. However, in individuals with a history of non-melanoma skin cancers and of solar keratoses, both markers of combined UV toxicity, the risk of malignant melanoma is greater. When ozone levels are reduced, the atmosphere is gradually losing its antioxidant filter function, as more solar UV radiation enters the

surface of the Earth. A 10 per cent drop in ozone levels is expected to result in an further 300,000 cases of non-melanoma and 4,500 cases of skin cancer melanoma. Because of their apparent lack of skin pigmentation, Caucasian people typically have a significantly greater chance of contracting non-melanoma or melanoma skin cancers than those of dark-skin.

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