SCOPE OF THE STUDY

Ultraviolet radiation (UV), particularly ultraviolet B (UVB) with a wavelength range (290–320 nm), represents one of the more important environmental factors affecting human health. UVB-radiation is regarded as the “burning ray” and it makes up 4–5% of UV light, it is a minor but the most active constituent of solar light. The toxic effects of UVB from natural sunlight and therapeutic artificial lamps are a major concern for human health. An additional potential factor is thinning of the ozone layer which results in increased UVB-exposure. UVB is 1,000 times more capable of causing sunburn than UVA; it also causes more genotoxic than UVA.

Normal skin invariably suffers from the cytotoxic effects of UVB-radiation; it produces both direct and indirect effects on the skin and subcutaneous tissues. Many in vitro and in vivo studies on skin cells demonstrated that UVB-radiation can damage many molecules and structures; this may result in changes of cellular functions. In recent years, accumulated evidence has demonstrated that UV-induced oxidative damage occurs through the formation of reactive oxygen species (ROS) and the induction of pyrimidine dimers and other photoproducts such as carbonyl derivatives. UVB-radiation induced skin lesions involve immediate free radicals production and altered antioxidant defensive system.

Further, UVB-induced macromolecular changes lead to the induction of specific signal transduction pathways like inflammatory, immunosuppressive and apoptotic processes in the skin. Chronic UVB-irradiation increases the skin tumor incidence, angiogenic and photoageing signaling. Hence, UVB-radiation has been considered as a prominent environmental carcinogenic agent. The past decade has seen a surge in the incidence of skin cancer due to changes in lifestyle patterns that have led to a significant increase in the amount of UVB radiation that people receive. Reducing excessive exposure to
UVB-radiation is desirable; nevertheless this approach is not easy to implement. Therefore, there is an urgent need to develop novel strategies to reduce the adverse biological effects of UV-radiation on the skin. A wide variety of natural agents have been reported to possess substantial skin photoprotective effects. In recent years, a considerable attention has been focussed on the exploration of botanical agents to prevent skin damage resulting from solar UVB-irradiation. Many photochemoprotective agents have recently been identified from botanical origins and hold promissory value to combat UVB-radiation exposure. The most potential chemical substances are members of the polyphenol family. Polyphenols are a large class of chemical compounds present in the human diet and have possessed antioxidant properties. Many such agents are also present in various skin care products and thus offering photoprotection.

Ferulic acid (3-methoxy-4-hydroxycinnamic acid) is a dietary phytochemical that occurs primarily in the seeds and leaves of most plants such as rice, wheat, barley, oat, roasted coffee, tomatoes, and citrus fruits. FA is an effective component of Chinese medicine herbs and has been approved in certain countries as a food additive to prevent lipid peroxidation. Moreover FA is well-known antioxidant agent used to prevent cell damage caused by ultraviolet light. FA has been used as an ingredient in cosmetics, such as skin lighteners, sunscreens, antiageing creams and moisturizers. FA was described as a specific inhibitor of the antiapoptotic proteins Bcl-XL and Bcl-2, thereby inducing apoptosis. These findings suggest that FA might have potential as preventive agent against UVB-induced carcinogenesis. In this study, we investigated the photochemopreventive efficacy of FA based on changes in oxidant-antioxidant status, inflammation, apoptosis and angiogenesis in UVB-exposed HDFa and Swiss albino mice.
2.1. SPECIFIC OBJECTIVES OF THE PRESENT STUDY

Intervention of UVB-induced ROS generation, DNA damage and modulation of subsequent apoptotic, inflammatory, immunosuppressive and photoageing signaling seems to be more appropriate and practical. The objective of the present study is to evaluate the preventive effect of ferulic acid on ultraviolet-B radiation induced cellular and molecular changes in human dermal fibroblasts and in Swiss albino mice.

2.2. Effect of FA on UVB-induced cellular changes in HDFa

1. To evaluate the sun protective value of FA.

2. To study the effect of FA on UVB-induced cytotoxicity in HDFa (MTT assay).

3. To study the effect of FA on UVB-induced ROS generation in HDFa.

4. To study the effect of FA on UVB-induced lipid peroxidation in HDFa.

5. To study the effect of FA on antioxidant status in UVB-irradiated HDFa.

6. To study the effect of FA on UVB-induced DNA-damage in HDFa.

7. To study the effect of FA on UVB-induced mutagenesis in Ames tester strains.

8. To study the effect of FA on inflammatory markers (COX-2 and TNF-α) expression in UVB-irradiated HDFa.

9. To study the binding interaction of FA on COX-2 and PPARα/γ proteins using molecular docking.

10. To study the effect of FA on DNA repair enzymes (XRCC-1, GADD45a, ATM and hOGG1) and peroxisome proliferator activated receptor (PPARα/γ) expression by qRT-PCR in UVB-irradiated HDFa.
11. To study the effect of FA on UVB-induced alteration of mitochondrial membrane potential in HDFa.

2.3. Preventive effect of FA on UVB-radiation induced carcinogenesis in Swiss albino mice

12. To study the effect of FA on UVB-induced photocarcinogenesis i.e. tumor volume and tumor size in Swiss albino mice.

13. To study the effect of FA on histopathological changes in the skin of UVB-irradiated Swiss albino mice.

14. To study the effect of FA on lipid peroxidation status in the UVB-induced tumor bearing mice skin.

15. To study the effect of FA on antioxidant status in the UVB-induced tumor bearing mice skin.

16. To study the effect of FA on inflammatory cytokines (TNF-α and IL-6) expression in the skin of tumor bearing mice.

17. To study the effect of FA on the cell proliferation markers (VEGF and iNOS) in the skin of UVB-induced tumor bearing mice.

18. To study the effect of FA on pro-apoptotic (p53 and Bax) and antiapoptotic (Bcl-2) protein expression in the skin of UVB-induced tumor bearing mice.