SUMMARY AND CONCLUSION

Solar ultraviolet-B (UVB) radiation has been implicated as a primary cause of skin cancer by multiple numbers of intracellular signalling. Recently, increasing attempt has been made to reduce the risk factors for skin cancers, including the damages from repeated exposure to solar UV-radiation, in particular from its UVB component. In this study, we investigated photoprotective potential of linalool against UVB-induced inflammation and carcinogenesis in experimental models. The summary of the present findings are given below.

- **Sun protection factor of linalool:** In this study, linalool showed SPF value of 9.12. Further, linalool exhibits a maximum UV absorbance at 269 nm and 360 nm near the range of UVB (290-320 nm) and UVA (320-400).

- **Effect of linalool against UVB-exposed cytotoxicity in HDFa:** UVB-exposure produced a significant decrease in cell viability. We observed linalool prevented UVB-induced cytotoxicity in a concentration dependant manner.

- **Linalool inhibits the ROS generation in UVB-treated HDFa:** The intracellular ROS was significantly higher in UVB-irradiated HDFa cells. Linalool pretreatment significantly prevented UVB-induced ROS generation in HDFa cells.

- **Effect of linalool on UVB-induced lipid peroxidation in HDFa:** In this study, pretreatment of linalool showed progressively decreased levels of TBARS when compared with UVB-irradiated HDFa cells.

- **Effect of linalool and/or UVB-exposure on antioxidant status in HDFa:** Activities of SOD, CAT, GPx and GSH were significantly restored by linalool (30 µM) in single UVB-irradiated HDFa cells.
Summary and conclusion

- **Linalool on UVB-induced CPD by T4endoV modified comet assay:** Fluorescence microphotographs show distinct comet tail in UVB-irradiated HDFa. Linalool prevented UVB-induced comet formation in a concentration dependant manner.

- **Linalool and/or UVB on mitochondrial membrane potential:** UVB-irradiation significantly altered mitochondrial polarization. Pretreatment with linalool (30 µM) significantly prevented the loss of UVB-mediated mitochondrial membrane potential.

- **Effect of linalool on UVB-induced apoptotic morphological changes:** UVB-irradiated HDFa cells showed condensed nuclei and apoptotic bodies (EtBr stained cells). Linalool pretreatment prevented the UVB-induced apoptosis in a concentration dependant manner.

- **Effect of linalool on UVB-mediated inflammatory markers expression:** UVB-irradiation caused overexpression of NF-κB, TNF-α, IL-6, IL-10 and COX-2. Linalool (30 µM) treatment modulated NF-κB, TNF-α, IL-6, IL-10 and COX-2 expression in HDFa cells.

- **Effect of linalool on UVB-induced apoptotic expression patterns in HDFa cells:** We observed increased expressions Bax and p53 and down regulation of Bcl-2 expression in the single UVB-exposed HDFa. Conversely, linalool pretreatment significantly modulates Bcl-2 expression and prevents Bax and p53 overexpression in UVB-irradiated HDFa.

- **Linalool on UVB-induced matrix metalloproteinase expression:** UVB-radiation caused increased expression of MMP-2 and MMP-9 in HDFa cells. Conversely, pretreatment with linalool prevented MMP-2 and MMP-9 expressions in HDFa cells.
Summary and conclusion

- **Linalool on short-term UVB-induced skin edema**: The exposure of the mice to UVB (180 mJ/cm²) for 10 consecutive days resulted in a significant increase in bifold skin thickness, ear thickness and ear punch weight. Pretreatment with linalool resulted in a significant inhibition of bifold skin thickness, ear thickness and ear punch weight compared to UVB-irradiated mice skin.

- **Linalool on UVB-induced histological changes in mouse skin**: Histopathological observation showed that UVB (180 mJ/cm²) exposure of the mice for 10 consecutive days resulted in increased epidermal thickness, hyperplasia, acanthosis and epidermal damage. Pretreatment of linalool 1 hour before UVB-exposure significantly reduced epidermal thickness, hyperplasia, acanthosis and epidermal damage in the mice skin.

- **Linalool prevents UVB-induced lipid peroxidation and oxidative damage**: Levels of TBARS and CD were increased significantly in UVB-irradiated mice skin. Linalool prevented UVB-induced TBARS and CD in the mice skin. Further, UVB-irradiation caused antioxidants depletion in the mice skin. Pretreatment with linalool significantly increased activities of SOD, CAT, GPX and GSH in mice skin.

- **Linalool inhibits UVB-mediated cytokines activation**: Expression of COX-2 and ODC were significantly increased in UVB-irradiated mice skin. Linalool treatment before each UVB-exposure significantly prevented COX-2 and ODC expression in mice skin.

- **Linalool inhibits UVB-induced skin carcinogenesis**: Chronic UVB-irradiated mice developed skin tumor. Linalool topical and intraperitoneal administration before each UVB-exposure prevented tumor formation in the mice skin.
Summary and conclusion

- **Linalool attenuates SCC features in the mice skin:** Chronic UVB-irradiated mice developed SCC, keratinous pearls, hyperplasia and dysplastic features in the skin dermis. Conversely, pretreatment of linalool 1 h before UVB-exposure inhibits the formation SCC features in the mice skin.

- **Linalool prevents UVB-carcinogenesis through apoptosis induction:** Chronic UVB-exposure downregulates the expression of proapoptotic proteins such as Bax, Caspase-9 and Caspase-3 in mice skin. Furthermore, mutated p53 and Bcl-2 expression was found to be increased in chronic UVB-irradiated mice when compared to control. Conversely, pretreatment with linalool modulates the expression of mutated p53, Bcl-2 and upregulates Bax, Caspase-9 and Caspase-3 in mice skin.

- **Linalool on long-term UVB-induced VEGF and TGF-β1 expressions:** Chronic UVB-exposure induces overexpression of VEGF and TGF-β1 in the mice skin. Linalool treatment prior to each UVB-exposure modulates the expression of VEGF and TGF-β1 in mice skin.

**Conclusion**

In the present work, we found that linalool prevents single UVB-radiation induced oxidatative damage, antioxidants depletion, inflammatory, photoaging and apoptosis in HDFa cells. We found that linalool prevents short-term UVB-exposure (7 consecutive days) mediated skin edema, ear thickness, inflammatory and cytokines expression in the skin of Swiss albino mice. Linalool modulates chronic UVB-induced skin carcinogenesis through attenuating tumor growth, oxidative imbalance, inflammatory reactions, cell proliferation, angiogenesis and apoptosis. This indicates that linalool not only acts as sunscreen and also works at the molecular level to inhibit UVB-induced inflammation and carcinogenesis. The use of linalool in skin care lotions may be an effective approach to prevent UVB-mediated carcinogenesis.