Photopreventive effect and mechanism of azd4547 and Curcumin C3 Complex® on UVB-induced epidermal hyperplasia.

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As indicated by the American Cancer Society, skin cancer is the most common of all type of cancers in the USA due to increased exposure to UV light due to ozone layer depletion. Higher risk prone individuals are those with fair complexion and sun-damaged skin. Squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) together account for non-melanoma skin cancer (NMSC). The SCC is clinically very aggressive and undergoes metastasis, which may result in spreading of cancer around the body. Therefore a “photo-preventive” agent is needed to prevent damage caused due to exposure to UV radiation.

In a previously published study Curcumin C3 Complex® has already shown positive effect in inhibiting UVB-induced tumor indices and multiplicity. In current study, it has been suggested that this effect of Curcumin C3 Complex® is via the FGFR/mTOR mechanism.

Objective:

To investigate the efficacy of Curcumin C3 Complex® for protection against acute UVB induced hyper proliferation by FGFR/mTOR signaling pathway.

Study Design:

JB6 P+ cells were exposed to UV light (290-320 nm) and lysed at given point of time for experimental analysis

Female SKH-1 mice were pretreated with Curcumin C3 Complex® (15 mg/kg) or vehicle (Corn oil) 5 days a week for two weeks on dorsal surface, after two weeks of acclimatization

After two weeks of administration of intervention, mice were exposed to single dose of UVB (180 mj/cm^2) radiation. After 24 hours of exposure, mice were sacrificed, blood samples were collected and plasma was isolated by centrifugation for ELISA test

In control group, mice were pretreated with AZD4547 (5mg/kg) for two weeks and similarly exposed and processed as intervention group

Squamous cell carcinoma cells and adjacent normal cells were derived from 21 patients diagnosed NMSC, whose sections were immunostained for FGFR2 (a fibroblast growth factor indicative of cancer) and quantified. The scores were given as: No stain =0, weak or focal staining record= 1+, moderate staining=2+ and strong staining=3+

Results and Discussion:

Curcumin C3 Complex® was found to inhibit FGF-2-induced JB6 cell proliferation and mTOR1, mTOR2 activation

Curcumin C3 Complex® also inhibited UVB-induced epidermal hyper proliferation and hyperplasia in mouse model and it was attenuated by FGFR inhibition

In case of normal skin samples, the staining was weak. Tumor sections showed higher staining intensity pattern. Eight patients showed 30% of tumor and 13 patients showed 50% of tumor tissue immunostained for FGFR2

The data of the current study suggested that pretreatment with Curcumin C3 Complex® was able to inhibit the phosphorylation of FGFR2 caused by UVB exposure

As per the authors, this study found evidence of interaction between FGFR and mTOR signaling

Conclusion:

Curcumin C3 Complex® inhibited both mTOR and FGFR2 signaling, which can be considered as a new therapeutic strategy for advanced cancer with dual pathway dysregulations.