Topical curcumin-based cream is equivalent to dietary curcumin in a skin cancer model.

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According to the American Cancer Society, 1–1.3 million cases of nonmelanoma skin cancer (NMSC) are detected annually. Around 20% of all skin cancers is cutaneous skin cell carcinoma (SCC) and 75% of all deaths attributed to skin cancers. Frequency of metastasis is as high as 12.5% for SCC, unlike the more prevalent basal cell carcinoma (BCC), which is non-aggressive.

It is well known that early cancer detection offers the best window of opportunity for treatment because early stage skin cancer has a high cure rate, whereas advanced stage cutaneous SCC often develops resistance to chemotherapy. Hence, focus on developing novel chemopreventive agents is necessary to delay or prevent cutaneous SCC formation. One such agent is Curcumin, which has in the recent past been examined for its effect in inhibiting skin carcinogenesis.

Objective:

To determine if topical Curcumin was as efficacious as oral Curcumin in a SCC skin xenograft model, to elucidate the pathways down-regulated by Curcumin as potential biomarkers for future chemopreventive studies and observe the potentially additive effects of topical application and oral dosing.

Study Design:

In vitro cell proliferation assay was performed on SRB12-p9 SCC cell line

Severe combined immunodeficiency (SCID) mice (6 to 8-week-old) pretreated prior to xenograft injection with either corn oil (control), 15 mg Curcumin by oral gavage, 15 mg Curcumin topical paste or combined 15 mg oral gavage and 15 mg Curcumin topical paste once daily for 3 days

Treatment was further continued through day 29 and parameters like body weight and tumor volume measurement was done daily

On day 29, tumors were harvested after the mice were anesthetized

Expression of human and murine IL 6 was evaluated in pooled serum from mice (n=3/group) by ELISA kit

Immunohistochemical analysis of molecular markers in skin squamous cell carcinoma was carried out

Soluble proteins extracted from SRB12-p9 cell lysates treated 20 μM Curcumin for 24 h or xenograft tumors were analyzed by western blot

Results and Discussion:

Curcumin (20 μM) showed growth inhibitory effects in SRB12-p9 cells as early as day 2 ($p<0.05$) compared to control

On day 2 and 3 Curcumin (20 μM and 40 μM) showed effective inhibition of proliferation of SRB12-p9 cells compared to control

SRB12-p9 xenograft tumor model suggested that oral administration of Curcumin as well as the combined group showed significant inhibition of tumor growth compared to control ($p<0.001$)

Tumor volume in topical group also statistically smaller than the control group ($p = 0.02$)

Ex vivo tumor measurement also revealed that oral, topical and combination group showed significantly reduced tumor volume ($p<0.001$, $p= 0.006$ and $p=0.02$, respectively) when compared to control group

Curcumin treatment significantly inhibited various signaling pathways viz; pAKT, pS6, p-4EBP1, pSTAT3 and pERK1/2 in SRB12-p9 cells

Western blot analysis of showed that both Curcumin groups inhibited of pERK1/2, whereas inhibition of pSTAT3 was only noted in the combination group

Conclusion:

Curcumin slowed progression of aggressive skin SCC by inhibiting several signaling pathways; hence it can be explored as a chemopreventive and therapeutic agent for skin cancer treatment.