Liposomal Curcumin Suppresses Growth of HNSCC

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Purpose

Head and Neck Squamous Cell Carcinoma (HNSCC) represents 5% of all cancers diagnosed annually in the United States. The significant morbidity associated with current treatment modalities has been motivating investigations of potential alternatives to current toxic therapies. The introduction of EGFR monoclonal antibody to the chemotherapeutic regimen has increased interest in therapies for HNSCC directed at biochemical pathways. In vitro cell viability studies on two HNSCC cell lines showed that there is significant inhibition of cell growth with liposomal curcumin (p=0.0125). The results in UM-SCC1 also showed that liposomes are significantly less toxic than DMSO and did not show any systemic toxicity associated with liposomal curcumin. Immunohistochemistry showed that liposomal curcumin treatment resulted in inhibition of NFkB activation through an AKT-independent pathway.

Materials and Methods

Liposomal Curcumin

Liposomes were used representing oral cavity carcinomas. Cells were plated and allowed to grow for 24 hours, then serum starved for an additional 24 hours. Cells were treated with DMSO, DMSO + curcumin, liposomes, or liposomal curcumin at various concentrations for 8 hours and then allowed to rest for 12 hours. After treatment, MTT reagent (1 mg/mL in media) was added for 4 hours. OD was measured at 570 nm.

NFkB Reporter Gene Assay

CAL27 and UM-SCC1 cells were plated at 5 x 10^5/well and transfected 24 hours later with a NFkB-responsive plasmid (luciferase) along with a firefly luciferase plasmid. Firefly luciferase was constitutively expressed for normalization of transfection. Cells were treated for 4 hours with liposomal curcumin and treated overnight. Proteins were collected and luciferase activity measured on a luminometer using a Dual Luciferase Assay kit (Promega, Madison, WI).

Results

In vitro cell viability studies on two HNSCC cell lines showed that there is significant inhibition of cell growth with liposomal curcumin (p=0.0125). The results in UM-SCC1 also showed that liposomes are significantly less toxic than DMSO and did not show any systemic toxicity associated with liposomal curcumin. Immunohistochemistry showed that liposomal curcumin treatment resulted in inhibition of NFkB activation through an AKT-independent pathway.

Conclusions

• Liposomal curcumin suppresses growth of HNSCC cell lines in vitro and exhibits less toxicity than curcumin in DMSO.
• Liposomal curcumin inhibits activation of NFkB, which may be its mechanism of tumor suppression.
• Intravenous liposomal curcumin suppresses growth of xenograft tumors in vivo.

Toxicology studies on mice injected intravenously with liposomal curcumin did not reveal any systemic toxicity.

The pathway by which curcumin inhibits NFkB activation appears to be independent of the AKT pathway. This may have clinical applications for the treatment of tumors which are resistant to EGFR antibody.

References


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