Head and neck squamous cell carcinoma (HNSCC) is diagnosed in over 30,000 patients annually in the United States, while approximately 8,000 patients die of the disease every year. The significant morbidity associated with current treatment modalities, which include disfiguring surgery, chemotherapy, and radiation, has led to continuing investigation of potential alternative and less toxic therapies.

Current treatment regimens for HNSCC often include use of a platinum-based chemotherapy, such as cisplatin (CDDP). Its toxic effects are dose-dependent and include renal, otologic, and bone marrow suppressive sequelae.

If an agent is found that acts synergistically with cisplatin, permitting decreased doses, tumor suppression could be maximized, while toxic side effects are minimized.

Previous studies by our group have demonstrated that liposome-encapsulated curcumin can suppresses growth of HNSCC by a mechanisms different than CDDP (figure 1).

In this study, we assess the potential of combining liposomal curcumin with cisplatin in the treatment of HNSCC.

**MATERIALS AND METHODS**

- HNSCC proteins from CAL 27 and SCC-1 cell lines were isolated and western blots analysis was performed.
- HNSCC cells were treated with curcumin and cisplatin, individually and together, and assayed for growth using MTT, western blotting, and immunofluorescence. Five-week old female athymic nude mice were utilized for in vivo experiments. HNSCC cells were injected to form xenograft tumors.
- Liposomal curcumin (50 ug/kg, maximum volume of 100ul) was administered intravenously three times per week for four weeks via tail vein injection. Mice were divided into three groups: no injection, liposomes alone, or liposomal curcumin. At the end of the fourth week, a single dose of intraperitoneal cisplatin [7.5 mg/kg; 1mg for the 20g mice treated with liposome alone (represented in figures 3,4,5)] was administered intraperitoneally three times per week for four weeks via tail vein injection. Mice were euthanized and tumors were dissected and weighed.

**RESULTS**

- Tumor growth inhibition in vivo: Our studies demonstrated almost a 50% reduction in tumor growth in the curcumin + CDDP treatment when compared to either controls, cisplatin alone, or control liposome + CDDP by week 3 of treatment (Fig 2) [p < 0.05 for curcumin + CDDP compared to controls]. Representative tumors are shown in figure 4 (Fig 3).
- Addition of curcumin or cisplatin alone or in combination resulted in cell death. Introduction of suboptimal levels of both agents in vitro demonstrated a synergistic suppression of HNSCC cell line growth compared to individual agents. Xenograft tumors in nude mice treated with combination curcumin and cisplatin showed superior tumor growth suppression compared to control mice and mice treated with liposome alone (represented in figures 3,4,5).

**CONCLUSIONS**

1. Cisplatin is currently being administered in the clinical setting as a chemotherapeutic agent for head and neck squamous cell carcinoma, but not without significant potential treatment toxicity.
2. Curcumin potentiates the anti-tumor activity of cisplatin in vivo (potential curcumin mechanism outlined in figure 1)
3. Thus, there is potential for the use of a combination of subtherapeutic doses of cisplatin in combination with curcumin in the clinical setting, which will still allow effective suppression of tumor growth while minimizing cisplatin’s toxic side effects.
4. Our data supports further investigation into the potential use of curcumin in combination with cisplatin in the treatment of HNSCC.

**BIBLIOGRAPHY**