

Compound's dual action inhibits oral cancer without observable side effects

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The compound licofelone inhibited oral cancer growth by inhibiting the cyclooxygenase and 5-lipoxygenase pathways, with no observable side effects, according to data from a rat study presented at the 11th Annual AACR International Conference on Frontiers in Cancer Prevention Research, held here Oct. 16-19, 2012.

Cyclooxygenase (COX) inhibitors have been shown to suppress oral and other cancers, but side effects, such as gastric bleeding, tend to disqualify them as preventive agents. Researchers hypothesized that suppressing COX might instigate cancer-causing inflammation through lipoxygenase (LOX). Because licofelone inhibits both pathways, researchers investigated whether it could provide superior cancer prevention while lowering toxicity.

"Toxicology is always a limitation because you're giving these preventive treatments to otherwise healthy people, so the threshold for toxicity is very low," said lead researcher David McCormick, Ph.D., senior vice president and director at the ITT Research Institute in Chicago. "Dual inhibitors may provide superior chemopreventive activity, as well as a better toxicologic profile."

Using a well-studied rat model, McCormick and colleagues induced oral cancer and tested different licofelone doses, including 37.5 mg/kg per day and 75 mg/kg per day, as well as 75 mg/kg per day after a six-week delay following the induction of cancer.



In a control group, 75 percent of rats developed <u>squamous cell</u> <u>carcinoma</u>, the predominant oral cancer in humans, most often at the base of the tongue. They also developed a variety of <u>precancerous</u> <u>lesions</u>.

Forty-three percent of rats assigned to high-dose licofelone and 55 percent assigned to the low-dose administration developed cancer. Those assigned to the compound after a six-week delay had a 34 percent incidence of oral cancer. McCormick noted that delayed administration can compromise the anticancer activity in some compounds. The fact that licofelone retained its anticancer action bodes well for its preventive potential, as patients may have already developed precancerous lesions before they seek treatment.

Researchers also observed a decreased incidence of the most advanced (highly invasive) cancers with licofelone: a 17 percent incidence with both doses compared with 54 percent in controls.

Although cancer incidence was reduced in the treated rats, the incidence of precursor lesions increased, again confirming licofelone's ability to suppress the development of <u>oral cancer</u>, according to the researchers.

"The data suggest the compound inhibits cancer progression," McCormick said. "The lower incidence of invasive cancer and higher incidence of cancer precursors indicate we may be stabilizing progression at the earlier, precancerous stage."

Provided by American Association for Cancer Research

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