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How do four caged xanthones inhibit cholangiocarcinoma cell growth?

May 12 2010

Programmed cell death (apoptosis) is a key mechanism in the cell exploited by several currently used anticancer drugs to kill tumor cells. A study from Thailand found that the four caged xanthones from Garcinia hanburyi: isomorellin, isomorellinol, forbesione and gambogic acid, have strong growth inhibition effect in cholangiocarcinoma cells selectively. Growth suppression by these compounds was due to apoptosis.

Cholangiocarcinoma (CCA) is a malignant tumor, characterized by a poor prognosis and unresponsive to conventional chemotherapeutic agents. Therefore, searching for novel and effective therapeutic agents for CCA is necessary. In previous studies, several caged xanthones from *G. hanburyi* have been reported to be potent antiproliferatives as well as having anticancer and anti-tumor activities and they induce apoptosis in various cancer cell lines. However, the molecular target of these compounds remains unclear.

A research article to be published on May 14, 2010 in the World Journal of Gastroenterology addresses this question. Chariya Hahnvajanawong and her colleagues of the Khon Kaen University and Mahidol University found that the four caged xanthones can significantly inhibit the growth of CCA cell lines by modulating the expression of apoptotic-regulated genes and proteins.

This is the first report which shows that these compounds induce apoptosis by increasing the levels of proteins which promote apoptosis (Bax, apoptosis-inducing factor (AIF), activated caspase-9 and -3) while

decreasing the levels of proteins which inhibit apoptosis (Bcl-2 and survivin).

In the view of the authors, the chemical structure diversity of the four compounds reflects the biological activities. At the molecular level, isomorellinol exhibited the highest potential, indicating that functional groups on the prenyl side chain may be important.

It is premature to conclude what the definite structure-activity relationship may be, but this preliminary insight provides a basis for further medicinal chemistry studies. Based on these results, the authors suggest that these four caged xanthones are compounds with great promise and may serve as a potential source and lead-structure for the development of a drug for the treatment of CCA.

More information: Hahnvajanawong C, Boonyanugomol W, Nasomyon T, Loilome W, Namwat N, Anantachoke N, Tassaneeyakul W, Sripa B, Namwat W, Reutrakul V. Apoptotic activity of caged xanthones from Garcinia hanburyi in cholangiocarcinoma cell lines. World J Gastroenterol 2010; 16(18): 2235-2243
www.wjgnet.com/1007-9327/full/v16/i18/2235.htm

Provided by World Journal of Gastroenterology