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Natural sesquiterpenes β-caryophyllene and β-caryophyllene oxide as chemopreventive agents for cholangiocarcinoma

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Cholangiocarcinoma (CCA) represents a particular type of liver cancer originating from the epithelial cells lining the intrahepatic and extrahepatic biliary tree. It is often clinically silent until it becomes an advanced disease with obstructive symptoms and a poor prognosis for patients [1]. In this context, searching for alternative therapeutic strategies becomes a pivotal goal in the battle against liver cancer. In present research, β-caryophyllene (CRY) and β -caryophyllene oxide (CRYO), two natural sesquiterpenes with protective properties [2], have been investigated for their ability to inhibit the growth of the human Mz-ChA-1 cholangiocarcinoma cells from extrahepatic bile ducts and the H69 non-malignant cholagiocytes. The cells were exposed to the test compounds for 24 h, then the cytotoxicity was measured by MTT assay [3]; doxorubicin was included as a standard cytotoxic agents. Both sesquiterpenes reduced the cholangiocytes proliferation. Particularly, CRY produced a marked cytotoxicity in the Mz-ChA-1cells at concentrations lower than that required for CRYO. Surprisingly, the antiproliferative effects produced by both CRY and CRYO were higher than that of the standard doxorubicin. In the non-malignant cholangiocytes, in spite of a low cytotoxicity of CRYO, CRY reduced the cell proliferation already at lower concentrations, acting in a similar way to doxorubicin. Being CRYO an epoxide analogue of CRY, the different cytotoxicity found could be due to their structural features and bioavailability. Present results encourage further studies on CRY and CRYO as chemopreventive agents for cholangiocarcinoma.

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Keywords

Natural sesquiterpenes; beta-caryophyllene; cholangiocarcinoma cells; chemoprevention; chemosensitizer.