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Antiproliferative Activity of the Netherlands Propolis and Active Constituents

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[Introduction] Propolis is a resinous hive product collected by honeybees from various plant sources. It has a long history of being used in folk medicine and also been reported to have broad spectrum of biological activities. In recent years, propolis has gained popularity as a health drink and also been extensively used in food and beverage, which is thought to improve the human health and prevent diseases such as inflammation, heart disease, diabetes and even cancer. Because of its broad spectrum of biological activities and uses in health food as well as in folk medicine, there is a renewed interest in the composition of propolis and their biological activities. In our previous work, we examined the antiproliferative, hepatoprotective and anti-*Helicobacter pylori* activities of Brazilian propolis and their constituents. The Netherlands propolis was differed than the Brazilian one because of climatic variation. Thus chemical analysis of the Netherlands propolis was undertaken, in order to isolate antiproliferative compounds,

[Result and Discussion] It was observed that the MeOH extract of the Netherlands propolis possessed potent antiproliferative activity towards highly liver metastatic murine colon 26-L5 carcinoma with an EC_{50} value of $3.5 \mu\text{g/mL}$. Further fractionation by antiproliferative activity guided of the MeOH extract led us to isolate five cinnamic acid derivatives together with four flavonoids. Isolated compounds were tested for their antiproliferative activity against murine colon 26-L5, murine B16-BL6 melanoma and human HT-1080 fibrosarcoma and human lung A549 adenocarcinoma cell lines. Caffeic acid benzyl ester (**1**) and caffeic acid phenylpropenyl ester (**2**) possessed strongest antiproliferative activity towards all tested tumor cell lines and selective against murine colon 26-L5 with an EC_{50} value of 0.28 and $0.11 \mu\text{M}$, respectively.