Saudi Propolis as a Source of Anti-Cancer Drugs: Chemical Analysis and Biological Activity

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Introduction:

Propolis is a gluey material collected by honeybees from plants that they use to seal cracks in hives and protect them from infection by bacteria and fungi (1- 4). Propolis was used during the accent times by Egyptians, Romans and Greeks as a medicine for some diseases (5). The properties of propolis as a remedy are due to its bio-active chemical composition (5-8). Therefore, its chemical constituents and biological properties are of interest to researchers to investigate. Geographical settings, plant sources and collecting season are important factors in the diversity of the propolis chemical compositions and biological activities (5). Most of the studies on propolis composition and pharmacological effects have been performed on samples from Europe and Latin America whereas few or likely non, have reported on propolis from Saudi Arabia. In this report we show the chemical composition and the biological activities of an acetyl acetate fraction of Saudi propolis and we discuss the possibility of using it as a source of anti-cancer drugs.

Aim of the work:

The main purpose of this study is to determine the chemical composition, of biologically active fraction of propolis sample collected from the southern part of Saudi Arabia (Elbaha-Region) and to examine its bio-active properties.

Methodology:

In this study we used a multidisciplinary approach to analyze Saudi propolis and to explore its biological activities. Our method spectrum includes GC-MS, high-speed countercurrent chromatography (HSCCC) and metabolite profiling by *off-line* injection to APCI-MS/MS, MTT-assay, flow cytometry, drug affinity responsive target stability (DARTS), immunofluorescence techniques, and other cell based assays.

Results:

Our results showed that the biologically active fraction of Saudi propolis inhibits the proliferation of number of cancer cell lines including HepG2 (human liver carcinoma), A549 (human lung carcinoma), and Jurkat (T lymphocyte leukemia) at low microgram level. DARTS, immunofluorescence and other cell based assays suggest cellular tubulin and microtubules as a molecular target of Saudi propolies (Figure 1). Furthermore, cell cycle investigations showed that Saudi propolis induces a G2/M arrest of the cell cycle followed by induction of apoptosis (programmed cell death) in Jurkat cells.

Moreover, our GC-MS data indicate that titerpenoids and diterpenoids represent the major components of the biologically active fraction of Saudi propolis (72% and 8% of total extract,

respectively). In addition, HSCCC with pre-fractionation and successive purification steps resulted in the isolation and characterization of various bioactive components from the highly complex propolis fraction. (12*E*)- and (12*Z*)-communic acid, sandaracopimaric acid, (+)-ferruginol, (+)-totarol, 3*ß*-acetoxy-19(29)-taraxasten-20*a*-ol were purified and elucidated by EI-, APCI-MS and 1D/2D-NMR. Cycloartenol and 24-methylene-cycloartenol, as well as five triterpene acetates were isolated in mixtures and elucidated by EI-MS and 1D-NMR. Free fatty acids, and two labdane fatty acid esters, the 15-O-oleoyl-, and 15-O-palmitoyl-isocupressic acid were also identified by APCI-MS/MS. In summary a total of 19 metabolites could be identified, from the biologically active fraction of Saudi propolis. The chemical metabolite profile of the Saudi Arabian propolis from Al-Baha showed similarities to the results published for propolis from Crete (9), and Greece (10). Depending on the identified diterpene chemical profile, the resin sources for propolis might be *Juniperus procera* or any other plant from the Cupressaceae family (11-14). The confirmation of these findings will require more field studies to trace the plants which are generally visited and this is also depending on the vegetation period.

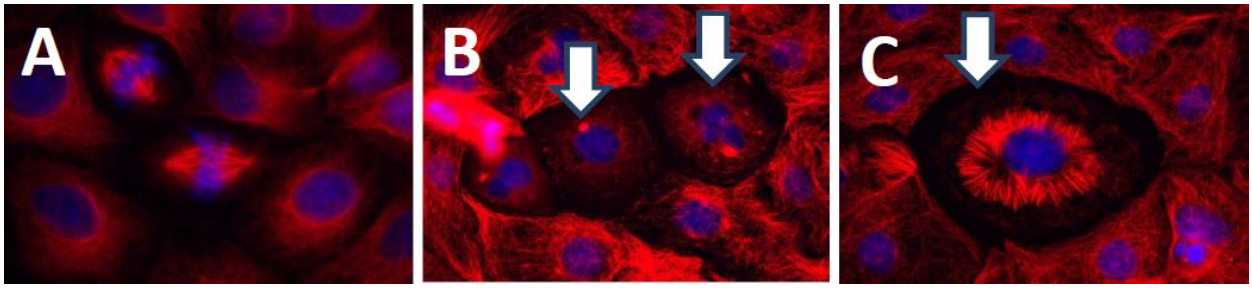

Figure 1: Effect of Saudi Propolis extract on the microtubules of PtK2 cells as shown by immunofluorescence techniques using anti-α-tubulin antibodies (red). Nuclei were stained with DAPI (blue). A) Control Cell, B, and C treated cells (100 µg/ml, 24 h).

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