Cell cycle arrest and induction of apoptosis in human cancer cells lines by date palm kernels extracts and isolated cytotoxic compounds

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This study conducted to identify the mechanism of cell death that induced by these isolated flavonoids, either by induction of apoptosis or necrosis. Three flavonoids namely nobiletin (NOB), tectorigenin (TEC) and persicognin (PERSI) were isolated from the optimised extractable polyphenols (EPP) crude extract of date palm kernels (DPK). The effect of crude EPP, NOB, TEC, PERS and the non-extractable polyphenols (NEPP) from DPK and paclitaxel on human lung cancer A549 and human colon cancer HT29 cell lines and on the normal murine fibroblast 3T3 cell line were investigated using MTT crystal violet and trypan blue exclusion assays.

Apoptosis, one type of programmed cell death, is a well-defined self-suicide process counteracting tumor growth. Many chemotherapy drugs produce antitumor effects by triggering the apoptosis through a variety of molecular mechanisms. Apoptosis is either created by death receptors, which are called extrinsic pathway utilizing caspases 8 and 10. The other pathway is mitochondrial path or intrinsic pathway involving caspase. Recognizing involved mechanisms in cancer development is of great importance for developing neoplastic treatment.

The morphological changes of treated cells inspected by light inverted microscopy. Cell cycle progression using propidium iodide staining examined by flow cytometry. The apoptotic effect of the crude extracts and purified compounds were investigated using annexin V-FITC and propidium iodide staining. The underlying mechanism of apoptosis induced by crude extracts and the isolated compounds was investigated using caspase-3, -8 and -9 assays and the mitochondrial membrane potential assay. The findings indicated that the both DPK extracts and purified phytochemicals did exert induced cell death on A549 and HT29 cell lines. The results perceived from MTT- assay and trypan blue exclusion showed that the cytotoxic effects of the plant extracts and the isolated compounds are dose-dependent with higher cell death within 72 hours treatment. Treatment of human lung and colon cancer cells with EPP, NOB, TEC, PERSI and NEPP induced late stages of apoptosis, as there was indication of the DNA degradation and high percentage of the cells population situated at sub-G1 phase, indicating a high population of apoptotic cells. Study of the apoptotic mechanism demonstrated that EPP and NEPP exhibited dependent mitochondrial signalling pathway as seen with caspase-9 and induced receptor-mediated (extrinsic) apoptotic pathway as seen with caspase-8. Therefore, our results suggest that DPK extracts and the three isolated flavonoids could be worthy candidates for developing anticancer agents.

Keywords: Apoptosis, date palm kernels, cancer cell lines, flavonoids, polyphenols.