



Kharazmi University

Faculty of Science - Biological Science Department

Biochemistry Division

Thesis Title:

Role of hesperidin (a natural flavonoid) and its aglycon form on ceramid metabolism in MDA-MB-231 human breast adenocarcinoma cell line – A comparative study

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Abstract:

Objective: The role of rutinoid (rhamnose+glucose) substitution has been examined extensively in the metabolism of flavonoids, however the effect of rutinoid on apoptosis-inducing activity of flavonoids is still unknown. Inhibition of cell death by

interference on ceramide signaling is a key strategy for tumorigenesis escape from apoptotic stimuli. Therefore, for the development of cancer therapy, ceramide metabolic pathways have become candidate target currently. In the present study, two flavonoids of hesperetin (HT) and hesperidin (HD; HT-7-rutinose) were used to study their effects on ceramide metabolism in cancer cells, MDA-MB-231.

Method: The cells were treated with various concentrations of each reagent hesperetin and Hesperidin. Cell survival, sphingomyelinase, glucosylceramide synthase and ceramidase enzyme activity and cellular ceramide levels were measured by spectrophotometer fluorescence and HPLC.

Result: The results of this study showed that HD in comparison with HT had significant cytotoxic effect on the MDA-MB-231 cells. At 175 μ M treatment of HD there were highest increasing effects on sphingomyelinase, glucosyl ceramide synthase activities and also in cellular ceramide level in the treated concentration range. These parameters were considerably higher with respect to HT. Ceramidase activity did not vary significantly in HD and/or HT treated conditions in comparison to control and also with respect to each other.

Conclusion: Retinoid substitution in flavonoids played important roles on apoptosis induction in MDA-MB-231 cells via ceramide metabolism involvement.

Key words: apoptosis, cancer, flavonoid, sphingomyelinase, glucosylceramide synthase, ceramidase.