The Impact of Nitrogenous Heterocyclic Compounds on Apoptosis in HCC in Rats

Thesis submitted to

Faculty of Science

In partial fulfillments required for M.Sc. degree in Biochemistry

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Abstract

Liver cancer is the fifth most common cancer among men and the seventh most common cancer among women worldwide. It is the third leading cause of cancer death globally. The oncogenic signal transduction of Sirt-1 and β-catenin were found to be constitutively activated in wide variety of cancers including liver cancer and so, it has become important therapeutic target in HCC treatment.

The aim of our study is to investigate the effect of two nitrogenous heterocyclic compounds which are (E)-2-(2,4,5 trimethoxybenzylidene) hydrazinecarbothioamide coded (H-21B) and N-(4-acetyl-5-methyl-5-(pyridin-2-yl)-4,5-dihydro-1,3,4-thiadiazol-2-yl) acetamide coded (H-13B) from two different families against HepG2 liver cancer cell line.

The effect these compounds was evaluated by checking the IC_{50}, cell morphology, apoptotic induction via DNA fragmentation assay, Sirt-1 and β-catenin signaling and caspase release. The cytotoxic effect of the two compounds was tested in vivo, in addition to the effect on the level of AST and ALT levels and the immunohistochemical assay.

H-21B and H-13B led to cell morphological changes and caspase release but in case of DNA fragmentation, H-21B was more effective than H-13B. Moreover, these compounds showed significant reduction of β-catenin and SIRT-1 expression levels in the tested cell line.

All in all, our results showed that the two tested compounds exhibit antitumor effects.