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Azilsartan induces oxidative stress and NF-kB medicated apoptosis in hepatocellular carcinoma cell line HepG2

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Over expression of renin angiotensin system (RAS) and nuclear factor-kappaB (NF-kB) has a key role in various cancers. Blockade of RAS and NF-kB pathway has been suggested to reduce cancer cell proliferation. This study aimed to investigate the role of angiotensin II and NF-kB pathway in liver hepatocellular carcinoma cell line (HepG2) proliferation by using azilsartan (as a novel Ag II antagonist) and Bay11-7082 (as NF-kB inhibitor). HepG2 cells were treated with different concentrations of Azilsartan and Bay11-7082. Cytotoxicity was determined after 24, 48 and 72 hours by MTT assay. Reactive Oxygen Spices (ROS) generation and cytochrome C release were measured following Azilsartan and Bay11-7082 treatment. Apoptosis was analyzed qualitatively by DAPI staining and quantitatively through flow cytometry methodologies and Bax and Bcl-2 mRNA and protein levels were assessed by real time PCR and ELISA methods, respectively. The cytotoxic effects of different concentration of Azilsartan and Bay11-7082 on HepG2 cells were observed as a reduction in cell viability, ROS formation, cytochrome C release and apoptosis induction. These effects were found to correlate with a shift in Bax level and a downward trend in the expression of Bcl-2. These findings suggest that Azilsartan and Bay11-7082 in combination or alone have strong potential for development as an agent for prevention against liver cancer.

Recent Publications

1. Ahmadian E, Eftekhari A, Babaei H, M Nayebi A and A Eghbal M (2017) Anti-cancer effects of citalopram on hepatocellular carcinoma cells occur via cytochrome c release and the activation of NF-kB. *Anticancer Agents Medicinal Chemistry;* 17(11): 1570-1577.
2. Ahmadian E, Eftekhari A, Fard J K, Babaei H, Nayebi A M, Mohammadnejad D and Eghbal M A (2017) *In vitro* and *in vivo* evaluation of the mechanisms of Citalopram-induced hepatotoxicity. *Archives of Pharmacal Research;* 40(11): 1296-313.

Biography

Elham Ahmadian has her research interests in drug/xenobiotic induced liver toxicity. She also studies on drug development against cancer, including pancreas and liver. Her current project is aimed at development of anticancer drugs that have the potential to compact cancer and also to understand the role of renin angiotensin related drugs in the hepatocarcinoginesis as a pleotropic effect.

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