Abstract

Cancer is a generic term used for a group of diseases being characterized by growth, proliferation and spread of abnormal cells. Globally, cancer is the second cause of death after cardiovascular diseases. The number of new cases of cancer is increasing in many countries, leading to a serious burden on the universal health system. The main treatments for cancer include surgery, radiation, chemotherapy and hormone therapy. Although prevention and advancement in treatment strategies have reduced cancer-related deaths, problems such as low selectivity, drug resistance and severe side effects of emerging drugs emphasize on design and development of new chemical entities (NCEs) with higher potency and specificity.

According to the studies on cytotoxic properties of different compounds, a number of novel N-heteroaryl enamino amide derivatives were synthesized in this project via a cost-effective method. Subsequent to purification, characterization and structural confirmation by using ^{1}H-NMR, IR and MS methods, cytotoxic effects on human cancer cell lines AGS, Hep-G2 and MCF-7 were evaluated by MTT assay. In the next step, to evaluate the induction of cell death (apoptosis and cell necrosis), superior cytotoxic agent (5 in AGS cell line) was elucidated by flow cytometry using annexin V and propidium iodide staining.

According to the results of cytotoxicity, compound 5 with IC_{50}= 9.9 μM in AGS, IC_{50}=15.2 μM in MCF-7 and IC_{50}= 40.5 μM in Hep-G2 produced the highest cytotoxicity and flow cytometry results showed that 24 h treatment of AGS cells with IC_{50} concentration of this compound mainly caused cell death by inducing necrosis (26.43%) and apoptosis (18.35%).

Based on structural evaluations, cyclic N-heteroaryl enamino amide structures (3,4-dihydropyrimidinone/dihydropyrimidinthiones) were more cytotoxic than acyclic structures. Within cyclic structures, the most important characteristic for creating higher cytotoxicity was presence of a strong electron withdrawing group with the ability to form hydrogen bonds at meta position of phenyl ring.

Key words: Cancer, Cytotoxicity, N-amino amide, Dihydropyrimidine,