Evaluation of Interaction between nitrogen-containing polycyclic heterocyclic compounds and c-Met receptors and their cytotoxic effects on pancreatic cancer cells

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Cancer is the second leading cause of death in the world after cardiovascular diseases. Cancer develops when normal cells in a particular part of the body begin to grow out of control. Despite the advancement in cancer biology, it is still one of the most common diseases with high mortality and due to the resistance of cancer cells to existing drugs the treatment have been difficult, For this reason, targeted therapies have increased in recent years. One of the pathways that play an important role in different kinds of cancers is the HGF_c-MET pathway and abnormal c-MET signal activity has been reported in a variety of cancers, thus it is important to produce c-MET inhibitores.

In this study, the interaction of phenanthro (e-9,10) (1, 2 , 4) triazine derivatives, poly aromatic acenaphtho[1,2-e]-1,2,4-triazine derivatives and amino naphthoquinone (1,2,3) triazole with MET receptor was evaluated via docking and Gold Score software. And biological effects of these compounds was evaluated by using SRB cytotoxicity test and Hoechst test on four cell lines AsPc-1, SUIT-2, PANC-1, MIAPaCa-2 with different expersion of MET

Some of these compounds, such as p4-10 with the structure of 3- (2- (3-Nitrobenzylidene) hydrazinyl) phenanthrene [9,10-e] [1, 2, 4], have good growth inhibition effects in this study. The major interactions observed in this compund include a pi-pi stacking bond with Tyr1159 with 1, 2, 4 triazine ring and a hydrogen bond between Tyr1230 with the carbonyl group as well as a hydrogen bond between Met1160 with N in triazine ring. These bonds contribute to better binding of the structure to the protein and enhance the growth inhibitory effect. IC50 of this

compound in SRB studies and in AsPc-1 cell lines with high MET expression is 5.07. The data from the Hoechst test also show that some of these compounds can induce apoptosis in cancer cells, thus more specific tests are needed to evaluate the anticancer effect of these compounds. Accroding to this study some of these compounds, especially p4-10 may have c-Met inhibitory effects and further studies to evaluate their effect as Targeted anti-cancer drugs is needed.

Key words: cancer,c-Met, SRB test, Hoechst test, AsPc-1 ،SUIT-2 ،PANC-1 ،MIA PaCa-2