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ABSTRACT

The present research work deals with the synthesis, characterization and biological activity of some heterocyclic compounds. The thesis comprises of seven chapters. First chapter deals with the general introduction and literature review of heterocyclic compounds.

Second chapter describe the synthesis, characterization and anticancer activity of pyridine-thiazolidinone conjugates. All the synthesized compounds were evaluated against two cancer cell lines (MCF-7; breast cancer cell line and HepG-2; liver cancer cell line) and one normal cell line (HEK-293; Human embryonic kidney cell line). Most of the synthesized compounds showed moderate to good cytotoxicity against these cancer cell lines. Some compounds showed good selectivity against MCF-7 and HepG-2 with the SI value more than 3. Two compounds were the most promising as both showed SI value more than 13 for both the cancer cell lines.

Third chapter deals with metronidazole-thiazolidinone conjugates which were synthesized by Knoevenagel condensation and screened *in vitro* against the HM1: IMSS strain of *Entamoeba histolytica*. All the compounds were characterized by various spectroscopic techniques like IR, ^{1}H NMR, ^{13}C NMR and ESI-MS mass spectrometry. Out of the thirteen synthesized compounds, six evinced propitious antiamoebic activity with IC_{50} values ranging from 0.18–1.65 μM lower than the standard drug metronidazole (IC_{50} = 1.64 μM).

Chapter four describe the synthesis and characterization of a series of metronidazole-hydrazone conjugates which were synthesized by condensation reaction of 4-[2-(2-methyl-5-nitro-1*H*-imidazole-1-yl)ethoxy]benzaldehyde and different aryl hydrazides in ethanol. All the synthesized conjugates were screened against HM1: IMMS strain of *Entamoeba*

histolytica. Among all the synthesized compounds, six compounds were found to be better inhibitors of *Entamoeba histolytica* than the reference drug metronidazole. These compounds showed greater than 50-60% viability against HeLa cervical cancer cell line after 72 h treatment. Molecular docking study was undertaken on *E. histolytica* thioredoxin reductase, which showed significant binding affinity in the active site. Out of the six active compounds, some showed lipophilic characteristics.

Fifth chapter deals with 5,6,7,8-tetrahydrobenzo [4,5]theino[2,3-d] pyrimidine based chalcones which were synthesized by Claisen-Schmidt condensation reaction of 1-(4-((5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]pyrimidin-4-yl)amino)phenyl) ethan-1-one with different aldehydes. The structure elucidation of all the synthesized compounds was elucidated on the basis of various spectral studies and the purity of all the synthesized compounds was confirmed by elemental analysis.

Sixth chapter describe the synthesis, characterization, antiamoebic and molecular docking studies of furan-thiazolidinone hybrids. All the hybrid compounds were prepared by Knoevenagel condensation of 3-(furan-2-ylmethyl)-2-(phenylimino)-1, 3-thiazolidin-4-one with different aryl aldehydes in presence of strong base. Some members of the series exhibited remarkable antiamoebic activity and cell viability. Three compounds showed excellent binding energy for *Entamoeba histolytica* O-acetyle-L-serine sulfohydrolase and *Entamoeba histolytica* thioredoxin reductase. These compounds demonstrated significant inhibition of O-acetyle-L-serine sulfohydrolase. The promising antiamoebic activity and enzymatic assay make them promising molecules for further lead optimization in the development of novel antiamoebic agents.

Seventh chapter deals with 4-(7-chloroquinolin-4-yl) piperazin-1-yl)pyrrolidin-2-yl) methanone derivatives which were synthesized, characterized and evaluated for antiprotozoal activity. The compounds were screened *in vitro* against the HM1: IMSS strain of *Entamoeba histolytica* and NF54 chloroquine-sensitive strain of *Plasmodium falciparum.* Among the synthesized compounds six compounds showed lower IC_{50} values (0.14-1.26 μM) than the reference drug metronidazole (IC_{50} = 1.80 μM). Nine compounds exhibited antimalarial activity (IC_{50} = 1.42-19.62 μM), while maintaining a favorable safety profile to host red blood cells. All the compounds were less effective as an antimalarial and more toxic (IC_{50} range: 14.67-81.24 μM) than quinine (IC_{50} = 275.6± 16.46 μM) against the human kidney epithelial cells.