Synthesis, Characterization and Biological Evaluation of Some Heterocyclic Compounds

Abstract of the Ph.D. Thesis

Submitted to

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OBJECTIVES

- Design of the novel hybrid molecules
- Synthesis of some novel heterocyclic derivatives
- Characterization by different spectroscopic techniques
- Evaluation of biological activities

Keywords: heterocycles, nitroimidazole, piperazine, quinoline, pyridine, indole, 3,5-bis(trifluoromethyl)phenyl]methanamine, chalcones, thiazolidinones, anticancer activity, cytotoxicity, molecular docking, *Entamoeba histolytica*

ABSTRACT

This thesis is a compilation of tedious research in synthesis, characterization and biological study of some heterocyclic compounds. This thesis contains five chapters which are as follows:

This study gives basic insight to heterocyclic compounds discussed in the thesis. Synthesis and applications offew compounds like Nitroimidazole, Piperazine, Quinoline, Pyridine, Indole, 1-[3,5- bis(trifluoromethyl)phenyl]methanamine and thiazolidinones have been reviewed further. A few anticancer, antiprotozoal, antiamoebic and antimicrobial diseases have also been discussed in precisely. The compounds consisting of 2-methyl-5-nitroimidazole and piperazine substituted derivatives showed results of cytotoxicity that in the tested concentration range. Compounds **NJ3, NJ4, NJ8** and **NJ14** show the considerable cytotoxicity towards HEK293 cells.

The compounds containing 2-(quinolin-8-yloxy) acetohydrazide conjugates (**QC1-QC11)** and their aldehydes were examined using HM1: IMSS strain of *E. histolytica* and the results showed that the derivatives having a quinoline nucleus with a hydrazone linkage [-NH-N=CH-R] (**QC1-QC11**) exhibited higher antiamoebic activity as compared with the aldehydes (**C1-C11**). There was a small inhibitory effect of the **QC2** and **QC4** derivatives on the malaria parasite in comparison to quinine, with negligible effects on the red blood cells.

The compounds consisting of 3,5-bis(trifluoromethyl)benzylamine and thiazolidinone is a favourable combination due to its action against MDA-MB-231 cancer cells. Compounds **T4, T5**, **T6**, **T7**, **T8, T9** and **T10** have shown adequate anticancer activity. These compounds have shown promising structural features towards MDA-MB-231 cancer cells which need to be further investigated to enhance biological activity. Molecular docking also revealed that compound **T2** and **T4** have high binding energy.

The compounds consisting phenylacetyl-indol-pyridine **P2, P4** and **P7** showed good to modest anticancer activity against MDA-MB-231 cancer cells. In silico study also indicated the good binding affinity and interactions with a cancer protein named Tumor- Associated Human Carbonic Anhydrase IX.

Among all the synthesized compounds **NJ3, NJ4, NJ8**, **NJ14, QC2**, **QC4, T4, T5**, **T6**, **T7**, **T8, T9**, **T10, P2, P4** and **P7** hold appreciative structural traits which require further investigation to increase biological pursuit.