Name : Faisal Hayat

Supervisor: Prof.Amir Azam

Thesis Title: *"Entamoeba histolytica* Inhibitors: Synthesis and Antiamoebic Screening of Some Heterocyclic Compounds."

Department of Chemistry

Jamia Millia Islamia (New Delhi)

Abstract:

The present thesis comprises of general introduction and four chapters. General introduction comprises of the literature of the work done in the area of amoebiasis and defines the objectives of the introduction.

The **First Chapter** deals with the synthesis, characterization and antiamoebic activity of chloroquinoline based chalcones(**4-18**). The reaction of 2-chloro-3-formylquinolines (**1-3**) with different commercially available aromatic ketones in presence of aqueous sodium hydroxide in ethanol gave the quinolinyl chalcones in good yield. All quinolinyl chalcones (**4-18**) were screened *in vitro* against HM1: IMSS strain of *E. histolytica* by microdilution method. Compounds **10**, **11, 15** and **17** have shown the most promising antiamoebic activity and less cytotoxicity.

The **Second Chapter** describe the synthesis, characterization and antiamoebic activity of pyrazoline derivatives bearing quinoline tail. A series of chalcones (**1a-1j**) were prepared by base-catalyzed Claisen-Schmidt condensation. The cyclization of chalcones (**1a-1j**) with 2-(quinolin-8-yloxy) acetohydrazide (**2**) in presence of base led to the synthesis of novel series of pyrazoline derivatives (**3a-3j**). *In vitro* antiamoebic activity was performed against HM1:IMSS strain of *Entamoeba histolytica.* The results showed that compounds **3d**, **3g**, **3h**, and **3j** exhibited most promising antiamoebic activity and less cytotoxicity

The **Third Chapter** deals with the synthesis, characterization and antiamoebic activity of 1, 2, 3-Thiadiazole and 1, 2, 3-Selenadiazole derivatives. The 1,2,3-thiadiazole and 1,2,3-selenadiazole derivatives **8-19** were prepared by the cyclization of novel 2-(quinolin-8-yloxy) acetohydrazones **2-7.** The key intermediates, 2-(quinolin-8-yloxy) acetohydrazone derivatives **2-7** in our study were synthesized by the condensation of 8-quinolinoxyacetic acid hydrazide with the different aromatic ketones. The cyclization of corresponding 2-(quinolin-8-yloxy) acetohydrazone derivatives **2-7** on treatment with thionyl chloride gave the target compounds 1,2,3-thiadiazoles **8-13**, whereas the same 2-(quinolin-8-yloxy) acetohydrazone derivatives **2-7** when treated with selenium dioxide/acetic acid gave the second target compounds 1,2,3-selenadiazoles **14-19**. *Invitro* antiamoebic activity was performed against HM1:IMSS strain of *Entamoeba histolytica*. The results showed that all the 2-(quinolin-8-yloxy) acetohydrazones were more active than their cyclized products (1,2,3-thiadiazole and 1,2,3-selenadiazole derivatives) and non cytotoxic.

The **Fourth Chapter** deals with the synthesis, characterization and antiamoebic activity of pyrazolo[3, 4-d]pyrimidine-6-one derivatives. A mixture of urea, aromatic aldehyde and 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one in absolute ethanol (30 ml) contain 2-3 drops of 37% HCl as catalyst was refluxed for 5 hours. The crude product which precipitated on cooling was filtered and washed with cold ethanol and then recrystallized from appropriate solvent.

In vitro antiamoebic activity was performed against HM1:IMSS strain of *Entamoeba histolytica*. The results showed that the compounds **2b**, **2i** and **2j** with IC_{50} values of 0.37 μM, 0.04 μM and 0.06 μM respectively, exhibited better antiamoebic activity and less cytotoxicity.