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Title of the Thesis: Development of Novel Heterocyclic Compounds and Their Anti-Protozoal Activity

Abstract

The present research work deals with the study of Development of novel heterocyclic compounds and their anti-protozoal activity. Thesis consists of six chapters.

Chapter-1 defines the objectives of the present research work.

Chapter-2 presents the Synthesis, Characterization and structure optimization of a series of Thiazolidinone derivatives as *Entamoeba histolytica* inhibitors. A series of 4-thiazolidinone derivatives was synthesized and screened *in vitro* against HM1: IMSS strain. Out of sixteen compounds, eight compounds having *N, N*- dimethylamino, nitro, dimethoxy, pyridine, 3-methoxy, 3-substituted thiophene, 4-hydroxy, *meta* - chloro and ethyl group at *para* position of the phenyl ring were found to be better inhibitors of *E. histolytica* than the standard drug metronidazole. Cell line study on Human hepatocellular carcinoma (HepG2) revealed the non-toxic nature (upto 3.15-25 μM.) of the active compounds .

Chapter-3 deals with the study of Synthesis, Characterization of analogues of thiazolidinone derivatives and their Stereochemistry Confirmation. This chapter comprises of the basic moiety phenylisothiocyanate and *ortho*-Chloro benzylamine. The structure of the compounds was established by IR, ^{1}H-NMR, ^{13}C NMR and CHN analysis. The stereochemistry of the molecules was determined by COSY, NOESY ^{1}HNMR spectroscopy. It was found that the molecules adopted (*Z, Z*)- configuration.

Chapter-4 Describes the Synthesis, Characterization and Confirmation of Stereochemistry of Pyrazole containing Thiazolidinone derivatives. A novel series of thirty compounds of combination of the two basic biologically active moieties pyrazole and thiazolidinone was synthesized. The structure of the molecules was determined by IR, ^{1}H NMR, ^{13}C NMR, mass spectroscopy and CHN analysis. The stereochemistry of the compounds was determined by COSY, NOESY spectroscopy. Furthermore, the structure was determined by X-ray single crystal structure. It was found that the molecules occupied (*Z, Z*)-configuration.

Chapter-5 Discusses the Synthesis, Characterization and Their Stereochemistry Confirmation of Bisthiazolidinone derivatives. A series of eight compounds was synthesized using different thiazolidinones and benzene 1, 4 & 1, 3- dialdehydes. The structure of the compounds was determined by IR, ^{1}H NMR, ^{13}C NMR and mass spectroscopy and CHN analysis. The stereochemistry of the molecules was determined by COSY, and NOESY spectroscopy. It was found that the synthesized molecules adopted (*Z, Z*) configuration.

Chapter-6 Consists of Synthesis, Characterization of dihydroquinazoline derivatives. The structure of the molecules was confirmed by IR, ^{1}H-NMR, ^{13}C NMR spectroscopy and CHN analysis.

Conclusion

In order to develop potent amoebicidal agents, seventy two (72) compounds containing various heterocyclic moieties (Thiazolidinones, pyrazole, bisthiazolidinone and dihydroquinazoline) were synthesized. Out of which sixteen compounds were screened *in vitro* against HM1:IMSS strain of *E. histolytica* by microdilution method. It was found that eight compounds were better inhibitors of *E. histolytica* than the standard drug metronidazole and non-cytotoxic against Human hepatocellular

carcinoma cell line (HepG2). This is the first time report of thiazolidinone derivatives as potent *E. hitolytica* inhibitors.