"Synthetic, Characterization of Some Heterocyclic Compounds and Evaluation of Their Antiprotozoal Activities"

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The present thesis comprises general introduction and four chapters. General introduction includes the literature of the work done in the area of parasitic disease and defines the objectives of the investigation. Ninety-nine compounds of variegated nature were prepared by multi-step synthesis belonging to dithiocarbazate, thiosemicarbazone, triazine derivatives and the modification of Metronidazole drug. These compounds were subjected for screening against parasitic disease i.e. amoebiasis.

The First Chapter deals with the synthesis, characterization of dithiocarbazate derivatives and evaluation of their antiprotozoal activity. Dithiocarbazates attracted our attention because they possess a broad spectrum of potentially useful chemotherapeutic properties.

Literature survey reveals that by introducing metal into an organic moiety enhance the activity of the compound. To enhance the activity of these compounds, transition metal {Pd (II), Pt (II) and Ru(II)} were used to synthesis the complexes of dithiocarbazates by the reaction of appropriate metal precursor.

The Second Chapter describes the synthesis, characterization of thiosemicarbazone derivatives and screening of these compounds for their antiprotozoal activity. In the past few years, thiosemicarbazones derived from 2-formylpyridine and related aldehydes have been of great interest because of their reported antiparasitic and antitumor action. Thiosemicarbazones were prepared by simple method in which N4-thiosemicarbazone moiety was replaced by aliphatic, arylic and cyclic amines.

It is observed that the presence of certain bulky groups at position N4 of the thiosemicarbazone moiety greatly enhances biological activity. On screening against (HM-1:1MSS) strain of E. histolytica, thiophene-2-carboxaldehyde-4-benzylpiperidine thiosemicarbazone showed IC50 0.38 µg/ml which is comparable to metronidazole IC50 0.32 µ g/ml.

The incorporation of transition metals into the molecular structure of thiosemicarbazones derivatives has been done. All the thiosemicarbazones behave as bidentate ligand by coordinating through azomethine nitrogen and thionic sulphur. Metal ions are known to accelerate drug action and the efficacy of therapeutic agent enhanced upon the coordination with metal ion. Among all the metal complexes, the highest activity was shown by Ru (II) complex of thiophene-2-carboxaldehyde-4-

benzylpiperidine thiosemicarbazone.

The Third Chapter presents the synthesis, characterization of triazine derivatives and in vitro evaluation of their antiprotozoal activity. The Chemistry of condensed heterocyclic systems especially containing triazine moiety has been largely investigated because they are effective in many pharmacological areas. Their derivatives posses a great number of biological activities such as antitumor, antiparasitic, antifungal, antiviral and anti-inflammatory activities. A series of triazine derivatives has been synthesized by the reaction of 3,7-Dimethyl pyrazolo [3,4-e] oxadiazine with substituted thiosemicarbazides. These compounds were screened in vitro and found that one showed better activity (IC50 0.27 µ g/ml) than metronidazole.

The Fourth Chapter describes the synthesis of metronidazole-ferrocene analogs and evaluation of their antiprotozoal activity. In recent years a considerable amount of research has been devoted to the synthesis of various substituted ferrocenes. Such compounds can effectively be used in asymmetric catalysis and enantioselective synthesis. Enhanced antibiotic activity of penicillin & Cephalosporine has been noted by replacing aromatic groups with the ferrocenyl moiety. C. Biot et al synthesized some chloroquine – Ferrocene derivatives and concluded that these compounds showed potent antimalarial activity as compared to chloroquine. A series of Ferrocene- metronidazole derivatives has been synthesized. These compounds were screened in vitro and found that compound 4 showed 2 times better activity than metronidazole.

Ninety-nine compounds were synthesized and subjected for screening against amoebiasis. Out of these compounds, only nine compounds were found active. It is interesting to note that by introducing metal into an organic moiety, the activity enhances. Two novel Ferrocene-metronidazole analogs showed activity better than metronidazole. It is suggested that these compounds should be tried for in vivo and pharmacokinetic studies and to look insight the cell for mechanism of action.