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ABSTRACT

In this chapter general introduction, literature reviews of heterocyclic compounds is discussed. The applications of heterocycles in medicinal chemistry has lead to many breakthroughs and further research in this field is ongoing. General synthesis and medicinal importance of thienopyrimidine have been discussed. A few protozoal diseases have also been discussed in brief. A series of eleven hybrid molecules containing the thienopyrimidine scaffold and the sulphonamide piperazine skeleton having a DHPS inhibitor site were synthesized and characterized with various spectroscopic techniques such as NMR, mass, IR. They were evaluated against chloroquine and pyrimethamine resistant K1 strain of *P. falciparum* and HM1: 1MSS strain of *E. histolytica* respectively. Compounds SC1 and SC4 showed better results than the standard drugs. Toxicity of the hybrids was measured on the HepG2 cell line. Majority of the compound had low toxicity. Docking studies revealed that the inhibitors place themselves nicely into the active site of the enzyme and exhibit interaction energy which is in accordance with the activity profile. In an endeavor to develop efficacious antiamoebic agents of 4- piperazin-1-yl-5,6,7,8-tetrahydrobenzo [4,5]theino[2,3-d] pyrimidine based acetamides derivatives were synthesized and screened *in vitro* against the HM1:IMSS strain of *E. histolytica*. All the compounds

were characterized by various spectroscopic techniques like NMR, IR, elemental analysis, mass etc. Crystal structure of two compounds (AC5 and AC10) was also determined. Out of the thirteen synthesized compounds, six evinced propitious anti-amoebic activity with IC50 values ranging from 0.96±0.01 to 1.39±0.01μM lower than the standard drug metronidazole (IC50 1.86 μM). The compounds that showed better activity than metronidazole were evaluated for their toxicity profile on the Chinese hamster ovarian cell line and showed low toxicity in the concentration range of 2.5-250 μM and 2.5-100 μM. Synthesis and characterization of a series of 2- [4-(5,6,7,8-tetrahydro[1]benzothieno[2,3-d]pyrimidin-4-yl)piperazin-1-yl]acetohydrazide derivatives and their antiamoebic activity was carried out. Twelve compounds (H1- H12) were synthesized and characterized by spectroscopic techniques. *In vitro* antiamoebic activity was performed for all the twelve compounds. An analysis of the antiamoebic properties for the *N*-acylhydrazones H1-H12 revealed an impressive potency enhancement when the R group contained a monosubstituted benzene with a lone pair possessing hetero atom. The compounds displayed low toxicity in the concentration range of 2.5-250 μM and 2.5-100 μM. The *in vitro* antiamoebic results and cytotoxicity profile revealed that the compounds can further be explored. A series of chalcones (4-21) possessing N-substituted ethanamine were synthesized by the aldol condensation reaction of 1-(4-(2-substituted ethoxy)phenyl)ethanone with different aldehydes preceded by the reaction of 2- chloro N-substituted ethanamine hydrochloride and 4-hydroxy acetophenone. The structure elucidation of all the synthesized compounds was done by various spectral and X-ray diffraction studies. All the compounds were screened against HM1: IMSS strain of *Entamoeba histolytica.* Out of 18 compounds synthesized 12 showed better activity then the standard drug metronidazole. The compound 9, 14 and 19 showed good cell viability and the least toxicity.