DISCOVERY OF POTENT AND SELECTIVE INHIBITORS OF SERINE ACETYLTRANSFERASE, AN ENZYME UNIQUE TO *Entamoeba histolytica*

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Introduction

E. histolytica is the etiologic agent of amoebiasis, a major public health problem in developing countries. The drugs that are used currently are not tolerated well on repeated use, manifest toxicity and cannot eradicate intestinal form of the disease. Therefore there is a need for identifying new anti-amebic agents. *Entamoeba* being a microaerophilic organism is sensitive to high level of oxygen and the enzymes that are involved in protecting against oxygen-stress are crucial for its survival. Therefore, serine acetyltransferase (SATase), an enzyme involved in cysteine biosynthesis was used as a target for identifying potential inhibitors.

Methods

Virtual screening of NCI chemical database with *E. coli* SATase was carried using molecular docking tools GOLD and FlexX. The initial analysis yielded 11 molecules of which three compounds were procured and tested for enzyme specificity, in vitro antiamoebic activity and cytotoxicity.

Results

These compounds inhibited the *E. coli* enzyme and also blocked the growth of *E. histolytica*. IC_{50} for the most potent compound was found to be 0.61 μM, comparable to metronidazole. Moreover, these compounds did not exhibit any anti proliferative effect on Vero-C-1008 cell line suggesting that they are non-toxic and specific to *E. histolytica*.

Conclusion

In conclusion, the virtual screening of a chemical library against *E. coli* SATase was able to identify low molecular weight potential inhibitors that blocked growth of the protozoan pathogen *E. histolytica*. Furthermore, these compounds did not have any effect on the growth of a Vero-C-1008 cell line suggesting that these compounds with new structural scaffolds have anti-amoebic activity and need to be studied further as potential lead candidates.