Abstract

Introduction

Leishmaniasis is one of the common diseases between humans and animals. Use of drugs that is used to treat leishmaniasis have limitations such as prolonged treatment, expensive medications, drug resistance and severe toxicity to the heart, liver, and kidneys. Therefore, drug development is essential in the treatment of disease. In this study, towards drug development of the treatment of leishmaniasis, new tetrahydropyrimidine and dihydropyridine derivatives were designed and synthesized through the Bijingle and Hansh procedures, respectively and their the anti amastigote and promastigote effects of major Leishmania parasites were investigated.

Materials and methods

Afther design, the derivatives were synthesized and purified. Then, their structurally confirmed using spectroscopic methods of FT-IR, ^{1}H-NMR and MS, as well as determination of melting point as a physical constant. Their antiparasitic effects were investigated on standard strain (MRHO/IR/75/ER) of major Leishmania.

Results

In general, the highest efficacy among the tetrahydropyrimidine compounds on the amastigote and promastigote forms were compounds 8 and 4 with EC_{50} = 16.80 and EC_{50} = 12.9 μg/mL, respectively, and among the dihydropyridine compounds of compound 11 with EC_{50} = 16.10 and EC_{50} = 10 μg/mL were observed. Also, the toxicity results of these compounds were studied on macrophages and the results showed that almost of compounds did not show any toxicity or showed slight toxicity.

Discussion and conclusion

Based on the results, position of chlorine atom on aromatic ring, the lipophilicity of the compounds, the chain length of ester on ring and the presence of oxygen or sulfur atom on the ring are effective on the activity. The efficacy of all the compounds was lower than standard drugs, but it was more than the monastrol. Also, dihydropyridine deriviatives showed stronger anti-leishmanial effects with less toxicity compared to tetrahydropyrimidine compounds.

Keyword: Multicomponent Reaction, Tetrahydropyrimidine, Dihydropyridne Leishmaniases