Abstract

Introduction and Goal

Although, leishmaniasis is a member of the forgotten diseases, it involves about two million people in the year, it kills 70,000 people and there are currently 12 million cases infected with the disease.

All leishmaniasis cases, except for various clinical manifestations and target organs, are caused by a parasite called Leishmania. The main hosts of disease are human, dogs and rodents.

Each drug used in the treatment of leishmaniasis has its advantages and disadvantages depending on its characteristics. However, its benefits are currently limited due to the increased parasite resistance to treatment with these drugs. Due to the development of drug resistance, the simultaneous use of two anti-Leishmania drugs with different mechanisms in most cases can cause more coverage of these resistant parasites. The design and development of the vaccine was shaped by the fact that people with asymptomatic leishmaniasis became resistant to post-clinical infections.

A number of undesirable properties of the available drugs have caused the satisfaction and appropriate response to drug therapy with these compounds is not achieved. Therefore, trying to synthesize a new drug with good anti-leishmania properties, less side effects and more economic is so important. In this research, a series of tetrahydropyrimidine derivatives were designed and synthesized. In order to increase efficiency and reduce costs and time, Biginelli method in acidic medium was used to synthesize compounds. Finally, the anti-leishmaniasis effect of compounds was investigated under *in-vitro* tests against promastigote and amastigote forms of the *L. major*.

Materials and Methods

In this project, a series of 1,2,3,4-tetrahydropyrimidine derivatives were designed, synthesized and purified. Their structural identification was performed by ^{1}H-NMR, FT-IR and Mass spectra. Their antiparasitic effect was investigated on standard strain (MRHO/IR/75/ER) of major Leishmaniasis, and also to measure the toxicity of these compounds against macrophages, mouse macrophage cells called J_{774} were used.

Results

Among 1,2,3,4-tetrahydropyrimidine derivatives against promastigote and amastigote forms *of L. major*, MV5 with IC_{50} equal to 3.15 μM and MV6 with IC_{50} equal to 5.74 μM showed the highest activity. Also, almost screened compounds showed slight toxicity against macrophages and MV5 with CC_{50} equal to 1258.41 μM is the most toxic compound.

Discussion and conclusion

According to the results, the type and position of groups in phenyl ring at C4 position of tetrahydropyrimidine ring, the type of atoms at C2 position of tetrahydropyrimidine ring, the length of the ester chain at C5 postions of tetrahydropyrimidine ring and lipophilicity character of compound had positive effect against Promastigot and Amastigot forms of parasite. Although these compounds are less effective than standard anti-leishmaniasis drugs, they can lead to more effective compounds.

Key words

Leishmaniases, 1,2,3,4-tetrahydropyrimidine, Biginelli Method.