Abstract

Introduction

Infectious diseases are disorders caused by organism such as bacteria, viruses, fungi or parasites. In the recent years bacterial infection is known as risk factor of cancer. Helicobacter pylori is one type of bacterium that can cause digestive diseases. Also, it can cause gastric cancer and Malt lymphoma or increased the risk of these cancers. Drugs that to treatment of Helicobacter pylori are used have limitations such as prolonged treatment and drug resistance. Therefore, drug development is essential in the treatment of disease. In this study, hybrid derivatives of 1,2,3-triazole and 1,2,3,4-tetrahydropyrimidine were designed and synthesized in order to inhibit the urease enzyme of Helicobacter pylori. Then the inhibitory activity of urease enzyme of these hybrid compounds was investigated.

Materials and methods

In this study after design of seven hybrid compounds of triazole and tetrahydropyrimidine, the derivatives in the three steps were synthesized through Click and Biginelli reactions and purified. Then, their structurally confirmed using spectroscopic methods of FT-IR, 1H-NMR and Mass. Thus, their anti-urease effects were evaluated by using modified Berthelot (phenol-hypochlorite) method.

Results

In general, the highest efficacy among the hybrid compound of triazole and tetrahydropyrimidine were compounds benzyl 4-(4-((1-(2-chlorobenzyl)-1H-1,2,3-triazol-4-yl)methoxy)phenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate(8) (IC_{50}= 25.02 ± 2.8096 µM) and methyl 4-(4-((1-(2-chlorobenzyl)-1H-1,2,3-triazol-4-yl)methoxy)phenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate(6) (IC_{50} = 28.09 ±4.5891µM) and lowest activity belongs to compound methyl 4-(4-((1-(2-chlorobenzyl)-1H-1,2,3-triazol-4-yl)methoxy)phenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate(3) (IC_{50}= 129.64 ± 4.6596 µM), respectively.

Discussion and conclusion

Investigation of structure-activity relationship showed that, the presence of thioxo group in the C2 position of tetrahydropyrimidine probably increases the lipophilicity and formation of disulfide bond. Also, presence of aromatic ring at ester moiety in the C5 probably increases the lipophilicity and charge transfer interaction with amino acids active site. Also, presence of methoxy group as an electron withdrawing in the *meta* position of phenyl ring in C4 position of tetrahydropyrimidine increases activity against urease enzyme. By compering synthesized hybrid compounds in this project and other triazole,

tetrahydropyrimidine compounds that reported in previous articles, concluded that hybrid compounds showed higher activity.

Keyword: Helicobacter pylori, 1,2,3-Trizole, 1,2,3,4-Tetrahydropyrimidine, Click reaction, Biginelli reaction