## Abstract

**Introduction**:

According to previously reports, leishmaniasis is one of the diseases that has caused health concerns in more than 98 countries, with a prevalence of more than 2 million people per year. Since no approved vaccine for this disease has been reported so far, and on the other hand, safe drugs with high efficacy are very limited, it is essential to find effective and biocompatible drugs. Due to the relatively high prevalence of this disease in the country, the present study aimed to synthesize, evaluate anti-leishmaniasis, and molecular modeling of new 2-amino thiazole derivatives.

**Materials and methods:**

In this study, new derivatives of 2-amino thiazole compounds were synthesized and characterized using infrared (IR), mass (MS), and proton nuclear magnetic resonance (H-NMR). The biological effects on Leishmania major parasites were evaluated at different concentrations, and $IC_{50}$ values were determined. In the next step, the structure activity relationship of the compounds was determined. Finally, the binding strength of the compounds to the enzyme N-myristoyltransferase was evaluated by molecular docking using Autodock software. It should be noted that the basis for the selection of this enzyme for molecular docking studies is its role and importance in the biological mechanisms of Leishmania major parasite, which causes the transfer of myristate saturated fatty acid from myristoyl-coA to the amino glycine terminus at the protein binding site. According to authoritative scientific articles, this enzyme plays a vital role in the life cycle of Leishmania major.

**Results:**

The results obtained from IR, NMR, and MS identification tests approved that all the structures were well synthesized. Anti-leishmaniasis effects were assessed on Leishmania major species, and the results showed that the N-((4-methyl-5-phenyl thiazol-2-yl) carbamothiol) cyclopropane carboxamide (4c) with $IC_{50}$ 38.54±0.45 µg / ml had the best effect as the anti-leishmanial agent. Also, the results of molecular docking showed that the 4b compound had the highest binding energy of -8/45 kcal/mol in binding to N-myristoyltransferase enzyme. Also, the presence of bromine atoms in compound 4b allows hydrophobic interaction with Gly205 in the binding pocket.

**Discussion and Conclusion:**

Based on the obtained results, compound 4c had a stronger anti-leishmaniasis effect than other compounds. In general, the substitution pattern of 5-methyl-4-phenyl on the thiazole ring seems

to be a more appropriate model for the development of stronger compounds. According to the molecular docking data, compound 4b had the highest interaction energy, which solves the problem of solubility for this compound for drug development with higher efficacy. Also, considering the effects of bromine substitution on the phenyl ring in compound 4b, it seems that the design of different substituents in the phenyl ring can be important in the development of stronger anti-Leishmania compounds.

**Keywords**: Leishmaniasis, Synthesis, MTT, 2-Amino Thiazole