

Determination of the Inhibitory Effects of N-Methylpyrrole Derivatives on Glutathione Reductase Enzyme

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Abstract : Glutathione reductase (GR) is a crucial antioxidant enzyme which is responsible for the maintenance of the antioxidant GSH (glutathione) molecule. Antimalarial effects of some chemical molecules are attributed to their inhibition of GR; thus inhibitors of this enzyme are expected to be promising candidates for the treatment of malaria. In this work, GR inhibitory properties of N-Methylpyrrole derivatives are reported. Firstly, GR was purified by means of affinity chromatography using 2',5'-ADP-Sepharose 4B as ligand. Enzymatic activity was measured by Beutler's method. Synthesis of the compounds was approved by thin layer chromatography and column chromatography. Different inhibitor concentrations were used and all compounds were tested in triplicate at each concentration used. It was found that all compounds have better inhibitory activity than the strong GR inhibitor N,N-bis(2-chloroethyl)-N-nitrosourea, especially three molecules, 8m, 8n, and 8q, are the best among them with low micromolar I_{50} values. Findings of our study indicate that these Schiff base derivatives are strong GR inhibitors which can be used as leads for designation of novel antimalaria candidates.

Keywords : glutathione reductase, antimalaria, inhibitor, enzyme

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