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The Effect of Artesunate on Myeloperoxidase Activity of Human Polymorphonuclear Neutrophil

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Abstract : Myeloperoxidase is the most abundant enzyme found in the polymorphonuclear neutrophil and is known to play a central role in the host defense system of the leukocyte. The enzyme has been reported to interact with some drugs to generate free radical which inhibits its activity. This study investigated the effects of artesunate on the activity of the enzyme and the subsequent effect on the host immune system. In investigating the effects of the drugs on myeloperoxidase, the influence of concentration, pH, partition ratio estimation and kinetics of inhibition were studied. This study showed that artesunate is concentration-dependent inhibitor of myeloperoxidase with an IC50 of 0.078mM. Partition ratio estimation showed that 60 enzymatic turnover cycles are required for complete inhibition of myeloperoxidase in the presence of artesunate. The influence of pH on the effect of artesunate on the enzyme showed least activity of myeloperoxidase at physiological pH. The kinetic inhibition studies showed that artesunate caused a competitive inhibition with an increase in the Km value from 0.12mM to 0.26mM and no effect on the Vmax value. The Ki value was estimated to be 2.5mM. The results obtained from this study show that artesunate is a potent inhibitor of myeloperoxidase and it is capable of inactivating the enzyme. It is considered that the inhibition of myeloperoxidase in the presence of artesunate as revealed in this study may partly explain the impairment of polymorphonuclear neutrophil and consequent reduction of the strength of the host defense system against secondary infections.

Keywords : myeloperoxidase, artesunate, inhibition, nuetrophill
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