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Immunosupressive effect of chloroquine through the inhibition of myeloperoxidase

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Polymorphonuclear neutrophils (PMNs) play a crucial role in a variety of infections caused by bacteria, fungi, and parasites. Indeed, the involvement of PMNs in host defense against *Plasmodium falciparum* is well documented both *in vitro* and *in vivo*. Many of the antimalarial drugs such as chloroquine used in the treatment of human malaria significantly reduce the immune response of the host *in vitro* and *in vivo*. Myeloperoxidase is the most abundant enzyme found in the polymorphonuclear neutrophil which plays a crucial role its function. This study was carried out to investigate the effect of chloroquine on the enzyme. In investigating the effects of the drug on myeloperoxidase, the influence of concentration, pH, partition ratio estimation and kinetics of inhibition were studied.

This study showed that chloroquine is concentration-dependent inhibitor of myeloperoxidase with an IC_{50} of 0.03mM. Partition ratio estimation showed that 40 enzymatic turnover cycles are required for complete inhibition of myeloperoxidase in the presence of chloroquine. The influence of pH on the effect of chloroquine on the enzyme showed significant inhibition of myeloperoxidase at physiological pH. The kinetic inhibition studies showed that chloroquine caused a non-competitive inhibition with an inhibition constant K_i of 0.27mM.

The results obtained from this study shows that chloroquine is a potent inhibitor of myeloperoxidase and it is capable of inactivating the enzyme. It is therefore considered that the inhibition of myeloperoxidase in the presence of chloroquine as revealed in this study may partly explain the impairment of polymorphonuclear neutrophil and consequent immunosuppression of the host defense system against secondary infections.

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