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Mechanochemical Synthesis, In vivo Anti-malarial and Safety Evaluation of Amodiaquine-zinc Complex

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SUMMARY

So far, some prospective metal-based anti-malarial drugs have been developed. The mechanochemical synthesis and characterization of Zn (II) complex with amodiaquine and its anti-malarial efficacy on *Plasmodium berghei*-infected mice and safety evaluation were described in this study.

Solvent-free mechanochemical synthesis and characterization of Zn (II) complex with amodiaquine as well as its anti-malarial efficacy on NK-65 *Plasmodium berghei*-infected mice and safety were evaluated.

Derivatization of amodiaquine with zinc (II) ion enhanced the activity of the drug through significant ($p < 0.05$) enhancement of parasitemia suppression in established malaria infection in comparison with the controls, while its capacity to clear malaria parasite was similar to that of chloroquine. A significant reduction in the liver, kidney and small intestinal activities of alkaline phosphatase, lactate dehydrogenase and alanine and aspartate aminotransferases was observed, while their levels increased significantly in the plasma. Levels of PCV, Hb, RBC and lymphocytes were significantly reduced ($p < 0.05$), and significant elevation ($p < 0.05$) in WBC and neutrophil concentrations across all the treatment groups when compared with control was observed.

The result indicates that coordination of zinc (II) to amodiaquine by mechanical induction improved its anti-malarial activity, while the alterations in the investigated biochemical parameters suggest functional and structural toxicity. Thus, Zn (II) complex with amodiaquine may not be completely safe for prolonged and repeated use as an oral anti-malarial remedy.

Key words: **antimalarial, amodiaquine-zinc, mechanochemical synthesis, *in vivo* and safety evaluation**

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