PREPARATION AND CHARACTERIZATION OF NANOCRYSTAL SUSPENSIONS CONTAINING DECOQUINATE FOR EXPERIMENTAL TREATMENT OF MALARIA

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INTRODUCTION: Malaria remains one of the most challenging parasitic diseases in the world. Decoquinate (DQ), a quinoline derivative that acts on the *bc$_1$* complex of *Plasmodium* ssp. cytochrome, exhibits potent antimalarial activity and a favourable safety profile. However, DQ has limited aqueous solubility and consequently low absorption and bioavailability via the oral route. In this context, drug delivery systems based on nanocrystals (NCs) emerge as a promising strategy to overcome these biopharmaceutical limitations. **METHODS:** This study aimed to prepare and characterize stabilized DQ nanocrystal suspensions, designated DQ-NC$_{0.5}$ and DQ-NC$_1$, and to evaluate their antimalarial activity against multiple developmental stages of *Plasmodium ssp*. **RESULTS:** Both DQ-NC$_{0.5}$ and DQ-NC$_1$ suspensions contained NCs with particle size of approximately 200 nm, a zeta potential of around –20 mV, and a DQ content around 70–80%. Additionally, DQ inhibited the growth of asexual blood stages of *P. falciparum*, with IC$_{50}$ values of 1.1 ± 1.1 nM for DQ-NC$_{0.5}$ and 0.9 ± 0.4 nM for DQ-NC$_1$.DQ-NCs also inhibited the formation of *P. berghei* zygotes and tissue schizonts. Both NCs suspensions were faster in the onset of action against asexual blood stages *in vitro*, resulting in a more rapid reduction in parasitemia compared with unformulated DQ. Notably, DQ-NC$_{0.5}$ was approximately 40-fold more potent in inhibiting the conversion of gametocytes into zygotes, showing activity comparable to atovaquone and suggesting a potential transmission-blocking effect. *In vivo*, oral and intraperitoneal administration of DQ-NCs led to parasitemia suppression close to 0% on day 7 post-infection compared with untreated controls. Furthermore, oral treatment with the nanocrystal suspensions extended median survival beyond 30 days. **CONCLUSION:** We conclude that nanocrystals represent a valuable technological approach for the pharmaceutical development of DQ as a promising antiplasmodial agent for therapeutic activities.

Keywords: Malaria, *Plasmodium ssp.*, antimalarial activity, decoquinate, nanocrystals, antiplasmodial agent, treatment of malaria.

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