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Oral administration of amphotericin B nanoparticles: Antifungal activity, bioavailability and toxicity in rats

Bushra T Al Quadeib, Mahasen A Radwan, Lidija Siller and **Matthew C Wright**
King Saud University, Saudi Arabia

Amphotericin B (AMB) is used most commonly in severe systemic life-threatening fungal infections. There is currently an unmet need for an efficacious (AMB) formulation amenable to oral administration with better bioavailability and lower nephrotoxicity. Novel PEGylated polylactic-polyglycolic acid copolymer (PLGA-PEG) nanoparticles (NPs) formulations of AMB were therefore studied for their ability to kill Candida albicans. The antifungal activity of AMB formulations was assessed in C. albicans. Its bioavalability was investigated in nine groups of rats (n¼6). Toxicity was examined by an *in vitro* blood hemolysis assay, and *in vivo* nephrotoxicity after single and multiple dosing for a week by blood urea nitrogen (BUN) and plasma creatinine (PCr) measurements. The MIC of AMB loaded to PLGA-PEG NPs against C. albicans was reduced two to threefold compared with free AMB. Novel oral AMB delivery loaded to PLGA-PEG NPs was markedly systemically available compared to Fungizone® in rats. The addition of 2% of GA to the AMB formulation significantly ($p<0.05$) improved the bioavailability from 1.5 to 10.5% and the relative bioavailability was 47.90% that of Fungizone. The novel AMB formulations showed minimal toxicity and better efficacy compared to Fungizone_. No nephrotoxicity in rats was detected after a week of multiple dosing of AMB NPs based on BUN and PCr, which remained at normal levels. An oral delivery system of AMB-loaded to PLGA-PEG NPs with better efficacy and minimal toxicity was formulated. The addition of glycyrrhizic acid (GA) to AMB NPs formulation resulted in a significant oral absorption and improved bioavailability in rats.

Recent Publications

1. M A Radwana, B T Al Quadeib, N M Aloudah, H Y Aboul Enein (2010) Pharmacokinetics of ketorolac loaded to polyethylcyanoacrylate nanoparticles using UPLC MS/MS for its determination in rats. International Journal of Pharmaceutics. 397(1-2):173-178.
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4. Bushra T AL Quadeib, Mahasen A Radwan, Lidija Siller, Benjamin Horrocks, Matthew C Wright (2015) Stealth amphotericin b nanoparticles for oral drug delivery: *in vitro* optimization. Saudi Pharmaceutical Journal. 23(3):290-302.
5. Mahasen A Radwan, Bushra T Al Quadeib, Lidija Siller, Matthew C Wright, Benjamin Horrocks (2017) Oral administration of amphotericin B nanoparticles: antifungal activity, bioavailability and toxicity in rats. Drug delivery. 24(1): 40-50.

bquadeib@ksu.edu.sa