



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

Editorial:

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 poly(lactic-co-glycolic acid) copolymer (PLGA-PEG) nanoparticles (NPs) formulations of AMB were therefore studied for their ability to kill *Candida albicans* (*C. albicans*). The antifungal

activity of AMB formulations was assessed in *C. albicans*. Its bioavailability was investigated in nine groups of rats (n=6). 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 4790% 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.