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## ACCEPTED MANUSCRIPT

# Enhanced delivery of fixed-dose combination of synergistic antichagasic agents posaconazole-benznidazole based on amorphous solid dispersions

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#### Abstract

Posaconazole (PCZ) and benznidazole (BNZ) are known to show synergetic effect in treating the acute and chronic phases of Chagas disease, a neglected parasitic disease. However, as both compounds are poorly water soluble, the development of amorphous solid dispersions (ASDs) of a PCZ/BNZ fixed-dose combination in a water-soluble polymer becomes an attractive option to increase their apparent solubility and dissolution rate, potentially improving their oral bioavailability. The initial approach was to explore solvent evaporated solid dispertion (SD) systems for a PCZ/BNZ 50:50 (wt. %) combination at several total drug loading levels (from SD with 10% to 50% drug loading) in water-soluble carriers, including polyvinylpyrrolidone (PVP K-30) and vinylpyrrolidone–vinyl acetate copolymer (PVPVA 64). Based on comparison of non-sink *in vitro* dissolution performance, ASD systems based Download English Version:

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