

Improved Solubility of Ivermectin by Complexation with Cyclodextrins and Amino acids †

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Abstract: Ivermectin (IVM) is an antiparasitic drug derived from avermectin with broad-spectrum activity against ectoparasites and endoparasites. IVM is used worldwide as a drug of choice for treating Lymphatic Filariasis and Onchocerciasis, two neglected infectious diseases. However, it is a poorly water-soluble drug that shows an unpredictable therapeutic response caused by a very low oral bioavailability. In this study, the effect of binary and ternary systems obtained with amino acids, and oligosaccharides was evaluated as an alternative to improve the aqueous solubility of IVM. The most promising solubilizing excipients were selected by solubility studies, while the complexes' formation constants were determined by phase solubility studies. The results revealed that the aqueous solubility was increased with binary systems using the amino-acids arginine (ARG) and glutamic acid, and the oligosaccharides hydroxypropyl- β -cyclodextrin (HP β CD), γ -cyclodextrin (γ CD) and sulfobutylether- β -cyclodextrin as ligands. The ternary systems with the combination HP β CD + ARG and γ CD + ARG exhibited a synergistic effect resulting in an 11-fold and 8-fold, respectively, improvement of the aqueous solubility of IVM. Thus, these supramolecular systems exhibited promising properties for developing pharmaceutical oral formulations of IVM with increased solubility.

Keywords: ivermectin; supramolecular systems; arginine; glutamic acid; hydroxypropyl- β -cyclodextrin; γ -cyclodextrin; sulfobutylether- β -cyclodextrin; solubility.

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Conflicts of Interest

The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.