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Original Research Paper

Development of albendazole sulfoxide-loaded Eudragit microparticles: A potential strategy to improve the drug bioavailability

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ABSTRACT

Albendazole sulfoxide (ABZSO), a broad spectrum anthelmintic drug extensively used in veterinary medicine, exhibits a low and erratic bioavailability due to its poor solubility in biological fluids. The aims of this study were the development, physicochemical characterization, and *in vitro* release profile evaluation of ABZSO-loaded Eudragit RS PO® microparticles (MPs) in order to improve the rate of dissolution and the dissolved percentage of the drug in pH 7.4. MPs were successfully obtained by the emulsification/solvent evaporation method, achieving entrapment efficiency and process yield of about 60% and mean size of 254 nm. The *in vitro* release profile study showed that dissolution of ABZSO followed a pseudo-second order kinetics and MPs were able to increase significantly ($p < 0.05$) the rate of dissolution of ABZSO compared to the micronized and non-micronized free drug, what could lead to an improvement in bioavailability and, consequently, in the antiparasitic activity.

1. Introduction

Helminthes can be classified as cylindrical (nematodes) and plate (cestodes and trematodes) worms. Helminthic infections are found worldwide, especially in tropical areas [1], constituting a serious sanitary problem in human and veterinary medicine, besides causing great economical problems [2]. Several parasites are very important to public health due to their high zoonotic potential, like the nematodes *Toxocara canis* and *Ancylostoma braziliensis* and the protozoans *Cryptosporidium*, *Leishmania*, and *Toxoplasma* [3]. On the other hand, there are the cestodes of *Taenia* gender, especially *Taenia solium*, responsible for causing cysticercosis, a disease found in animals and human beings. *Cysticercus cellulosae*, the larval stage of *T. solium*, is responsible for neurocysticercosis which is a disease caused by the presence of cysts containing this larva in the central nervous systems and could cause serious illness to the patient, even death [4].

Benzimidazole compounds are especially effective against nematodes found in the gastrointestinal tube in combating adult worms besides their larvae and eggs [1]. They are also highly effective against lung worms [5]. Their mechanism of action is related to several biochemical changes, particularly the inhibition of β-tubulin, leading to the suspension of cellular processes like mitotic division and transport of nutrients, and also the inhibition of the fumarate reductase enzyme in mitochondrial reactions blocking, in this manner, the metabolic route of the parasite [1,6].

Albendazole sulfoxide (ABZSO), a broad spectrum antiparasitic drug from the benzimidazole group, is used to control infections by nematodes, cestodes, and trematodes in big and small ruminants, besides companion animals. Apart from their broad spectrum, benzimidazole compounds have the advantage of causing relatively low toxicity to hosts compared to other antiparasitic drugs [7–9].

ABZSO is almost insoluble in water and sparingly soluble in water-miscible solvents like ethanol and propylene glycol. Usually, it is administered at a dose of 7.5 mg kg^{-1} and its bioavailability varies from 36.8% to 40.5% [9]. Besides, this drug is well distributed in the body after intravenous administration, achieving volume of distribution values ranging from 0.67 to 1.2 L kg^{-1} for cattle and sheep, respectively [10,11], due to its low and erratic bioavailability, when administered by other routes, a high dosage is required to achieve plasmatic therapeutic levels [12].

One of the advantages of micro- and nanoencapsulation processes is their ability to improve bioavailability of poorly water-soluble drugs [13,14]. According to Devalapally et al. [15], in general, conventional formulations show low and irregular bioavailability of poorly water-soluble drugs. Microencapsulation processes can be used to improve pharmacokinetic properties of these compounds. The reduced size of microparticles (MPs) and the consequent increase in surface area can substantially increase the rate

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