Synthesis and structural characterization of the Carvacryl acetate and (2-Hydroxypropyl)-β-cyclodextrin inclusion complex

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Abstract

Carvacryl acetate (CarvAc) is a semisynthetic derivative of Carvacrol, a monoterpene isolated from *Lamiaceae* family, which presents activity against *Schistosoma mansoni*. To improve its biodisponibility and pharmacokinetics properties, here we aim to synthetize and characterize the (2-Hydroxypropyl)-β-cyclodextrin (HP-β-CD) and CarvAc inclusion complex (IC).

Introduction

Control and treatment of Schistosomiasis is based only on praziquantel therapy, raising the urgent development of new antischistosomal drugs. CarvAc presets *in vitro* anthelmintic activity against *S. mansoni* at 6.25 μg/mL [2]. The HP-β-CD IC increases the biodisponibility of poor soluble drugs and it was produced through kneading, the first unit operation in extrusion and spheronization process [3].

Results and Discussion

IC were prepared according to Hedges [4], with 1:1 mol ratio of CarvAc and HP-β-CD, milled in a mortar with ethanol, and kept at 25°C, overnight. The frequencies for IC observed at 3392.8, 2922.1, 1159.2 and 1028,0 cm^{-1} which corresponds to the symmetric and antisymmetric stretching of v[OH], v[CH2], v[C–C] and bending vibration of v[O–H]. Comparing IC to HP-β-CD frequencies, we observed a range increasing due to benzyl ring electronic cloud from CarvAc inside the IC cavity (Fig. 1).

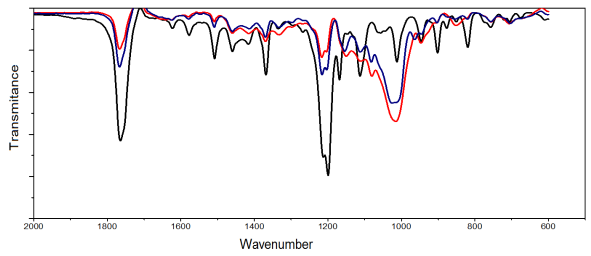

Figure 1. FT-IR spectra, CarvAc in black, HP-β-CD in red, and TM in blue.

Thermogravimetric analysis (TGA) was measured from 25°C to 700°C. HP-β-CD exhibits two separate weight losses due to loss of water molecules at 97°C, which were located in the cavity of HP-β-CD, and followed by the decomposition of macrocycles at 335°C. The IC underwent weight losses in three stages and lost 90% of its original weight at 700°C, in the endothermic process associated with the water release; the exothermic process from the crystallization and fusion after all.

From XRD patterns, we can conclude that CarvAc and HP-β-CD are crystalline solids however a structure complete amorphization is detected for the IC. Particle size and distribution were range 24.032 ± 0.644 to 71.218 ± 0.580 nm and a zeta potential equal to -27.1667 ± 0.3885, revealing a trend to aggregate. The SEM images clearly show that IC (Fig. 2a) were formed due to hollow structures with a thin HP-β-CD shell, either opened or closed (Fig. 2b).

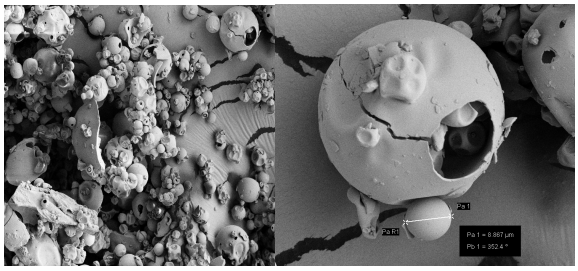

Figure 2. SEM images of (a) IC and (b) hollow structures, with size indicates by white line.

Conclusions

The FTIR spectra significantly indicate the formation of the inclusion complex. SEM images are an unequivocal proof of the IC type comprises a Trojan microparticles formation. Supramolecular associations, as nanostructures carried into microparticles, modulate the kinetic releases of drugs entrapped in the nanoparticles. The open structures evidence the easy delivery of CarvAc, however *in vivo* assays are required to check the effectiveness of TM.

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