Characterization Of Albendazole – Random Methyl Beta-Cyclodextrin Binary Systems By Infrared Spectroscopy

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Introduction: The purpose of this study is to investigate the host-guest interaction in solid state between anthelmintic drug albendazole and random methyl-beta-cyclodextrin using spectrophotometric method.
Material and method: Binary systems between albendazole and random methyl-beta-cyclodextrin were prepared in four molar ratios using two laboratory methods and the host-guest interaction was characterized by Fourier transform infrared spectroscopy.
Results: The absorption spectra of albendazole display some absorption bands in the 1800–1000 cm^{-1} domain and the absorption spectra of random methyl-beta-cyclodextrin present a wide absorption band the 1200–1000 cm^{-1} region. In order to examine the spectral changes of the binary systems, five characteristic bands in albendazole spectrum were chosen and their absorbances were represented for each molar ratio of albendazole in the binary systems.
Conclusions: The Fourier transform infrared spectroscopy analysis of the binary system reveals an emphasis of molecular interaction between albendazole and cyclodextrin as the amount of cyclodextrin in the binary system is increasing.

Keywords: albendazole, cyclodextrin, infrared spectroscopy, molecular interaction

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Introduction

Albendazole (ABZ) is a broad-spectrum anthelmintic benzimidazole derivative [1]. Albendazole is practically insoluble in water [2], which limits its oral bioavailability [3–5]. Also, the hydrophobicity of ABZ is a major drawback for the treatment of systemic helminthic infections [3,4].

The solubility and consequently, the bioavailability of a pharmacon may be successfully improved by complexation with cyclodextrins [5,6]. Random methyl beta-cyclodextrin (RAMEB) is a beta-cyclodextrin derivative with remarkable properties of forming inclusion complexes with pharmacons [5,6], used also in our previous researches regarding the influence of complexation with RAMEB upon the physico-chemical properties of ABZ [7]. Fourier transform infrared spectroscopy (FTIR) may be used to emphasize the formation of an inclusion complex involving cyclodextrin and to reveal the molecular interaction between the cyclodextrin and the guest molecules [8–13]. In present study, the possibility of formation of molecular interaction between ABZ and RAMEB is investigated using Fourier transform infrared spectroscopy.

Material and method

Albendazole, methyl[5-(propylthio)-1-H-benzimidazol-2-yl] carbamate was purchased from Biesterfeld Siemgluess, Hamburg, Germany. Random methyl-beta-cyclodextrin (RAMEB) (DS~12) was acquired from Cyclolab R&D (Budapest, Hungary). Other chemical reagents were of analytical grade purity according to Romanian Pharmacopoeia 10th ed. and to European Pharmacopoeia 7th ed.

Preparation of binary systems

Binary systems were prepared in four molar ratios (ABZ : RAMEB molar ratio = 2:1, 1:1, 1:2, 1:3).

Physical mixtures (PM): the calculated and exactly weighted amounts of ABZ and RAMEB were pulverized in a ceramic mortar and carefully mixed. Afterward, the products were sieved (100 μm).

Kneaded products (KP): the physical mixtures of ABZ and RAMEB were wetted with the same quantity of ethanol-water (1:1, w/w) mixture under continuous kneading until the evaporation of the bulk solvent. After drying at room temperature, the products were dried at 105 °C; subsequently they were pulverized and sieved.

Fourier Transform Infrared Spectroscopy

The Fourier transform infrared spectra of ABZ, RAMEB and their binary systems were recorded using a JASCO FT/IR - 670 PLUS spectrometer, at room temperature. The resolution was 4 cm^{-1}, the wave number range extending from 2000 cm^{-1} to 400 cm^{-1}. In order to obtain a better S/N ratio, accumulation of 64 spectra was performed during each record. The samples were included in KBr pellet.

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Table I. The values of the molar fractions of albendazole in the binary systems

	Molar fraction of albendazole in the binary systems			
	Molar ratio			
Binary system	2:1	1:1	1:2	1:3
ABZ - RAMEB	0.667	0.500	0.333	0.250

Results

Preparation of binary systems

For each binary system consisting of ABZ and RAMEB, the molar fraction of ABZ was calculated and the results are presented in Table I.

Fourier Transform Infrared Spectroscopy

Albendazole presents a simple absorption spectrum, characterized by the presence of a few absorption bands in the 1800–1000 cm^{-1} region (Figure 1a). In the RAMEB spectrum, the presence of a wide absorption band in the 1200–1000 cm^{-1} region is observed, attributable to the glucopyranosic ring (Figure 1b).

The spectra of the physical mixture are presented in Figure 2 (a–c) and the spectra of the kneaded products are presented in Figure 3 (a–d).

In order to observe the modification of spectra due to complexation, five absorption bands in ABZ spectrum, were chosen. These bands do not even partially overlap to the RAMEB spectrum. The five absorption bands correspond to the following wave numbers: 1725, 1590, 1525, 1320 and 1270 cm^{-1}. For each of this wave numbers, the values of the absorbances of ABZ are represented in the case of each binary system, depending on the values of the molar fractions of ABZ in the corresponding binary system. Figure 4 (a–e) and Figure 5 (a–e) reveal the absorbances corresponding to each molar fraction of ABZ for each absorption band chosen in the experiment. Figure 4 correspond to the physical mixture products and Figure 5 refers to the kneaded products.

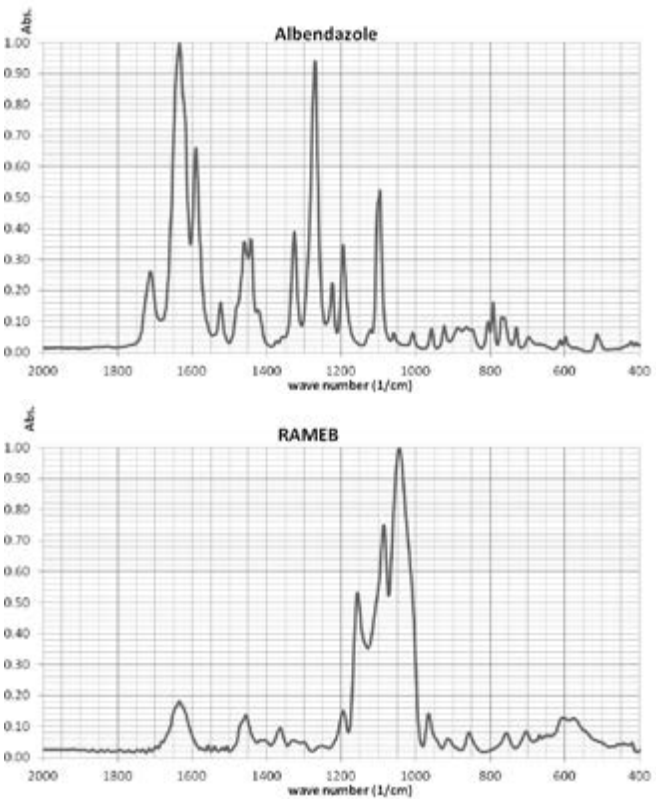

Fig. 1. FT IR spectra of albendazole (a) and of RAMEB (b)

Discussions

Fourier Transform Infrared Spectroscopy

The spectral changes caused by complexation [5,8] are difficult to emphasize due to the simple spectra of albendazole and the cyclodextrin [11,13]. From the graphics presented in Figure 4 and Figure 5 one may observe a positive, systematic deviation from the Bouguer-Lambert-Beer relationship. This result may be interpreted in terms of for-

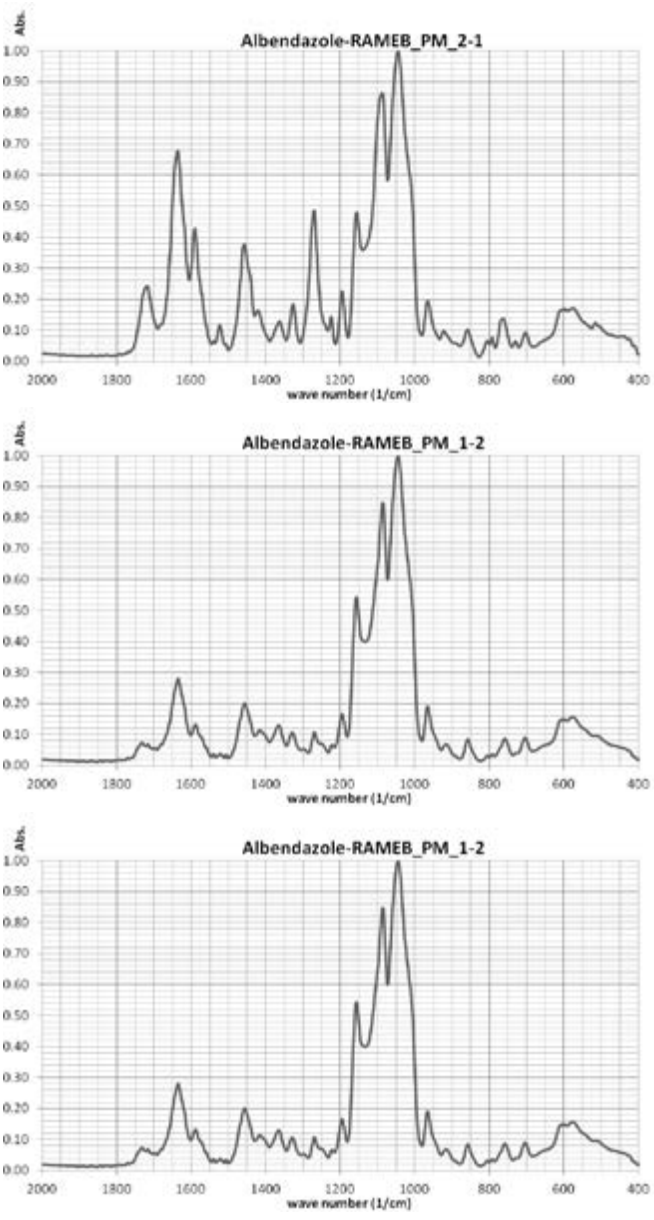

Fig. 2. FT IR spectra of physical mixtures: PM 2:1 (a), PM 1:1 (b), PM 1:2 (c)

mation of partial inclusion complexes between ABZ and RAMEB.

Conclusions

The Fourier transform infrared spectroscopy sustains the hypothesis of formation of partial inclusion complexes be-

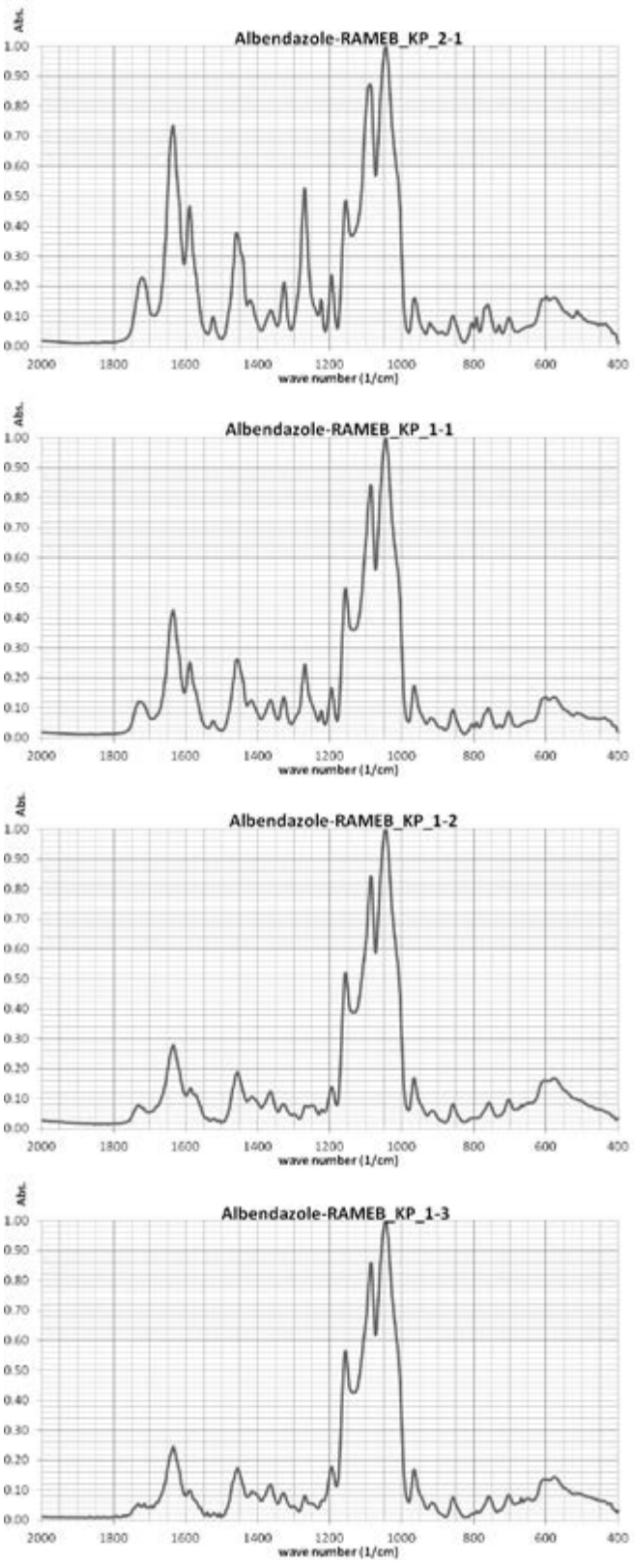

Fig. 3. FT IR spectra of kneaded products: KP 2:1 (a), KP 1:1 (b), KP 1:2 (c), KP 1:3 (d)

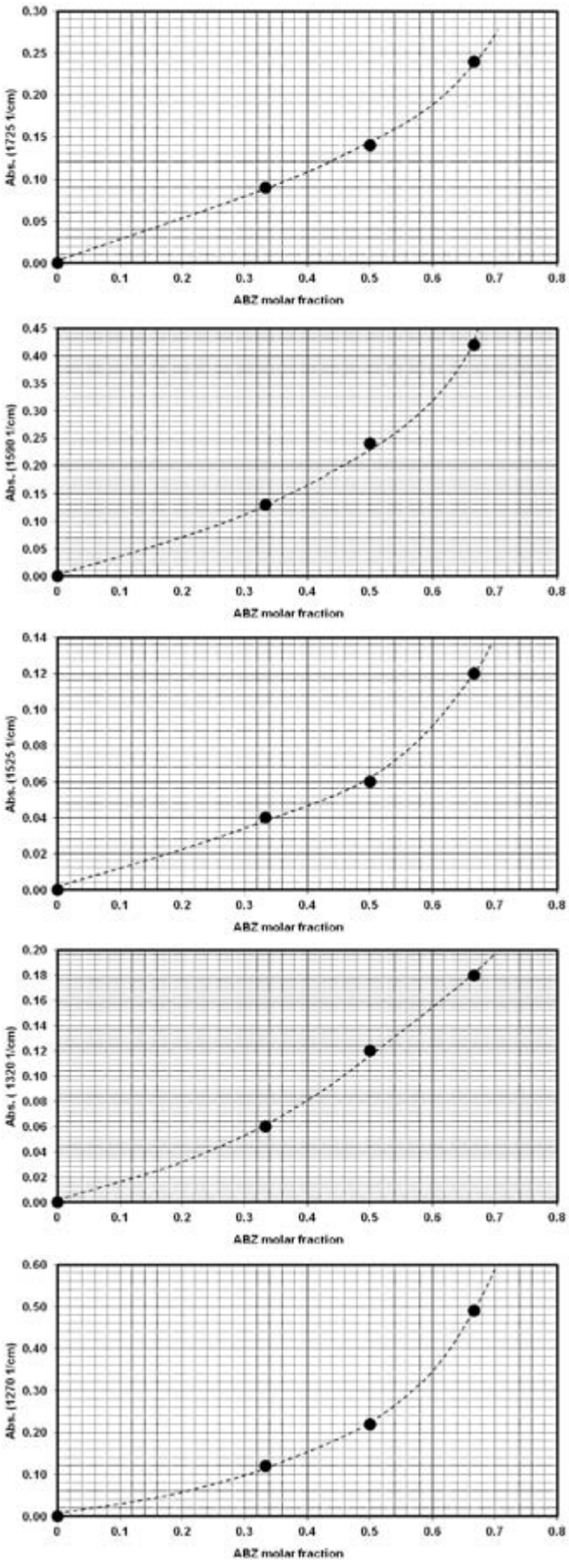

Fig. 4. The representation of absorbances of characteristic bands of ABZ for PM binary systems: 1725 cm^{-1} absorption band (a), 1590 cm^{-1} absorption band (b), 1525 cm^{-1} absorption band (c), 1320 cm^{-1} absorption band (d), 1270 cm^{-1} absorption band (e)

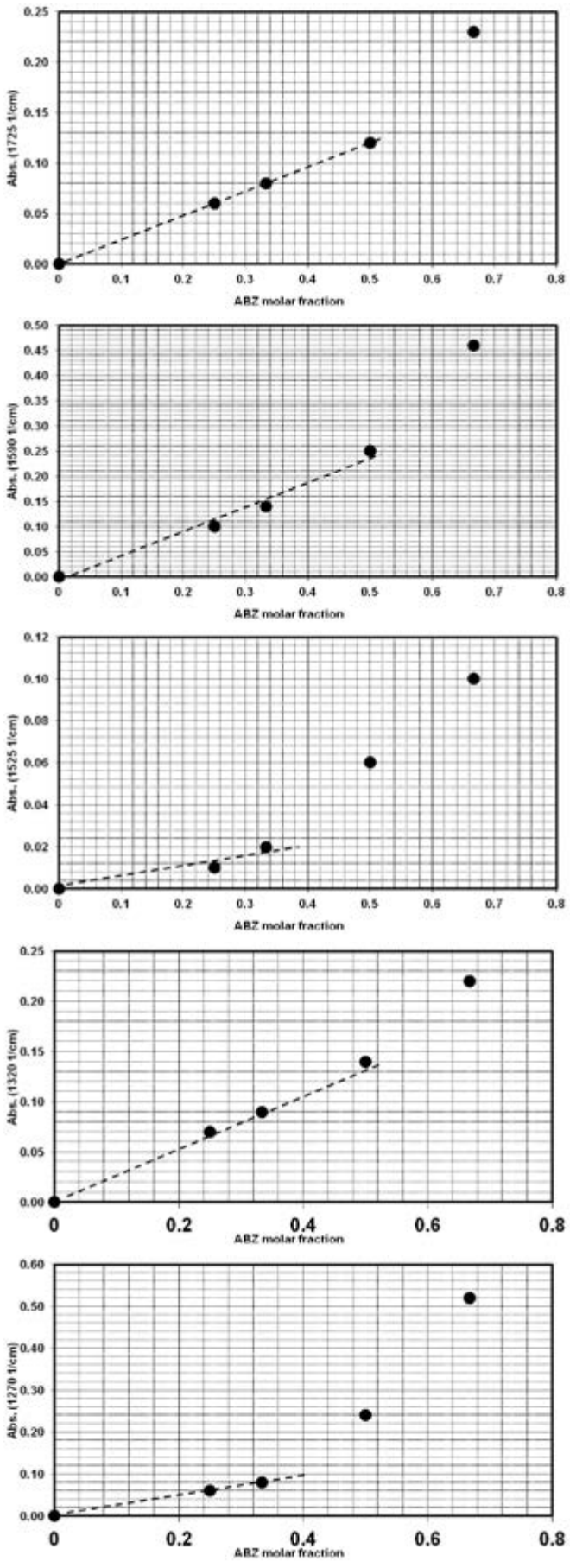

Fig. 5. The representation of absorbances of characteristic bands of ABZ for KP binary systems: 1725 cm^{-1} absorption band (a), 1590 cm^{-1} absorption band (b), 1525 cm^{-1} absorption band (c), 1320 cm^{-1} absorption band (d), 1270 cm^{-1} absorption band (e)

tween ABZ and RAMEB. The FTIR analysis emphasized a systematic deviation from the Bouguer-Lambert-Beer relationship of binary system, with the decrease of molar fraction of albendazole.

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