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Study on physical and chemical behavior of carbamazepine-β – cyclodextrin inclusion complex

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Abstract

Carbamazepine, (CBZ) is a sodium channel blocker recommended for the treatment of epilepsy and trigeminal neuralgia for over 40 years. Cyclodextrins are the most suitable candidate for the inclusion of CBZ due to the dimension of the internal cavity in which the active drug can fit properly. The aim of the current study is to evaluate the ability of β - cyclodextrin to include CBZ. The kneading method of complexation in solid state (1:1 molar ratio) was used to obtain the inclusion complex. For comparison a simple physical mixture was prepared. Physical and chemical characterization of raw materials, physical mixture and the inclusion complex were made using Fourier transform – infrared spectroscopy, X-ray diffraction, scanning electron microscopy and simultaneous thermal analysis. The results obtained using all these analytical techniques, proved that carbamazepine forms stable complexes with β-cyclodextrin in 1:1 molar ratio, and the complexation was almost complete.

Keywords: β-cyclodextrin; carbamazepine; kneading method.

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Method

FT-IR spectra were recorded using a JASCO FTIR-4200 spectrometer with an ATR PRO450-S accessory, on a spectral range of 4000-400 cm^{-1} and a resolution of 4 cm^{-1}.

Powder X-ray diffraction (XRD) patterns were recorded on a Rigaku Ultima IV diffractometer, with CuKα radiation λ = 1.5406 Å, in the 2θ = 5-60° range, with a scan speed of 5°/min and a 0.02 step size, at 40 kV and 30 mA.

Scanning electron microscopy (SEM) measurements were carried out in a FEI Quanta 3D FEG.

Thermal measurements were performed on a Netzsch STA 449 F1 Jupiter Simultaneous Thermal Analyzer apparatus in argon dynamic atmosphere, with a heating rate of 5 $^{o}C\ min^{-1}$ and the sample mass of ~ 5 mg.

Samples notation: carbamazepine – CBZ, beta-cyclodextrin - β-CD, CBZ- β-CD physical mixture, CBZ- β-CD inclusion complex.

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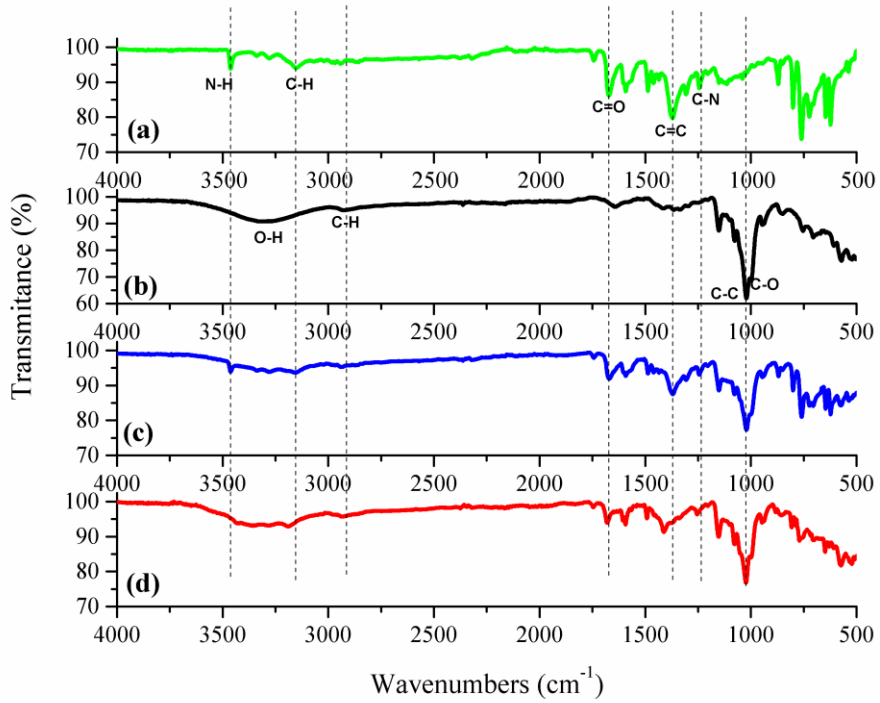
Results and Discussion

FTIR spectra of (a) CBZ, (b) β – CD, (c) CBZ - β - CD physical mixture and (d) CBZ - β - CD inclusion complex



The FTIR spectrum of physical mixture displays all characteristic peaks of individual compounds. The FTIR spectrum of inclusion complex shows a significantly decreases in intensity of the spectral zone of CBZ, due to its inclusion in the CD cavity.

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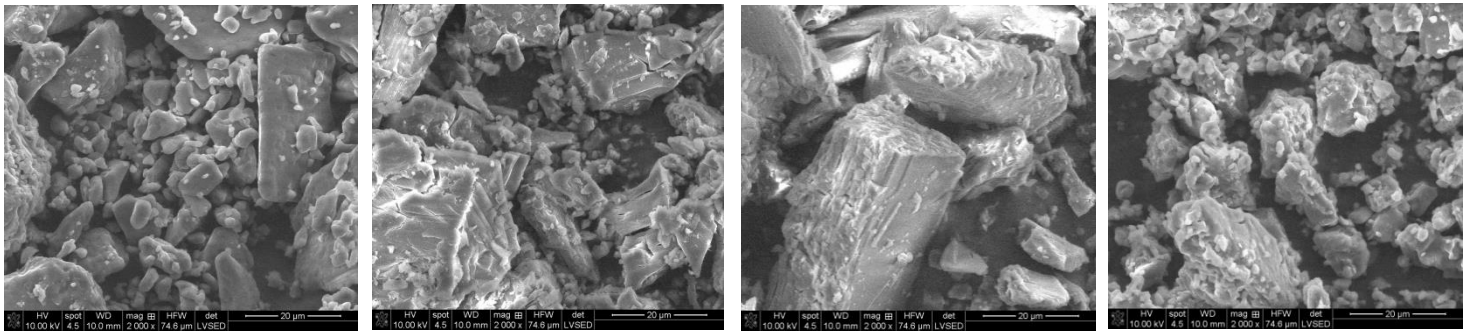
SEM analysis



(a) (b) (c) (d)

The SEM images for (a) CBZ; (b) β – CD; (c) CBZ - β - CD physical mixture; (d) CBZ - β - CD inclusion complex, at 2000x magnification

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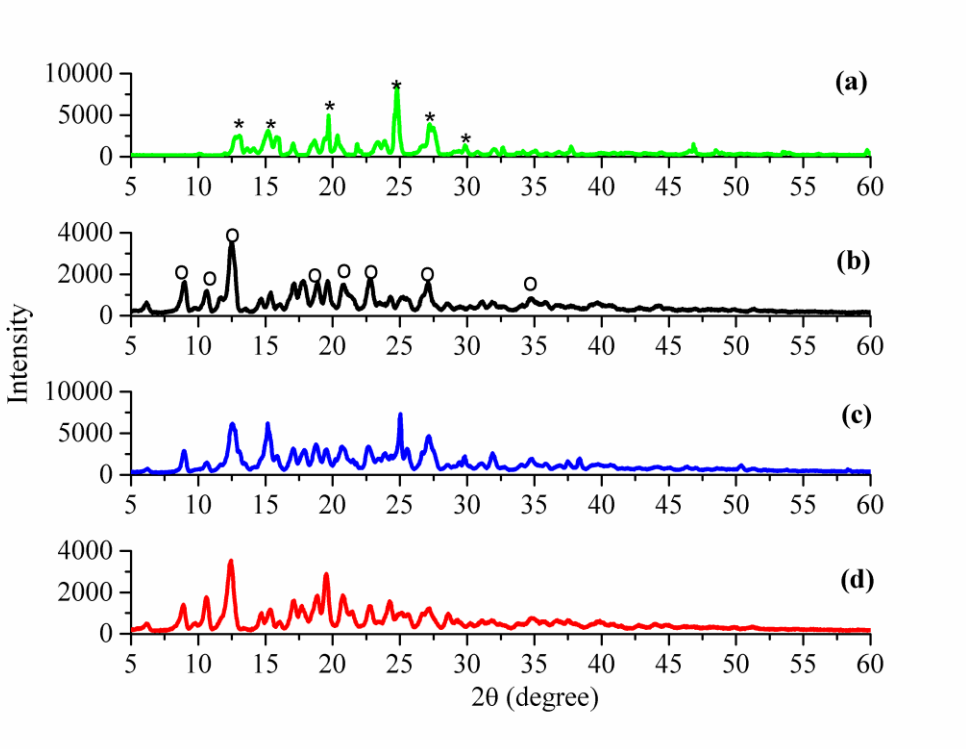
XRD analysis of (a) CBZ, (b) β – CD, (c) CBZ - β - CD physical mixture and (d) CBZ - β - CD inclusion complex



The XRD pattern of the inclusion complex shows the disappearance of the XRD pattern of CBZ, which supports the assumption of a stronger interaction between CBZ and β – CD.

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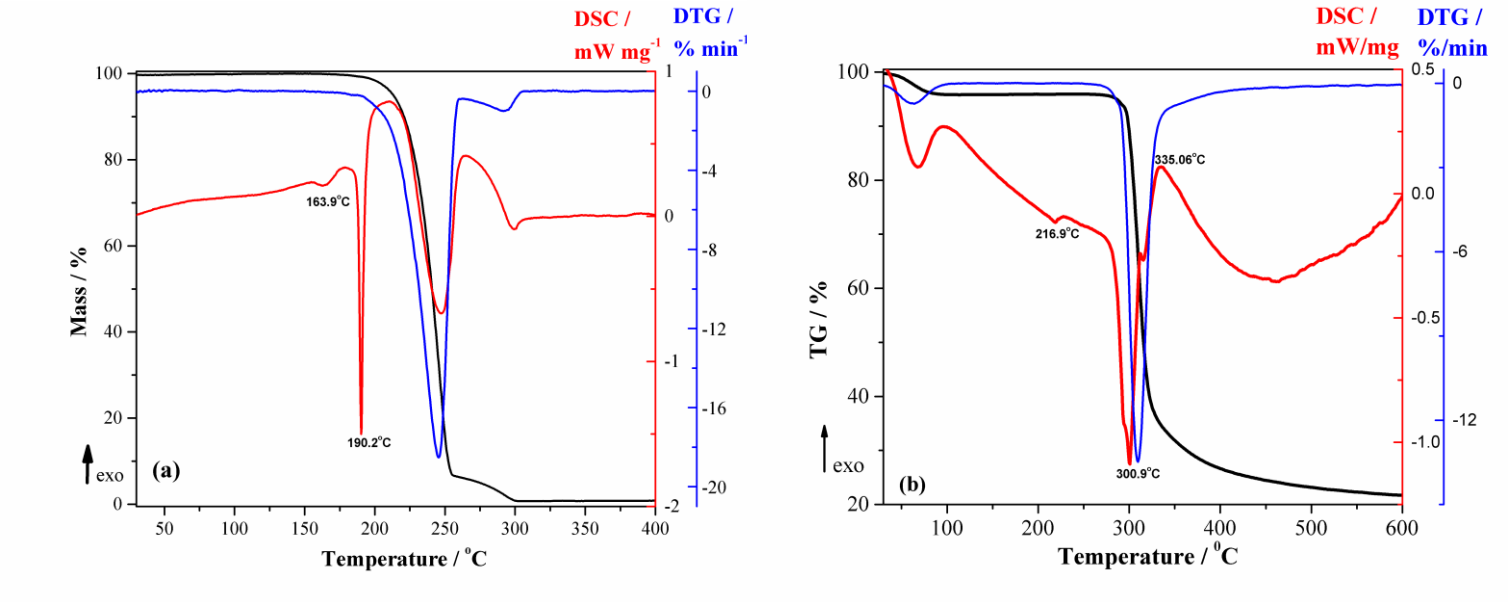
Thermal analysis



The themal curves of (a) CBZ and (b) β – CD (dynamic argon atmosphere, β = 5°C min^{-1})

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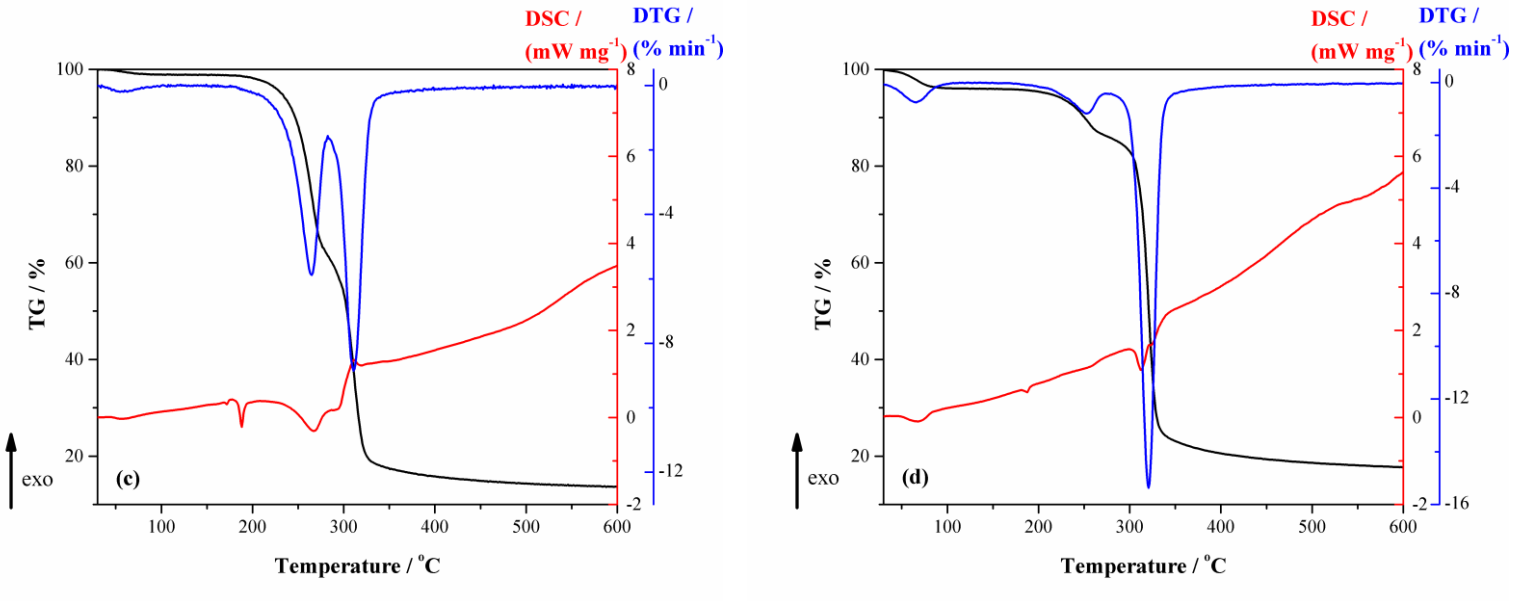
Thermal analysis



The themal curves of (c) CBZ- β – CD physical mixture and (d) CBZ- β – CD inclusion complex (dynamic argon atmosphere, β = 5°C min^{-1})

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Conclusions

- A new inclusion complex of CBZ and β-CD, obtained in a molar ratio of 1:1, by kneading method, was investigated as a promising candidate for the reparation of orodispersible tablets.
- SEM morphologies of the inclusion complex in comparison with the initial compouns and their physical mixture present change in the shape, sizes, and structure of the binary system, fact which leads to conclusion that the inclusion of CBZ in the cavity of β-CD occurred.
- The powder X-ray diffraction patterns showed that in the physical mixture are not registering important differences compared with CBZ, meantime by complexation process, a new compounds with more of β-CD characteristics appeared.
- The FTIR spectra of CBZ-β-CD inclusion complex also presents a series of spectral changes in comparison with the two separate compounds spectra and with their physical mixture.
- By all studied tests, it is obviously that CBZ forms a stable inclusion complex with β-CD in 1:1 molar ratio, and the complexation was almost complete.

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