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Research Article

STUDIES ON ETOPOSIDE AND α-CYCLODEXTRIN INCLUSION COMPLEXES

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A R T I C L E I N F O

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A B S T R A C T

Etoposide is a cytotoxic anticancer drug which is used as a form of chemotherapy for cancers. Inclusion complexes were prepared between Etoposide and α- cyclodextrin in solid and solution state. The obtained inclusion complexes were characterized using UV-VIS, Fluorescence FT-IR Spectroscopic Studies and SEM. The results obtained confirm the inclusion of etoposide in the cyclodextrin cavity.

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INTRODUCTION

Etoposide or **VP-16** (trade name Etopophos) is a cytotoxic anticancer drug which belongs to the topoisomerase inhibitor drug class. It is used in the form of its saltetoposide phosphate. The chemical name of the drug is 4' –Dimethyl – epipodophyllotoxin 9-[4,6-O-(R)-ethylidene – beta– D – glucopyranoside], 4' -(dihydrogen phosphate). The chemical formula of etoposide drug is $C_{29}H_{32}O_{13}$. The molar mass of this drug is 588.557 g/mol [1,2].Cyclodextrins (CDs) are cyclic oligosaccharides consisting of 6, 7, and 8 units of 1, 4-linked glucose units, and are named as alpha (α), beta (β) and gamma (γ)-cyclodextrins respectively [3].They have internal cavities capable of forming complexes with hydrophobic organic molecules in aqueous solutions [4]. They have a toroidal shape with an internal hydrophobic surface and an external hydrophilic surface and they are acting as a host molecule. These cyclodextrins are well known as they form stable host-guest inclusion complexes which have the interesting property of including organic, inorganic and biological molecules in their cavities[5,6].

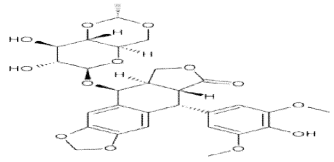

Fig 1 Structure of Etoposide

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MATERIALS AND METHODS

Instruments

The UV-visible spectra were carried out with Systronics Double-beam Spectrophotometer-2203. Fluorescent measurements were made using JASCO Spectrofluorometer FP-8200. FT-IR studies were carried out with BrukerAlphaT, made in Germany.

Materials

Etoposide, α-Cyclodextrinwere purchased from SigmaAldrich. All reagents were of analytical grade. Triply distilled water was used for the preparation of stock solutions. The solutions were prepared just before taking measurements.

Methods

Preparation of solid inclusion complex

The solid inclusion complex was prepared between etoposide and α-Cyclodextrin by co-evaporation method. Accurately weighed 0.0353g of etoposide was taken and dissolved in 30ml of methanol. About 0.2918g of α-CD was dissolved in 30 ml of distilled water. Both the solutions were taken in a 250ml beaker and put over electromagnetic stirrer to stir 48 hours at room temperature and evaporated. The precipitate was then subjected to characterization.

Preparation of liquid inclusion complex

About 0.0011g of etoposidewas dissolved in 10ml of methanol. About 0.2918g of α-Cyclodextrin was dissolved in 30ml of distilled water. Inclusion complexes were prepared by varying the concentration of α-Cyclodextrin ranging from 0.002M to 0.010M with constant amount of etoposide.

Absorption and Fluorescence Study

Absorption and Fluorescence maxima of Etoposide at different concentration of α – Cyclodextrin

Alpha Cyclodextrin				
[CD con]	λmax	Absorbance	λflu	Intensity
0	262.0	0.323	390	103.216
0.002	263.5	0.374	392	106.100
0.004	265.5	0.385	394	109.228
0.006	266.5	0.396	395	110.730
0.008	267.4	0.427	397	112.059
0.01	268.6	0.440	399	113.305

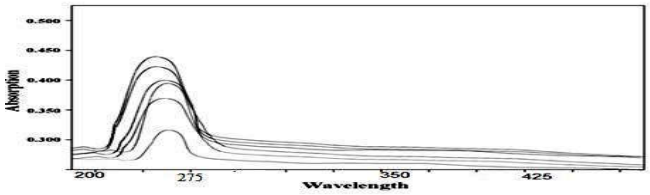

Fig 2 Absorption spectra of Etoposide at different concentration of α – CD

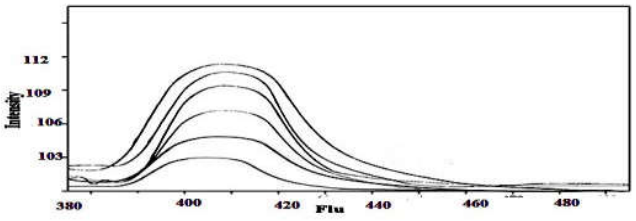

Fig 3 Fluorescence spectra of Etoposide at different concentration of α – CD

The absorption maxima of Etoposide appear at 262 nm. The absorption maxima is hypsochromically shifted to 268.6nm for α-CD complex. The inclusion complex had an increased intensity due to the formation of inclusion phenomena between α-Cyclodetrin and etoposide. The same phenomena have been observed by Wang *et al*[7]. The absorbance value increased with increasing α- CD concentration, while the concentration of etoposide remains the same. It indicates the solubility of guest molecule (etoposide) increases upon forming the inclusion complex. On increasing the cyclodextrin concentration the fluorescence intensity increased which indicates partial encapsulation of the drug molecules in the cyclodextrin cavity due to its larger size.

FT-IR Spectral Study

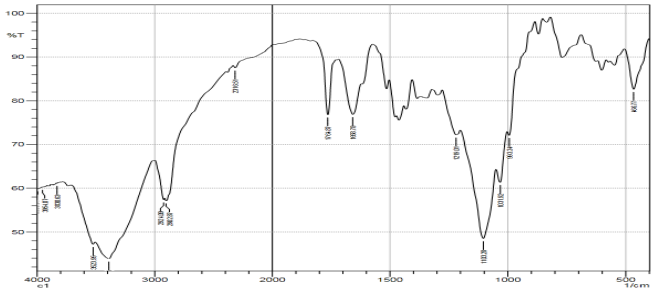

Fig 4 FT-IR spectra of Etoposide

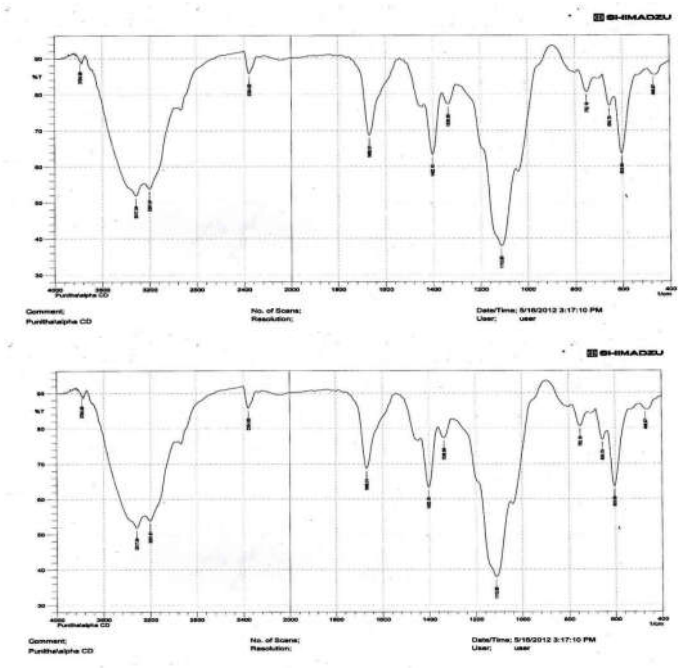

Fig 5 FT- IR spectra of α- CD

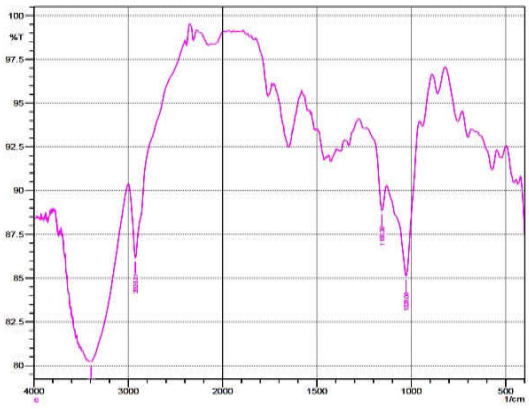

Fig 6 FT- IR spectra of α-CD:Etoposide inclusion complex

FT-IR spectra ofetopside, α-CD and α-CD: etoposide inclusion complex. C-H stretching appeared at 2902.87cm^{-1} in etoposide but it was shifted to 2926.01cm^{-1} in inclusion complex. In α-CD peak at 1668.31cm^{-1} is shifted to 1658.78cm^{-1} in the complex which indicates the presence of C=C stretching. In etoposide C-O stretching at 1028.06cm^{-1} shifted to 1031.92cm^{-1} indicates the presence of ether linkage. These spectral shift confirms the formation of inclusion complex.

Scanning Electron Spectroscopy (SEM)

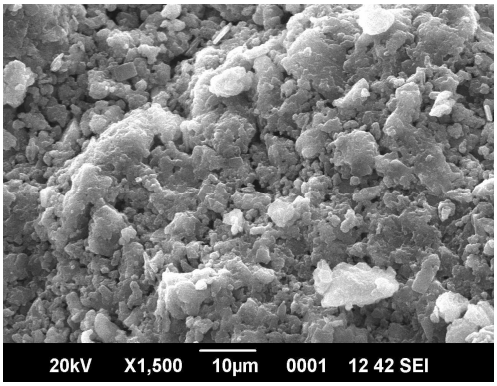

Fig 7 SEM of Etoposide

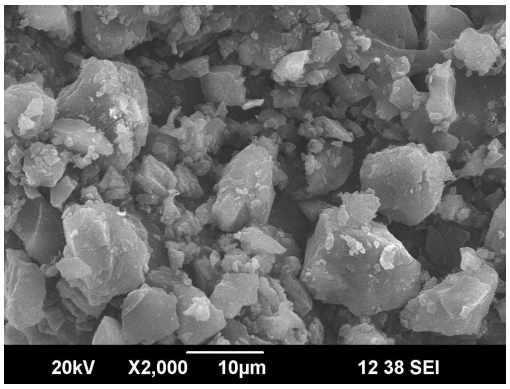

Fig 8 SEM of α-CD

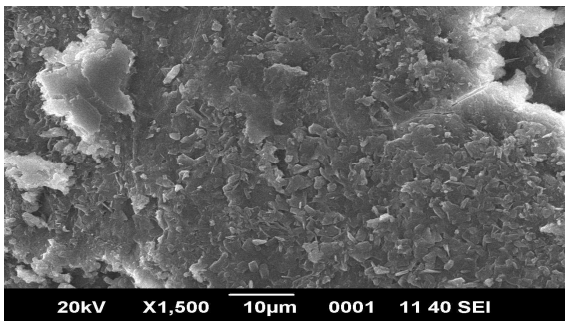

Fig 9 SEM of inclusion complex of α- CD: Etoposide

The SEM figures of the Etoposide, α-CD and Inclusion complex. The picture of Etoposide seems as sheeted structure. α-CD shows spherical structure. But the inclusion complex was entirely different from those two. This is an evidence for the formation of inclusion between etoposide and α-cyclodextrin.

CONCLUSION

Etoposide forms inclusion complexes with α-CD in aqueous solution. The formation of the inclusion complexes is confirmed by UV spectroscopy and fluorimetry studies. The absorption and emission maxima are red shifted with high formation constant values. This red shift is due to the presence of β-D glucopyranose unit. FT-IR spectra and SEM analysis are serve as an evidence for the inclusion process in solid state.

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