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Characterization of nimodipine/β-cyclodextrin inclusion complex

IRENA HOMŠEK, BRANKO KOLARIĆ, SLAVICA RISTIĆ AND IVANA KOLARIĆ

ICN Yugoslavia, Institute 29 November 111, 11000 Belgrade, Yugoslavia

Introduction

One problem with many of the active substances used today is their poor solubility in water and theirs limited bioavailability. Cyclodextrins have received considerable attention in the pharmaceutical field because of improved aqueous solubility, and chemical stability of various drug molecules through inclusion complex (1). In this study, solid dispersions are prepared by freeze dry technique in order to improve the solubility of nimodipine (NM), which belongs to the relatively small dihydropyridine group of calcium channel blocking agents. NM is practically insoluble in water. The present contribution deals with the potentiality of inclusion complexations of NM in β-cyclodextrin (β-CD).

Materials and methods

β-CD and NM were purchased from ICN, Costa Mesa, USA. The test sample was prepared in the same molar ratio of 1:1 drug to β-CD. The drug and β-CD were dissolved, under stirring at room temperature, in ethanol (30% w/w) in dark for 24 hours. The obtained solution was frozen by immersion in shell freezer and freeze-dried over 24^h in a freeze dryer apparatus (Labconco). Inclusion complex of NM/β-CD were studied by Differential Scanning Calorimetry (DSC) using a differential scanning calorimeter (DuPont) at a scanning speed of 2°C/min under a nitrogen steam. ^{13}C-NMR spectra were taken in DMSO using a Varian spectrometer at 200 MHz using β-CD as a reference. Infrared analyses were conducted with an IR spectrometer (Bomem Michelson Series), using KBr disc (1mg/100mg KBr).

Results and discussion

Formations of the drug-β-CD complex is explained by the results obtained from the structural and thermal analytical techniques used. The characterisation of the inclusion complexes by DSC thermograms was made considering the fact that signal emitted by the β-CD host appears if inclusion occurred. Thermal behaviour is not dependent of the amount of cyclodextrin in the system.

Further evidence of the inclusion of NM into the β-CD cavity in solution was obtained by NMR spectroscopy. Figure 1. shows the shift of ^{13}C-signal of β-CD in presence of NM at 40 ppm.

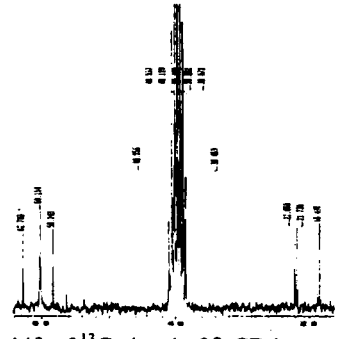

Figure 1. The shift of ^{13}C-signal of β-CD in presence of NM.

Results obtained by IR spectrometry showed that there were not differences between NM/β-CD complex and its physical mixture indicating that no chemical reaction happens during complexation process and NM stay unchanged inside β-CD cavity, after freeze drying.

Conclusion

This study has shown that examined complex of NM with β-CD, prepared by freeze-drying technique, can be proved in the solid state by DSC as well as in solution by ^{13}C-NMR. Further study will try to investigate whether complexation could increase NM solubility.

References

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