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Effect of Hydroxypropyl-β-cyclodextrin on the Solubility and Dissolution of Nicardipine

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ABSTRACT

In the present study, the influence of hydroxypropyl-β-cyclodextrin (HPCD) on the solubility and dissolution of nicardipine (NCDP) was investigated. The solubility of NCDP increased linearly in proportional to the concentration of HPCD. The phase-solubility diagram was classified as type A_L indicating the formation of a 1:1 inclusion complex with a stability constant (k_s) of 14.31 M^{-1}. The inclusion complex of NCPD-HPCD was characterized by differential scanning calorimetry (DSC) and infrared spectroscopy (IR). The dissolution rates of the prepared discs containing various proportions of HPCD were significantly greater than that of the pure drug. The enhancement of the dissolution rate is reflected by improvements of wettability and solubility by HPCD.
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INTRODUCTION

Nicardipine (NCDP), 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-3,5-pyridine-dicarboxylic acid methyl 2-[methyl-(phenylmethyl)amino]ethyl ester, is one of the 1,4-dihydropyridine derivatives and belongs to the family of calcium channel antagonists for use in patients with coronary insufficiency and high blood pressure.[1,2] However, the poor solubility of 1,4-dihydropyridine derivatives in water leads to the limitations of the development of useful dosage forms.[3] In addition, poor aqueous solubility is also believed to contribute to its low bioavailability.[4]

β-Cyclodextrin (β-CD) is a cyclic oligosaccharide of 7 glucose residues with a cavity capable of forming an inclusion complex with several poorly water- soluble compounds to modify their physicochemical properties, thereby enhancing their solubilities and dissolution rates in an aqueous environment.[5,6] β-CD has been shown to improve the solubility of some 1,4-dihydropyridine derivatives including NCDP.[3] Low aqueous solubility (about 1.8% w/v at 25 °C), inducing hemolytic activity, and the potential for renal toxicity upon parenteral administration[7,8] have limited the widespread use of β-CD. One means of enhancing the aqueous solubility and reducing the toxicity of β-CD without perturbing its ability to form inclusion complexes is chemical derivatization.[9] As a better option,

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