Introduction

Inclusion complexes of various drugs with cyclodextrin have been successfully applied in pharmaceutical formulation to enhance solubility, chemical stability and absorption (Szejtli, 1991; Uekama et al., 1998). A relationship between partition coefficient of drug and its tendency to form inclusion complexes has generally been found which indicates that hydrophobic cavity of cyclodextrins is more attractive to lipophilic guest molecules (Szejtli, 1991). There are considerable pharmaceutical benefits to be gained from a drug molecule forming an inclusion complex with natural and modified cyclodextrins (Rajewski et al., 1995; Szente and Szejtli, 2000). However, there was very few application in aerosols as a carrier. Pulmonary absorption of dimethyl-β-cyclodextrin (DMCD) and hydroxypropyl-β-cyclodextrin (HPCD) in rabbit was previously studies (Marques et al., 1991). Nevertheless, the aim of using those carriers was to sustain pulmonary release. If there is a proof that cyclodextrin-drug complex results in enhance drug delivery, this field would
be of interest, giving rises in the possibility of the eventual reduction of the dose of a given drug when employed with drug-cyclodextrins. In addition to that the cyclodextrin itself should be safe. Salbutamol was chosen as a model drug as it is very common drug use in dry powder inhaler. There was an evidence that the target site was present mostly in the alveoli (Barnes et al., 1984). At present the delivery efficiency of targeted drug to the lower airways was only 10% of the nominal dose (Newman et al., 1991; Vidgren et al., 1997). The researchers seek to develop new carrier in case of dry powder inhaler (Timsina et al., 1994). Natural cyclodextrins are orally non-toxic if the dose does not exceed 600 mg/kg. In human, the expected daily intake would not exceed 25 mg/kg/day and as a result, cyclodextrins have been used in tablet and capsule formulations (Szejtli, 1991; Antsperger, 1996). The administration of natural β-cyclodextrin parenterally at a dose of 200 mg/kg to rats and mice causes renal toxicity (Brewster et al., 1989). While the methylated β-cyclodextrin such as DMCD is more potent drug solubilizers,
they are also lipophilic and possess surface activity causing them to be hemolytic and parenterally toxic (Pitha et al., 1988). Intranasal administration of DMCD and β-estradiol or progesterone was studied by Schipper et al. (1990). It was found that the increase in steroid solubility by the formation of inclusion complexes with DMCD was an important factor in enhancing of absorption. The nasal dosage form of insulin complexed with DMCD was reported to provide a greatly increased serum insulin in rat as compared with the traditional dosage form. The enhanced rates of dissolution lead to an improved biological activities of the complexed drugs. A pilocarpine-β-cyclodextrin complex was prepared and encapsulated into niosome. Dispersed niosome in a gel produced a slow sustained release (Sheena et al., 1997). The in vivo studies of this formulation confirmed that a longer miotic effect was obtained as compared to non-encapsulated drug formulation. This observation showed that the drug had been released in a controlled manner from the niosome entrapped complex gel and
enhanced the bioavailability of the drug. As mention earlier, it has an advantage to develop new carrier which can enhance drug delivery. Two cyclodextrins were selected as a reason that GCD is evidently safe while DMCD is better solubiliser and has been used in an opthalmic preparation. Therefore, the irritation would be accepted. It is forcasted that cyclodextrin carrier is able to absorb in the lower airways as immediately as intravenous injection.

The interaction between salbutamol and cyclodextrin will be identified then this might be expected to have implications for the formulation of dry powder inhaler as an enhancing drug delivery to the lung. It is aimed to investigate the carrier entering the lower airways and the possibility of it in enhancing drug delivery. There is a certain amount of carrier reaching lower airways which is safe. The final aim was to investigate the dissolution rate of salbutamol in dry powder dosage form.