UNIVERSITI TEKNOLOGI MARA

SIMVASTATIN SOLUBILITY IN TERNARY SYSTEM CONTAINING B-CYCLODEXTRIN AND HPMC: PHASE SOLUBILITY AND IN VITRO DISSOLUTION STUDY

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ABSTRACT

Drug solubility plays an important role on influencing the dissolution rate and bioavailability of a drug. On this matter, Simvastatin (SV) exhibits a low solubility but high gastrointestinal permeability. Many studies had been conducted to increase the solubility of SV. This study was conducted to increase the solubility of SV by ternary system of SV with β-cyclodextrin (βCDT) and hydroxypropylmethylcellulose(HPMC). The system was prepared by physical mixing method. In the study series of SV-βCDT-HPMC ratio were synthesized prior to the objectives. The objectives of this study were to investigate the phase solubility study of SV-βCDT and SV-βCDT-HPMC as well as the dissolution rate of optimum formulation of SV-βCDT-HPMC. The in vitro dissolution study was accomplished by using USP-II apparatus. Results show that, ternary system can increase the SV solubility up to some extent. Based on the results, the occurring of physical adsorption arising from the system during physical mixing. This statement is strengthened by solid state characterization performed on the system.

CHAPTER 1

INTRODUCTION

1.1 Background Study

Drug solubility is important as it influences its dissolution rate and hence it bioavailability. Recent study shows that 75% of new drugs entity has low solubility. These insoluble drugs are classified as Class II and IV according to the Biopharmaceutical Classification System (BCS)(Di, Fish, & Mano, 2012). One of the drugs that fall in the BCS Class II is a statin group.

Statin group is classified in Class II as statin has low solubility and high permeability in gastrointestinal(GI) mucosa. Statin is a 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) inhibitor. The inhibition of the enzyme leads in reducing the blood cholesterol level and reducing the cardiovascular disorder risk.There are 5 type of Statin drug, lovastatin (LV), simvastatin (SV), fluvastatin (FV), atorvastatin (AV) androsuvastatin (RV). AV have the highest molecular weight followed by RV, SV, FV, and lastly LV by 540.6 g/mol, 481.5 g/mol, 418.5 g/mol, 411.4 g/mol and 404.5 g/mol respectively(Hojjati, Yamini, Khajeh, & Vatanara, 2007).

Simvastatin (SV) works by inhibiting the biosynthesis of cholesterol by inhibiting the 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase. This inhibition