Research Article

Dissolution enhancement of atorvastatin calcium by self-nanoemulsifying drug delivery system using cremophor RH 40 and Transcutol P as surfactants

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ABSTRACT

Backgrounds: Atorvastatin calcium is HMG-CoA reductase inhibitor, one of the most popular medicines for treatment high cholesterol. Atorvastatin calcium is BCS class II drug that have low aqueous solubility and low bioavaibility (14%). Self Nanoemulsifying Drug Delivery System (SNEDDS) known can increase dissolution and oral bioavailability of drugs. **Objective:** This study aims to increase the dissolution rate of Atorvastatin calcium by formulating into SNEDDS. **Materials and Methods:** The optimization formula was carried out using various comparisons of oil and mixed surfactants (1:9; 1:8; 1:7) and various comparison of surfactants and cosurfactant (3:1; 2:1; 1:1). The formulated SNEDDS were evaluated for transmittance percentage, dispersibility, robustness, thermodynamic stability, droplet size, and dissolution tests. **Results:**The best formula of SNEDDS contain atorvastatin calcium 10 mg/mL using oleic acid as the oil phase, cremophor RH 40 as the surfactant, and transcutol as the cosurfactant, with ratio between oil with mixture of surfactants was (1: 7) and ratio between surfactant and cosurfactant (3: 1). The preparation was meet the requirements of the transmittance percentage (93.56% ± 0.115), dispersibility time (34.67 seconds ± 0.644), stable on robustness to dilution and thermodynamic stability tests and has average droplet size 87 nm. The result showed that SNEDDS of atorvastatin calcium could improve the dissolution of atorvastatin calcium compared with pure drug (94,6% of drug was dissoluted in 45 minutes). **Conclusion:** SNEDDS containing atorvastatin calcium was met physical and stability requirements and could enhance the dissolution rate of Atorvastatin calcium.

KEY WORDS: Atorvastatin calcium, Cremophor RH 40, Dissolution, Self-nanoemulsifying drug delivery system, Transcutol P

INTRODUCTION

Atorvastatin calcium is one of the most popular medicines for the treatment of high cholesterol. Atorvastatin calcium can inhibit 3-hydroxy-3-methyl-glutaryl coenzyme A (HMG-CoA) reductase, the enzymes that catalyze the conversion of HMG-CoA to mevalonate.[1,2] Atorvastatin calcium is BCS Class II drug with low aqueous solubility and high permeability.[3,4] Oral bioavailability of atorvastatin calcium is very low (only 14%). The low oral bioavailability of atorvastatin calcium is caused by low aqueous solubility and high hepatic first-pass metabolism.[5] Efforts are needed to enhance dissolution rate and oral bioavailability of atorvastatin calcium.

Self-nanoemulsifying drug delivery system (SNEDDS) is isotropic mixture of oil, surfactant, and cosurfactant which forms fine o/w nanoemulsion when introduced in aqueous phase under condition of mild agitation. Agitation will be provided by body movement and gastrointestinal (GI) movement.[6,7] SNEDDS is formulation with high solubilization capacity for lipophilic drugs and thermodynamically stable. SNEDDS can increase drug dissolution with provide large interfacial area for partitioning drug between oil and aqueous phase in GI.[6] In addition, SNEDDS could increase permeation of drug across the intestinal membrane and enhance drug bioavailability.[8]

Bases for SNEDDS are using oil, non-ionic surfactant, and cosurfactant which are acceptable for oral route.[9] In this research cremophor RH40 and Transcutol P were used as surfactant and cosurfactant. Some study showed that atorvastatin calcium has good solubility in cremophor RH 40 and Transcutol P. Cremophor RH 40 is non-ionic emulsifying and solubilizing agent that obtained by reacting hydrogenated castor oil with ethylene oxide. Transcutol P or diethylene

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