



DEVELOPMENT OF A SOLID SELF-EMULSIFYING DRUG DELIVERY SYSTEM OF A WEAKLY BASIC BCS CLASS II DRUG

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INTRODUCTION

The rate limiting factor of the absorption of drugs from the GI system depend on the release of the active ingredients from the dosage form and dissolution in the physiological fluid. Drugs with a solubility in water below 100 µg/mL usually expresses low dissolution and low absorption (1). Approximately 70-90% of the new generation drug molecules have low solubility problems. According to BCS, these compounds belongs to BCS Class II (70%) and BCS Class IV (20%) (2).

Drug molecules with low solubility in water may cause low bioavailability, the necessity of using excipients, inappropriate dosing, uncontrollable collapse after dosing, and other similar problems (3). For this reason, various methods can be applied to increase the solubility of drug molecules that have low solubility in water and thus low oral bioavailability. Among these methods, lipid-based systems have been developed as a new technological approach that has recently attracted considerable attention. Self-emulsifying systems (SEDDs), which are a part of lipid-based drug delivery systems, are divided into subgroups according to the components that make up these systems, one of which is type IV formulations that do not contain oil, only surfactants and / or co-surfactants (4). The active ingredient Tadalafil (TDL) is our subject of study for BCS class II. Type IV formulations were prepared using surfactant and cosurfactant (S/CoS) to increase the solubility of this substance. The formulations prepared were turned into solid form using appropriate adsorbents (5).

MATERIALS & METHODS

Materials

- ✓ TDL was a gift from Jubilant Life Sciences (India)
- ✓ Transcutol® HP, Labrasol ALF®, Gelucire® 44/14 and 48/16 were obtained as gift samples from Gattefossé (France).
- ✓ Kolliphor® PS 20, PS 60, PS 80, HS 15, PEG 400, CS 12, CS 20, EL and ELP were obtained as gift samples from BASF (Turkey).
- ✓ Florite was gifted from Tomita Pharmaceutical Co., Ltd (Japan)
- ✓ Neusilin UFL2 and Neusilin US2 were gifted from Fuji Chemical (Japan)
- ✓ Syloid XDP 3050 and Syloid XDP 3150 were gifted from Grace GmbH (Germany).

Formulation Studies

The solubility of TDL in surfactant and cosurfactant to be used in the composition of oil-free lipid based formulations was examined. The amount of TDL was analyzed by HPLC at 285 nm.

Solubility Studies

Type-IV formulations containing 7.5 mg TDL were prepared using high solubility S/CoS mixtures, and the droplet sizes of these formulations, phase separation at different temperatures, and their sensitivity to pH change were analyzed.

Dissolution Studies

Solid-Type IV (S-Type IV) was prepared using adsorbents for the appropriate formulations, dissolution studies were carried out first in 0.1 N HCl environment, then the suitable solid formulations were analyzed at pH 4.5 and pH 6.8 and their dissolution rate profiles were examined. The tests were carried out in 900 mL medium at 50 rpm at 37 ± 0.5 ° C for 45 minutes. The test also performed for market product (Cialis 5mg).

RESULTS

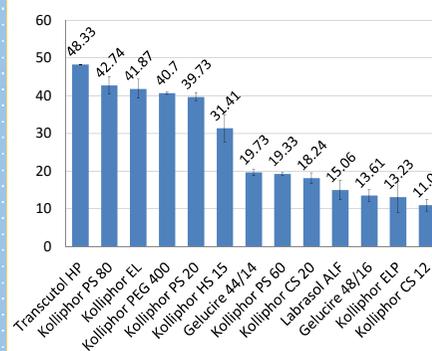


Figure 1. TDL Solubility in Surfactants and Co-Surfactant (mg/mL)

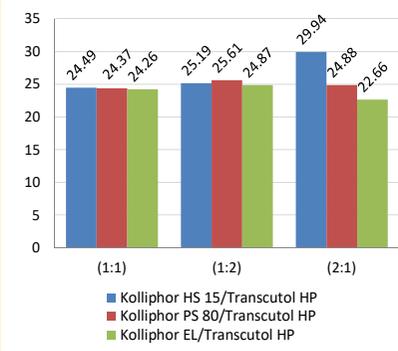


Figure 2. TDL Solubility in S/KoS (mg/mL)

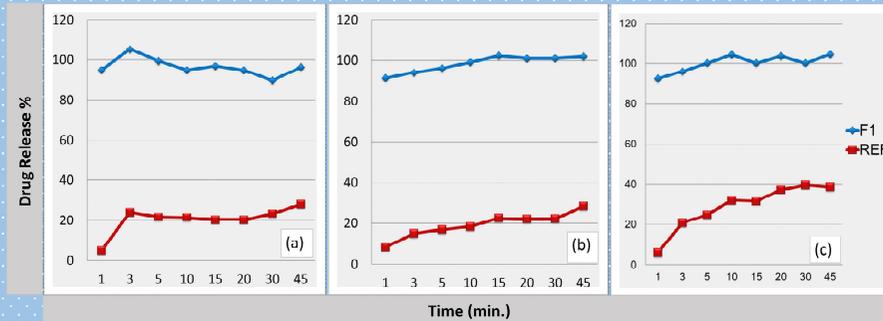


Figure 3. Dissolution graphics of TDL S-Type IV formulation (F1; Kolliphor PS80: Transcutol (2:1)) and Referans product in different pH's. (a): 0,1 N HCl, (b): pH4.5 Phosphat buffer, (c): pH: 6,8 Phosphat buffer.

CONCLUSIONS

- ✓ Transcutol® HP is the best cosurfactant among tested ones.
- ✓ Kolliphor® PS 80 ve Kolliphor® EL, have significantly higher TDL solubilization capacity among other surfactants.
- ✓ The solid formulations prepared with Neusilin US2 and Neusilin UFL2 at the ratio of 2: 1 of the formulations obtained with the mixture of Kolliphor® PS80 and Transcutol® HP at a ratio of 2: 1, provided over 80% dissolution at the end of 1 minute in 3 pH conditions.

ACKNOWLEDGMENT

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