

# Comparative review of self-nanoemulsifying drug delivery systems with Rosuvastatin

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## Introduction

Rosuvastatin (ROS) calcium is a synthetic drug in the statin group that has an anti-hyperlipidemic activity. Rosuvastatin as BCS class II drug, is characterized by low solubility and high permeability. It has poor water solubility (0.33 mg/mL in water), poor solubility in gastro intestinal fluids, undergoes extensive first-pass metabolism and shows a bioavailability of less than 20% after oral administration (Salem et al., 2017). Enhancement of ROS solubility in order to improve its effectiveness could be done by various approaches such as complexation with cyclodextrines, nanosponge delivery system, amphiphilic lipid vesicular systems called pharmacosomes, nanocrystals, hydrotrophy, micelle formation, microemulsions, nanoemulsions etc. (Butt et al., 2019). Also, formulation of self-nanoemulsifying drug delivery system could be listed as the attractive approach. SNEDDS is an isotropic mixture of oil, surfactants, and co-surfactants, which when administered in an aqueous medium such as gastro intestinal fluid forms a fine oil-in-water nanoemulsion (Wang et al., 2009). Compared to other methods, SNEDDS is a preferred solubility improvement approach for BCS class II drugs due to its simplicity and cost-effectiveness. However, SNEDDS formulation challenge is related to the selection of appropriate oil phase, surfactant and co-surfactant.

The aim of the study was to identify the most promising composition of ROS SNEDDS formulation via literature survey that will have potential to significantly improve ROS effectiveness.

## Materials and methods

A systematic search of the literature was performed through the free PubMed search engine that has access primarily to the MEDLINE databases with references and abstracts from the biomedical sciences. Literature data published in the last ten years were taken into consideration.

Keywords used: Self nanoemulsifying drug delivery system, SNEDDS, rosuvastatin, bioavailability, solubility, oil phase, surfactant, co-surfactant.

## Results and discussion

According to performed literature review it can be seen that ROS SNEDDS particle size is preferred to be less than 200 nm and it vastly depends from the type and amount of selected oil phase, surfactants and co-surfactants.

In the study by Balakumar et al. (2013), ROS showed the highest solubility in cinnamon oil (99.56±1.43 mg/mL), labrasol (99.46±2.34 mg/mL) as a surfactant and in Capmul MCM (99.12 ± 2.46 mg/ml) and Capmul MCM C8 (99.81 ± 3.21 mg/ml) as a co-surfactant. The optimal formulation composition was 30% cinnamon oil, 60% labrasol and 10% Capmul MCM 8 and was characterized with droplet size of 122 nm and in vitro ROS release of 90.29±1.11% in 24 hours that was significantly higher when compared to the commercial formulation which showed 52.42±1.30% release for the same time.

On the other hand, in the study of Amrutkar et al. (2014) the optimal formulation was composed with 20%

Capmul MCM as oil phase and 80% of surfactant Tween 20 and co-surfactant PEG 200 in ratio of 1:1. This formulation had droplet size of 88 nm and a 98.13% of ROS were released in 20 minutes that was significantly higher compared to the commercial product which showed release of 32.18% at the same time under the same conditions.

In the study of Abo Enin (2015) natural oils (olive oil, garlic oil, nigella oil and fish oil) with the rationale to increase the antihyperlipidemic efficiency of ROS were studied. Highest solubility of ROS was determined in olive oil ( $21.216 \pm 0.65$  mg/mL) and garlic oil ( $21.125 \pm 1.16$  mg/mL). The optimal formulation composition was as follows: and 20% olive oil:garlic oil in a ratio of 1:1 as an oily phase, 76.6% Tween 80 as surfactant and PEG 400 as co-surfactant in a ratio of 3:1 and 1.4% water. The droplet size was  $59.87 \pm 3.54$  nm and 85% of ROS were released in 10 min, while at the same conditions the release from commercial product was 70% in 60 min.

In the study by Verma et al. (2021), the optimal formulation contained 14% Capmul MCM EP as oil phase, 50% of Tween 20 as surfactant and 36% of Transcutol P as co-surfactant. It had globule size of 14.69 nm and 99.5% of ROS were released in 15 min.

## Conclusion

In the summary all formulated SNEDDS resulted with improved ROS solubility and faster ROS release when compared with commercial formulations thus making them promising candidates for enhanced ROS effectiveness.

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