# Development and Characterization of Different Formulations of Controlled-Release Lipid-based Delivery Systems of Carvedilol

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## Abstract

Cardiovascular diseases generally refer to a wide class of diseases that involve disorders in the blood vessels and heart which leads to heart attack, angina, and stroke. Carvedilol, a non-selective β-blocker, is commonly used to treat high blood pressure and congestive heart failure. However, carvedilol suffers from extensive first-pass hepatic metabolism by cytochrome P450, low solubility, and low bioavailability. The aim of this work was to develop controlled-release lipid based drug delivery systems (LBDDSs) for the oral delivery of carvedilol. The LBDDSs were prepared by loading the submicron-sized emulsions of carvedilol (carvedilol SMEs), prepared with different surfactant-cosurfactant ratios, into the oleaginous base Compritol® 888 to prepare carvedilol submicron-sized emulsion organogels (carvedilol SME organogels). Carvedilol SMEs with different surfactant-cosurfactant ratios were characterized in terms of their thermodynamic stability studies, droplet size, and surface tension. Whereas carvedilol SMEs organogels were characterized in terms of their rheological properties and *in vitro* release behavior of carvedilol. Finally, safety and stability studies were carried out on the optimized formulation of the carvedilol SME organogel. The results showed that carvedilol SMEs were thermodynamically stable, exhibiting an average droplet size below 100 nm and a surface tension of ~ 30 mN/m. Also, the

rheological properties and *in vitro* release of carvedilol of organogels were highly dependent on the surfactant-to-cosurfactant ratio. In the in vitro safety study, a negative correlation was found between Tween 20 (T-20) concentration and $IC_{50}$ of carvedilol SME organogels. In addition, the optimized carvedilol SME organogel did not pass the stability studies at 30°C/65 %RH and 40°C/75 %RH, where significant decline in carvedilol content (~ 30%) was found. The results obtained shed light on understanding the effect of the surfactant-to-surfactant ratio on the droplet size and surface properties of carvedilol SMEs, and the viscoelastic properties, rate and mechanism of drug release, safety, and stability of carvedilol SMEs organogels.