

# Niosomal carriers enhance oral bioavailability of carvedilol: effects of bile salt-enriched vesicles and carrier surface charge

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**Abstract:** Carvedilol (CRV) is an antihypertensive drug with both alpha and beta receptor blocking activity used to preclude angina and cardiac arrhythmias. To overcome the low, variable oral bioavailability of CRV, niosomal formulations were prepared and characterized: plain niosomes (without bile salts), bile salt-enriched niosomes (bilosomes containing various percentages of sodium cholate or sodium taurocholate), and charged niosomes (negative, containing dicetyl phosphate and positive, containing hexadecyl trimethyl ammonium bromide). All formulations were characterized in terms of encapsulation efficiency, size, zeta potential, release profile, stability, and morphology. Various formulations were administered orally to ten groups of Wistar rats ( $n=6$  per group). The plasma levels of CRV were measured by a validated high-performance liquid chromatography (HPLC) method and pharmacokinetic properties of different formulations were characterized. Contribution of lymphatic transport to the oral bioavailability of niosomes was also investigated using a chylomicron flow-blocking approach. Of the bile salt-enriched vesicles examined, bilosomes containing 20% sodium cholate (F2) and 30% sodium taurocholate (F5) appeared to give the greatest enhancement of intestinal absorption. The relative bioavailability of F2 and F5 formulations to the suspension was estimated to be 1.84 and 1.64, respectively. With regard to charged niosomes, the peak plasma concentrations ( $C_{max}$ ) of CRV for positively (F7) and negatively charged formulations (F10) were approximately 2.3- and 1.7-fold higher than after a suspension. Bioavailability studies also revealed a significant increase in extent of drug absorption from charged vesicles. Tissue histology revealed no signs of inflammation or damage. The study proved that the type and concentration of bile salts as well as carrier surface charge had great influences on oral bioavailability of niosomes. Blocking the lymphatic absorption pathway significantly reduced oral bioavailability of CRV niosomes. Overall twofold enhancement in bioavailability in comparison with drug suspension confers the potential of niosomes as suitable carriers for improved oral delivery of CRV.

**Keywords:** niosomes, bile salts, surface charge, bioavailability, oral delivery, lymphatic transport

## Introduction

Oral delivery is the most convenient route of drug administration, especially for chronic illness, with high patient compliance, ease of administration, cost-effectiveness, and other benefits.<sup>1</sup> Although high oral bioavailability is highly desirable, many important drugs in the clinic suffer from poor oral bioavailability and highly variable exposure. This can be due to various factors, including low solubility, limited permeability, first-pass metabolism and drug efflux.<sup>2</sup>

To reach the bloodstream, a drug should first dissolve in the gastrointestinal (GI) fluid. Thus, dissolution may be the rate-limiting step in oral administration of poorly

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# Niosomal Carriers Enhance Oral Bioavailability Of

**Huangqi Zhang**



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