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# Synthesis of Liposomal Vesicles by a Novel Supercritical Fluid Process

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**Abstract :** Organic solvent residues are always associated with liposomes produced by the traditional techniques like the thin film hydration and reverse phase evaporation methods, which limit the applications of these vesicles in the pharmaceutical, food and cosmetic industries. Our objective was to develop a novel and benign process of liposomal microencapsulation by using supercritical carbon dioxide (SC-CO2) as the sole phospholipid-dissolving medium and a green substitute for organic solvents. This process consists of supercritical fluid extraction followed by rapid expansion via a nozzle and automatic cargo suction. Lecithin and cholesterol mixed in 10:1 mass ratio were dissolved in SC-CO2 at 20 ± 0.5 MPa and 60 oC. After at least two hours of equilibrium, the lecithin/cholesterol-laden SC-CO2 was passed through a 1000-micron nozzle and immediately mixed with the cargo solution to form liposomes. Liposomal micro-encapsulation was conducted at three pressures (8.27, 12.41, 16.55 MPa), three temperatures (75, 83 and 90 oC) and two flow rates (0.25 ml/sec and 0.5 ml/sec). Liposome size, zeta potential and encapsulation efficiency were characterized as functions of the operating parameters. The average liposomal size varied from 400-500 nm to 1000-1200 nm when the pressure was increased from 8.27 to 16.55 MPa. At 12.41 MPa, 90 oC and 0.25 ml per second of 0.2 M glucose cargo loading rate, the highest encapsulation efficiency of 31.65 % was achieved. Under a confocal laser scanning microscope, large unilamellar vesicles and multivesicular vesicles were observed to make up a majority of the liposomal emulsion. This new approach is a rapid and continuous process for bulk production of liposomes using a green solvent. Based on the results to date, it is feasible to apply this technique to encapsulate hydrophilic compounds inside the aqueous core as well as lipophilic compounds in the phospholipid bilayers of the liposomes for controlled release, solubility improvement and targeted therapy of bioactive compounds.

**Keywords :** liposome, micro encapsulation, supercritical carbon dioxide, non-toxic process
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