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Characterization of Verapamil hydrochloride entrapped in poly (lactide-co-glycolide) (PLGA) particles

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Background: Verapamil hydrochloride is a commonly prescribed drug in the management of hypertension, angina and cluster headache prophylaxis. Verapamil hydrochloride has a disadvantage of low bioavailability because of extensive hepatic metabolism (only 10% to 20% becomes bioavailable) and short half-life (2 to 4 hours). As a result, it requires frequent dosing of the drug leading to the problem of noncompliance in patients and alternating over and under doses of the drug. A method of circumventing hepatic first pass effect is by making the drug particle microsized (<10 µm) and lipophilic.

Objectives: The aim of this study was to characterize the optimized microparticles of Verapamil hydrochloride entrapped in Poly (lactide-co-glycolide) (PLGA) (Verapamil HCl-PLGA) prepared through solvent displacement method followed by lyophilization.

Significance: This study sought to contribute to the improvement of the dosage form of Verapamil HCl by the application of polymeric drug delivery system. Through polymeric drug formulation, the low bioavailability due to hepatic first-pass effect is addressed by the transport of hydrophobic polymeric microparticles (size of <10 µm) to the lymphatic system instead of the hepatic portal transport, therefore, avoiding extensive hepatic metabolism.

Methodology: The Verapamil HCl-PLGA microparticles were prepared through solvent displacement method followed by lyophilization. The optimization parameters for the formulation include particle size, polydispersity index, zeta potential and entrapment efficiency. The optimized final formulation was further characterized based on percent particle recovery, redispersibility, percent drug loading, drug release kinetics and morphology.

Results: Based on the analysis of the data from solvent displacement method, increasing the PLGA 75:25 concentration resulted to an increase in the particle size, polydispersity index and entrapment efficiency and a decrease in zeta potential; while the increase in Poloxamer 188 concentration led to a decrease in zeta potential and an increase in the entrapment of drug; lastly, the increase in the pH of the non-solvent phase resulted to an increase in particle size. The addition of sucrose, led to an unfavorable increase in the particle size and polydispersity index, and a decrease in zeta potential and entrapment efficiency after lyophilization. The final product of the process was a heterogenous sized (<10 µm) irregularly shaped particles (fragment-like), with an acceptable particle recovery, redispersibility and percentage (%) drug loading, but poor release kinetic property (non-linear and decreasing concentration over time).

Conclusion: The Verapamil HCl-PLGA microparticles prepared through solvent displacement method followed by lyophilization were able to meet the conditions noted by Chu and Lui (2008) for lymphatic transport: Entrapment in a lipophilic polymer in terms of particle size requirement (<10 µm).

Biography

Bienvenido S Balotro, RPh, MBA, MS, is an Assistant Professor of the Department of Industrial Pharmacy, College of Pharmacy, University of the Philippines Manila where he has taught pharmaceutical dosage form and drug delivery systems, pharmaceutical product development, and pharmaceutical marketing. Ms, Paola Marie Sabban, RPh, MS, is a Regulatory Affairs Associate at Pfizer (Phils.) Inc. She finished her Master of Science degree (Industrial Pharmacy track) at the University of the Philippines Manila, College of Pharmacy.

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