Pharmaceutical Sciences Seminar Series

Wednesday, May 10, 2023
4:00pm
NCRC Building 10 Research Auditorium
Zoom

“Development of PLGA microspheres encapsulating exenatide acetate by solvent evaporation”

Presented by:

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Abstract The once-weekly Bydureon® (Bdn) PLGA microsphere formulation encapsulating the GLP-1 receptor agonist, exenatide acetate, is an important complex injectable product prepared by coacervation for the treatment of type 2 diabetic patients. Encapsulation by coacervation is useful to minimize an undesirable 24-hour initial burst release of exenatide and associated nausea upon administration, but Bdn suffers from manufacturing difficulties such as process scale-up and batch-to-batch variations. Herein we prepared exenatide acetate-PLGA formulations of similar compositions to Bdn by using the desirable alternative double emulsion-solvent evaporation technique. After screening several process variables, we varied the PLGA concentration, the hardening temperature, and the particle size range, and determined the resulting drug and sucrose loading, initial burst release, in vitro retention kinetics, and peptide degradation profiles using Bdn as a positive control. All formulations exhibited a triphasic release profile with a burst, lag, and rapid release phase, although the burst release was greatly decreased to <5% for some. In particular, the combination of a high polymer concentration and low hardening temperature led to a favorable burst release of 4.4 ± 0.5%. Marked differences were observed in the degradation profiles, particularly oxidized and acylated fractions when the polymer concentration was varied in the formulation. For one optimal formulation, the release and peptide degradation profiles were similar to Bdn microspheres, albeit with an induction time shift of one week, likely due to the slightly higher Mw of the Bdn polymer. These results indicate the potential of manufacturing the microsphere component of Bdn by solvent evaporation while still retaining the desirable low initial burst release and other important features of the drug product.