Development of Extended-release Capsules loaded with Albumin-based Microspheres

B. A. Orawiec¹, G. G. Enriquez¹, S. A. A. Rizvi², M. Newaz¹, and D. P. Do¹
¹Chicago State University, Chicago, IL 60628, USA
²Nova Southeastern University, Fort Lauderdale, FL 33328, USA
ddo@csu.edu

ABSTRACT SUMMARY

Extended-release delivery of BCS class II and III compounds is desirable in order to decrease dosing frequency and potential adverse effects during therapy. The objective of this research was to develop a polymeric microsphere drug delivery system that will effectively exhibit extended-release characteristics in the body via an orally administered capsule. Using acetaminophen and ibuprofen as model drugs, the microsphere drug delivery system provided a constant release of the drug for upwards of 36 hours.

INTRODUCTION

While a multitude of dosage forms exist on the market, one of the most common and effective is the oral capsule/tablet. However, the oral capsule is not without its disadvantages. Many drugs which possess a short half-life must be administered in multiple daily doses, which can be inconvenient, decrease patient compliance, and cause fluctuations in plasma levels which manifest as either side effects or a subtherapeutic effect¹. As a result, oral capsules which are efficacious and exhibit an extended-release profile are a highly desired product despite the difficulty in producing them. If such a delivery system is achieved, it can lead to a reduction in dose and administration frequency while improving patient compliance and convenience when compared to immediate release formulations¹-². While a wide variety of extended release formulations are currently available, drug delivery via microspheres holds several advantages over other technologies, including prolonged in-vivo half life and extended release of the drug¹.

Our research focused on the formulation of extended-release capsules using a microsphere delivery system. Spray drying was utilized to prepare microspheres capable of extended drug delivery. Multiple formulations were developed and analyzed for physicochemical properties and release profiles. Data revealed that several formulations successfully exhibited zero-order kinetics while maintaining optimal drug stability.

EXPERIMENTAL METHODS

Microsphere formulations were prepared using microencapsulation methods, previously described³. Bovine serum albumin (BSA) was dissolved in purified water at the desired concentration and cross-linked chemically using glutaraldehyde (GLU) overnight at room temperature. The drug (acetaminophen and ibuprofen were used as model drugs) was added to the crosslinked-BSA solution to achieve the desirable loading. The mixture was then spray-dried using the following parameters: Air flow rate: 800 Nl/h; pump feed rate: 2%; inlet temperature: 120°C; outlet temperature: 44°C.

Once prepared, the drug-loaded microsphere powder was placed into hard gelatin capsules. Size and surface morphology of microspheres were determined using scanning electron microscopy. A laser diffraction particle sizer was used to determine the size distribution and zeta potential of microspheres. In addition, FTIR and Raman spectroscopy were utilized to examine the chemical stability of the encapsulated drug.

Drug release studies were performed using a modified USP type 1 dissolution apparatus at 37°C and 75 rpm in phosphate-buffered saline (PBS), pH 7.2³. Samples were taken at predetermined intervals. After sampling, fresh PBS was added to keep the volume constant. Acetaminophen (APAP) and ibuprofen (IBU) concentrations were measured using a UV-Visible spectrophotometer at 243 and 264 nm, respectively.
RESULTS AND DISCUSSION

Our research aimed to develop extended-release capsules incorporating biodegradable albumin microspheres as the platform technology. Six formulations containing various amounts of BSA and glutaraldehyde were formulated and optimized to provide the desired release of the drug. Microspheres were found to be less than 2-µm in average size and exhibited a uniform size distribution (Figure 1). Additionally, they were spherical in shape, which is critical for maintaining constant drug release characteristics. Zeta potential measurements were -20 mV to -10 mV, which indicated that the microspheres are stable in aqueous media.

Figure 1. Representative microscopic image of microspheres at 10,000 magnification.

FTIR and Raman spectra indicated that the drug is stable throughout the process of microencapsulation (data not shown).

Capsules containing drug-loaded microspheres were also evaluated for their dissolution and release characteristics. Their release profiles displayed an initial burst release during the first hour and then remained constant for upwards of 36 hours (Figures 2 and 3). As shown, microspheres provided an optimal release profile of both acetaminophen and ibuprofen.

![Figure 2: Release profile of ibuprofen microsphere-loaded capsules. Drug concentrations were measured at 264 nm.](image)

![Figure 3: Release profile of acetaminophen microsphere-loaded capsules. Drug concentrations were measured at 243 nm.](image)

CONCLUSION

Drug-loaded microspheres were prepared via spray-drying techniques and incorporated into capsules. Dissolution studies of capsule formulations containing variable concentrations of drug and polymer provided promising evidence for the role of microspheres in oral extended-release dosage forms.

REFERENCES