ABSTRACT

During the last decade, many novel controlled-released methods in the field of controlled release drug delivery system have attracted the attention of researchers. Among them, drug-loaded biodegradable polymer and encapsulation of drug crystal with polyelectrolyte multilayer ultrathin films are prominent. On one hand, biodegradable polymer, when used as drug carrier, can be turned into nanoparticles via solvent-evaporation method. These nanoparticles can realize not only controlled release of the drug by degradation rate of the polymer but also drug targeting by their size. On the other hand, Layer-by-Layer (LbL) self-assembly is a promising technology that allows the precise tailoring over the composition, thickness, structure, and property of the particle surface in nanoscale. Since encapsulation of the drug crystal with polyelectrolyte mulilayer ultrathin films is achieved by LbL assembly, the release behavior of the drug can be highly controlled.

In this thesis, efficient preparation of Ibuprofen-loaded poly(hydroxybutyrate-co-hydroxyvalerate) (PHBV) nanoparticles was investigated. After that two controlled release methods mentioned above is combined, which means conducting LbL assembly on the surface of the nanoparticles. Furthermore, the release behavior of the nanoparticles before and after coated is compared. The main contents and results of the research are as follows:

Through O/W solvent evaporation method, series IBU-loaded PHBV nanoparticles with different preparation parameters, whose average diameter ranged from 500nm to 800nm, were fabricated. SEM images illustrated their fine sphere shapes. By varying preparation parameters, such as pH values of the aqueous phase, drug/polymer ratio, HV content of the PHBV and concentration of PVA, the highest encapsulation efficiency and drug loading was figured out. It is found that lowering the pH value and drug/polymer ration can enhance the encapsulation efficiency and drug loading. Varying HV content, on the contrary, takes no effect on them. Due to the loss of drug into the aqueous phase, increasing the PVA content leads to low encapsulation efficiency and drug loading.

In vitro release is performed to investigate the release behavior of the PHBV nanoparticles. The IBU release curve shows a biphasic release pattern: the initial burst in the first two hours and the subsequent steady release with constant rates. Decreasing the drug/polymer ratio and HV content can weaken the initial burst effect to some extent.
Chitosan (CHI) and alginate sodium (ALG) were successfully adsorbed onto PHBV nanoparticles by the layer-by-layer self-assembly technique. Zeta-potential and TEM indicated the alternative deposition of CHI and ALG onto the surface of nanoparticles. The encapsulation efficiency and drug loading of the nanoparticles after deposition decreased a little. In vitro release of the coated nanoparticles suggests that the initial burst effect was weakened dramatically. Only 15 wt% of the IBU release in the first 2 hours, and the half release time had expanded to 66 hours, which is 33 times of that of bare IBU-loaded nanoparticles.

**Keywords:** Nanoparticles; Solvent evaporation; In vitro release; Layer-by-Layer self-assembly