Abstract

The project attempts to develop an oral delivery system of BCG vaccine. The project will be proceeded in three years. In the first year, solid dosage forms had been investigated to evaluate the physicochemical properties of developed preparations. Oral vaccine delivery systems were prepared, and the release characteristics were determined by in vitro dissolution method. In the second year, formulation factors potentially affecting vaccine delivery systems were assessed for the establishment of an optimal formulation of oral vaccine preparation. In the third year, the major work is to establish the evaluation method for assessing vaccine stability. Additionally, we intend to develop an animal model to evaluate the therapeutic effect of vaccine preparations. The in-process factors related to the manufacturing procedure will also be evaluated.

In this year, we used a biodegradable copolymer, poly(lactide-co-glycolide) (PLG), to prepare PLG microparticles as carriers for adsorbing BCG vaccine. In addition, we established a BCA (bicinchoninic acid) analytical method for determining the concentration of BCG vaccine. A calibration curve was constructed with good linearity ranged from 150 to 1000 ？Hgg/ml. Carriers with vaccine could be further prepared as granules and capsules for convenience in oral administration. Excipients and adjuvants including: carbonates, magnesium and aluminum compounds were incorporated in the preparation to assess their effects on the potency of BCG vaccine. Capsules with enteric coating were prepared to prevent the digest of active vaccine in gastric fluid. Preparations were conducted by in vitro dissolution test to evaluate the protecting capability of enteric coating, vaccine preparations are tested in acidic fluid (pH 1.2)for 2 hrs, following in neutral phosphate buffer solution. Our results indicated that the protecting capability of enteric coating is enhanced as increasing the coating time. In the preliminary study, we found that the prepared enteric capsules disintegrate about 3~4 hrs in the stomach of rabbit, but remain intact at 2 hrs. Furthermore, we also investigated the temperature effect of preparing environment; the preparations of BCG vaccine had better potencies at lower temperature.

Overall the results of 2 years, we used suitable excipients to prepare BCG vaccine as a suitable enteric capsule, which were prepared and stored under low temperature. The prepared enteric capsules could maintain their activity at 18% for 1 month storage. Thus, BCG vaccine is potentially developed as an oral delivery system in the study. Another, the established preparing method can be applied to other vaccines for the development of oral vaccine preparations.

Keywords：Oral Vaccines；BCG Vaccine；Biodegradable Polymers；Vaccine Carriers