Abstract

Over the past several years, there has been a concerted effort to develop a new vaccine against tuberculosis. The existing vaccine, Mycobacterium bovis Bacillus Calmette-Guerin (BCG), has been used for many decades, but meta-analysis of controlled clinical trials has revealed a lack of effectiveness in adults. In order to develop the oral vaccine that could be stable during oral administration and be targeted to M cells, we prepared the poly-DL-(lactide-co-glycolide)（PLG） microspheres containing BCG by a water-in-oil-in-water emulsion solvent evaporation method. The BCG strain was inoculated in Middlebrook 7H9 broth and qualified by acid-fast staining, polymerase chain reaction, and Western blotting. The bioadjuvant Escherichia coli heat-labile enterotoxin subunit B (LTB) was expressed from prokaryotic expression system and qualified by GM1-enzyme-linked immunosorbent assay. Two prototypes of oral BCG were constructed. One was the BCG-LTB conjugate, the other was PLG microspheres entrapped BCG-LTB. The microsphere showed a 41.7% entrapment ratio and a slow release manner. The immunogenicity of BCG-LTB conjugate was further investigated and the results showed that LTB indeed enhanced the humoral response of BCG in young and old mice. Taken together, our data suggested that PLG-based microspheres could serve as a formulation for controlled-release oral vaccine.

Keywords：Bacillus Calmette-Guerin；Escherichia coli heat-labile enterotoxin；Microsphere；Oral vaccine