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# Chitosan microspheres for nasal delivery of model antigen bovine serum albumin

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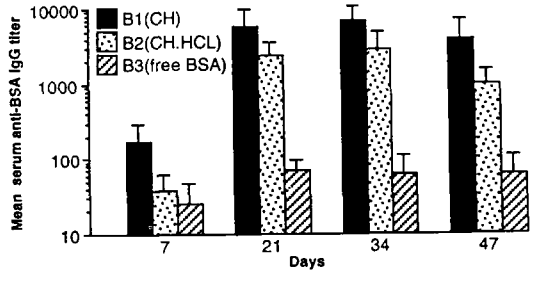
There is an increasing interest in the development of safe, efficient nasal delivery systems for proteins and vaccines. Due to its easier accessibility the nasal cavity is a potential alternative to parenteral and oral routes for the delivery of immunogenic substances (Almeida and Alpar (1996). Recently, efforts have been focused on the design of new and better vaccine delivery systems. Both synthetic and naturally derived polymers, especially in the form of microspheres have gained much attention as new ways for the controlled, and for targeted, delivery of therapeutic polypeptides and vaccines. Mucoadhesive microspheres, when used as antigen carrier for nasal delivery, may achieve increased residence time within the nasal cavity. Chitosan has been shown to have mucoadhesive properties. In this study we describe the use of chitosan as a delivery vehicle for a model antigen, bovine serum albumin (BSA). Chitosan (polyglycosamine), a polysaccharide prepared from crustacean shells, is biocompatible and naturally resorbed by the body and has been previously used for sustained drug release, bone induction material, and homeostasis Chandy et al., (1991), Klokkevold et al., (1992). Chitosan microspheres containing BSA were prepared by a spray-drying method. Microspheres were prepared from chitosan base (CH) (high molecular weight, Aldridge) and chitosan hydrochlroride (CH.HCL) (Seacure210 Pronova).The encapsulation procedure involved is a mild aqueous process which is ideal for the incorporation of labile proteins. Briefly, chitosan and BSA dissolved in either double distilled water (for CH.CHL) or in 1% w/v aqueous acetic acid solution (for CH) : 100 ml of this solution was taken in 250 ml beaker and used for spray dry process. CO-current spray drying was performed using SD-04 spray drier (Labplant, England) with standard 0.5 mm nozzle. The amount of BSA encapsulated was determined by bicinchoninic acid assay. The stability of BSA was determined by sodium dodecyl sulphate (SDS-PAGE method). Microspheres with an average diameter of ~5 μm and~ 2% w/w BSA loading is obtained. 5 μg of encapsulated BSA was delivered intranasally into the mouse nostrils with micropipeptte on day 1 and day 14. Four groups of mice (n=5 per group ) were used in this study. Group (B1) was dosed with CH microspheres containing 5 μg equivalent of BSA. Group (B2) was dosed with CH.HCL microspheres containing 5 μg equivalent of BSA. Group(B3) was dosed with 20 μg of free BSA. Free BSA and particles were delivered in PBS ( pH 7.4). Untreated animals were used as a control. Tail vein blood samples were collected periodically and their serum tested for the presence of BSA-specific antibodies using an ELISA method.

Fig.1 Anti-BSA specific IgG titers in serum of mice dosed nasally with BSA free or microencapsulated in CH or CH.HCL (Mean ±s.d; n=5)




BSA in CH (B1) and CH.HCL (B2) microspheres potentiated IgG response significantly above those induced by soluble BSA (B3). CH microspheres gave greater IgG response than the CH.HCL microspheres which were approximately 40 times higher than those obtained for free BSA. This may be due to reduced binding to the negatively charged mucosa and less penetration enhancing capacity of microspheres prepared with soluble CH.HCL (Schipper et al 1996). This study shows that delivery of BSA in mucoadhesive chitosan microspheres enhances systemic immune response after nasal delivery which is also dependent on the nature of chitosan used in the preparation of microspheres.

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