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Induction of high antitoxin titers against tetanus toxoid in rabbits by intranasal immunization with dextran microspheres

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View references (٣٩)

Abstract

Poor absorption of protein antigens through the mucosal membranes necessitates the use of mucoadhesive delivery systems. Regarding the advantages of mucosal immunization and also the penetration enhancement potential of dextran microspheres, in this study the adjuvant potential of these microspheres was compared with CpG-ODN. Cross-linked dextran microspheres (CDMs) were loaded with tetanus toxoid (TT). In vitro release studies were performed in a model, simulating the nasal cavity. The immunoreactivity of encapsulated TT was assayed by ELISA. Membrane toxicity and local irritating potential of CDM was examined by erythrocyte hemolysis and nasal administration to human nose, respectively. The various formulations were nasally administered to rabbits (n = ٤). Alum-adsorbed TT (AATT) was injected as the positive control. The serum IgG and nasal lavage sIgA titers were determined by ELISA method. Serum antitoxin titers were determined by toxin neutralization (TN) bioassay method. Mean diameter of CDM was ١٢٨,١ ± ٢٥,٨ μm. Mean encapsulation efficiency was ٢٠,٣ ± ٣,٢٪ (n = ٣). Antigenicity of encapsulated TT was ٩٠,٥ ± ١,٨٪ (n = ٣) that of original TT. Hemolysis studies showed no membrane disruption by CDM and none of the human subjects reported nasal irritation. Among the nasally immunized animals, the highest antitoxin titers was seen in the group immunized with CDM + TT (P < ٠,٠٠٠١). The serum IgG titers of the CDM + TT group was higher than the TT solution group (P < ٠,٠٥). The adjuvant potentials of CDM and CpG-ODN in inducing IgG titers was not significantly different (P > ٠,٠٥). The lowest sIgA titers in the bronchial lavage were seen in the group of animals received AATT parenterally. Considering the proper release characteristics, desirable preservation of the antigen activity of TT, good mucoadhesion properties and also safety of CDM + TT, these microspheres could be regarded as an efficient mucosal adjuvant and antigen delivery system. These microspheres could induce very high antitoxin titers following nasal administration, while the CpG-ODN could not induce such titers. The antitoxin titers induced by CDM + TT was ١٧٥ times higher than the protective levels.

Reaxys Database Information

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Author keywords

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Indexed Keywords

EMTREE drug terms: antitoxin; CpG oligodeoxynucleotide; dextran; immunoglobulin A; immunoglobulin G; microsphere; sephadex; tetanus toxoid

EMTREE medical terms: animal experiment; antibody detection; antibody titer; antigenicity; article; bioassay; burning sensation; clinical article; controlled study; coughing; enzyme linked immunosorbent assay; hemolysis; human; human cell; human experiment; lung lavage; nonhuman; normal human; nose irritation; priority journal; rabbit; side effect; sneezing

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