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Induction of systemic and mucosal immune responses by intranasal administration of alginate microspheres encapsulated with tetanus toxoid and CpG-ODN

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Abstract

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In the induction of systemic and mucosal immunity, particulate antigens are more effective than soluble antigens; possibly because they are more efficiently endocytosed by mucosal-associated lymphoid tissue (MALT) M cells. In this study, we determined the systemic and mucosal immune responses in rabbits following intranasal immunization with encapsulated tetanus toxoid (TT) and CpG-ODN in alginate microspheres. The microspheres were less than 4 μm in diameter. Encapsulation efficiency of TT and CpG-ODN was determined as 47.7 ± 6.6 and 34.2 ± 7.4 , respectively. Release of TT and CpG-ODN in a simulated model with nasal cavity was 14.2 ± 3.06 and $36.7 \pm 2.4\%$ after 4 h. Encapsulated TT preserved its intact structure, but its immunoreactivity was decreased to about $91 \pm 5\%$. The highest serum IgG and antitoxin, and nasal lavage IgA titers were observed in groups immunized with microsphere formulations. CpG-ODN as an adjuvant could increase the serum IgG and antitoxin titers when co-administered with TT solution, but its co-encapsulation with TT in alginate microspheres failed to potentiate the systemic immune response while induced high IgA titers in nasal lavages. No hemolysis was occurred on incubation of alginate microspheres and human RBCs. Also after nasal administration of plain microspheres to human volunteers, no local irritation was observed. Intranasal administration of microspheres encapsulated with vaccines showed to be an effective way for inducing a variety of immune responses and that a strong systemic IgG and mucosal IgA responses can be induced in rabbits with intranasal administration of alginate microspheres encapsulated with TT. © 2006 Elsevier B.V. All rights reserved.

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Author keywords

Alginate; CpG-ODN; Microsphere; Nasal immunization; Tetanus toxoid

Indexed Keywords

EMTREE drug terms: alginic acid; antitoxin; CpG oligodeoxynucleotide; microsphere; tetanus toxoid

EMTREE medical terms: animal experiment; animal tissue; article; controlled study; drug formulation; drug release; erythrocyte; hemolysis; human; human cell; immune response; immunization; immunoreactivity; microencapsulation; mouse; mucosal immunity; nonhuman; nose cavity; nose mucus; priority journal; rabbit

MeSH: Adjuvants, Immunologic; Administration, Intranasal; Alginates; Animals; Chemistry, Pharmaceutical; Drug Carriers; Drug Stability; Glucuronic Acid; Hexuronic Acids; Humans; Immunity, Mucosal; Immunoglobulin A; Immunoglobulin G; Microspheres; Nasal Lavage Fluid; Oligodeoxyribonucleotides; Particle Size; Rabbits; Solubility; Tetanus Antitoxin; Tetanus Toxoid
Medline is the source for the MeSH terms of this document.

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