

DIVALENT BIODEGRADABLE MICROSPHERE VACCINES INCUDE PROTECTIVE IMMUNE RESPONSE AGAINST TETANUS AND DIPHTHERIA

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INTRODUCTION: Biodegradable microspheres (MS) represent a promising approach in the development of single-injection vaccine delivery system. MS made of poly(lactide) (PLA) or poly(lactide-co-glycolide) (PLGA) and loaded with tetanus or diphtheria toxoid have demonstrated strong immune stimulation with lasting antibodies in mice and guinea-pigs after a single inoculation, and a first human trial with a tetanus vaccine is presently envisaged. So far, most of the studies have used single microencapsulated antigen, whereas the feasibility of combining several antigens in a single microsphere formulation is unknown.

In this study, we have tested the immunological performance of divalent MS vaccines against tetanus and diphtheria in guinea pig. The animals were subcutaneously immunised once with diphtheria and tetanus toxoids contained in PLGA-MS. All formulations were strongly immunogenic, irrespective of MS size and hydrophobicity. ELSIA antibodies, mainly of the IgG1 subtype, were quantitatively comparable with those induced after two immunisations with a licensed vaccine which contain the antigens adsorbed on aluminium hydroxide. The MS-formulations provided increasing levels of antibodies during the 16 weeks of testing. The antibody responses were also weakly polarised in favour of tetanus. After a challenge with tetanus and diphtheria toxins, the MS mediated protective immunity comparable or better than did the licensed divalent vaccine. The protection efficacy did not correlate well with toxin neutralisation, which demonstrated superiority of the licensed vaccine when given twice. However, MS-aided neutralising antibodies against both diphtheria (2-4 IU/ml) and tetanus (5-18 IU/ml) toxins were orders of magnitude above protective level (0.01 IU/ml) when immunised with MS. These levels were similar to those obtained with a single injection of the licensed vaccine.

In conclusion, this study showed that a single administration of biodegradable MS vaccines provided protective immunity against diphtheria

and tetanus and that this immunisation approach may be feasible for multivalent vaccines. However, direct challenge and toxin neutralisation assays yielded contrasting information on the product quality of the vaccine, so methods for testing the efficacy of slow-release formulation might need to be revised.

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