

Injectable polymer microspheres enhance immunogenicity of a contraceptive peptide vaccine

Chengji Cui^{a,1}, Vernon C. Stevens^b, Steven P. Schwendeman^{a,*}

^a Department of Pharmaceutical Sciences, University of Michigan, Ann Arbor, MI 48109-1065, United States

^b Division of Reproductive Biology and Vaccine Development, The Ohio State University, Columbus, OH 43210, United States

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Abstract

Advanced contraceptive peptide vaccines suffer from the unavailability of adjuvants capable of enhancing the antibody response with acceptable safety. We sought to overcome this limitation by employing two novel poly(lactic-co-glycolic acid) (PLGA) microsphere formulations to deliver a synthetic human chorionic gonadotropin (hCG) peptide antigen co-synthesized with a T-cell epitope from tetanus toxoid (TT), C-TT2-CTP35: surface-conjugated immunogen to induce phagocytosis; and encapsulated peptide to provide a depot effect, with MgCO₃ co-encapsulated in the polymer to neutralize acidity from the biodegrading PLGA polyester. A single immunization of encapsulated peptide in rabbits elicited a stronger antibody response with equivalent duration relative to a positive control—three injections of the peptide administered in a squalene-based water-in-oil emulsion. Surface-conjugated peptide was less effective but enhanced antibody levels at 1/5 the dose, relative to soluble antigen. Most remarkable and unexpected was the finding that co-encapsulation of base was essential to attain the powerful adjuvant effect of the PLGA–MgCO₃ system, as the MgCO₃-free microspheres were completely ineffective. A promising contraceptive hCG peptide vaccine with acceptable side effects (i.e., local tissue reactions) was achieved by minimizing PLGA and MgCO₃ doses, without significantly affecting antibody response.

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1. Introduction

For several decades the World Health Organization (WHO) has pursued development of safe, effective and long-acting (e.g., 6 months) nonsteroidal immunocontraceptives to obviate side effects, such as endocrine and other metabolic disturbances, often associated with long-acting steroid hormone preparations [1]. At the forefront of the newly recognized field of immunopharmaceuticals, vaccines against

hCG are among the most advanced contraceptive vaccines, utilizing the body's own immune defense system to provide protection against pregnancy [2,3]. A hormone synthesized in appreciable amounts exclusively during pregnancy by the early conceptus or in some cancers, hCG plays an essential role for establishing and maintaining early pregnancy [4,5]. Antibodies against hCG exert antifertility action at the post-fertilization/pre-implantation stage without disturbance of the normal ovulation function or hormone secretion. Once the effective antibody level has retreated after several months, immunity can be boosted to continue contraception or discontinued to recover fertility. A successful immunocontraceptive is expected to provide a new and improved method for family planning without the fear of side effects or need of access to high quality services, and lead to a significant public health benefit for millions of families [1].

Abbreviations: PLGA, poly(lactic-co-glycolic acid); hCG, human chorionic gonadotropin; CTP, C-terminal peptide; PBS, phosphate buffered saline; PBST, phosphate buffered saline containing 0.02% Tween 80

* Corresponding author. Tel.: +1 734 615 6574; fax: +1 734 615 6162.

E-mail address: schwende@umich.edu (S.P. Schwendeman).

¹ Present address: Formulation Development, Consumer & Personal Product Worldwide, Johnson & Johnson, 199 Grandview Road, Skillman, NJ 08558, United States.