Chapter 14
Effective Strategy for Delivering Nano-Liposomal Encapsulated Mycobacterial ESAT-6 Vaccine Adjuvant in Tuberculosis: Optimization, Characterization, and Preclinical Evaluation of Pharmaceutical Nanoparticles

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ABSTRACT

Nanoparticles-based biological products need to be explore for finding out newer adjuvants. Most of next generation adjuvants are in clinical trials. Vaccine funding agencies should consider and initiate specific funding programs for adjuvant science and clinical development; even it remains a major roadblock in new vaccine development, too. In current context of research, the authors elaborated the nano-liposomal encapsulated ESAT-6 vaccine subunit adjuvant with chitosan polymers. Methodology involves, for characterization of these, nano-liposomal formulation, particle size, in vitro drug release, and different pre-clinical pharmacology approaches for evaluation of nanovaccine anti-tubercular activity. This research is not exhaustive of all cellular compartments or agents and many subsets have been well reviewed. Indeed, many of these cells or antimicrobial mediators may play significant roles in prevention of Mtb infection, as signs of measurable memory immune responses in some cases are not evident, and could explain why some individuals are resistant to infection.

DOI: 10.4018/979-8-3693-6326-3.ch014

INTRODUCTION

Vaccine Adjuvant in Nanoparticulate Liposomal Formulation: Infectious disease has been one of the most common causes of morbidity since a very long time leading to an unprecedented burden on the healthcare system. Developing countries like India has experienced outbreak of varied Tuberculosis diseases leading to great loss of life as well as economy. For countries like India, geo-climatic conditions and overpopulation can be blamed for outbreak of many Tuberculosis diseases like malaria, influenza, chickenpox etc. Despite of vast armamentarium to curb the spread of microbes, infectious diseases still pose a threat globally. Due to emergence of vaccines and antibiotics, the number of cases has definitely decreased many folds. Vaccination has effectively averted millions of deaths from common Tuberculosis disease. It has been regarded as one of the most economical and effective means to prevent and control infectious disease. Despite the ever-increasing scope of vaccines, the battle against Tuberculosis diseases is still to be triumphed. Henceforth, much research has been carried out to strive and improve the immunogenicity and efficiency of the vaccine without compromising the safety parameter of the same. One such way to attain an improved immunogenicity of the vaccine without compromising the safety is by using adjuvants. Adjuvants had been used for more than half a century now to enhance the innate as well as the adaptive immunity response induced using a vaccination allowing for development of effective memory response and thereby better protection against the deadly infections. Despite the magnificent properties and advantages of adjutants, there are only a few adjuvants that have been approved by USFDA. Adjuvants like aluminium salts, saponins, monophosphoryl lipid A and unmethylated CpG oligodeoxynucleotides. Each of the adjuvant is destined to induce a specific immune response thereby resulting in a tailor-made vaccine to target a specific pathogen. However, since only a small number of adjuvants are clinically approved, there is a constant need to find more adjuvants to effectively fine tune the tailor-made vaccines. Continued investigations and research has shown the property of biomaterial like Chitosan to act as a possible adjuvant. Being a biomaterial, it is non-toxic and bio-compatible in nature and hence can act as an effective adjuvant in vaccine delivery. Moreover, the antiTuberculosis property of the chitosan adds as an added advantage in using chitosan as an adjuvant in antiTuberculosis vaccines *(Bode, C. et.al., 2011).*

Mechanism of Nano-Liposomal Drug Delivery System: Liposomes are synthetic spheres containing lipid layers that can encapsulate antigens that are desired and act as adjuvants. Classical liposomes are vesicles composed of phospholipids and often cholesterol. They act by slowly releasing encapsulated antigen on intramuscular injection and by passively accumulating within regional lymph nodes. Liposomes can induce both humoral and cellular immunity to protein and polysaccharide antigens. The potency of liposomes varies with the number of lipid layers, electric charge, composition and method of preparation. The liposomal based vaccines fuse with cell membranes of macrophages, enabling the delivery of proteins into the cytoplasm and enter in to major histocompatibility complex (MHC) class I pathway and activate CD8 cells. The major drawback of liposomes is manufacturing difficulties such as stability, high cost and may produce pain at the site of injection. Recently, liposome based vaccines against Lung cancer is in phase III while vaccines against *Neisseria meningitidis*, HIV and TB is in phase I clinical trial.

Vaccine Adjuvant (ESAT-6): Adjuvants are most important component of vaccine usually added with the immunogen in vaccine preparation. Since long back, adjuvants have been used to reduce immunogen dose, improve longevity and enhance the efficacy of vaccine. Though its wide use in pharma industries for vaccine manufacturing, it produce side effects, sometimes potent adverse reaction. From the earlier