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Development and Characterization of pH sensitive liposomes for macrophage targeting using prime-boost vaccination strategy for Pulmonary Tuberculosis

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Abstract

Tuberculosis (TB) caused by the bacterium *Mycobacterium tuberculosis* remains a major health problem worldwide. Although BCG seems to provide protection against miliary tuberculosis, its effect on pulmonary TB in adults is poor, and needs a better vaccine regimen to combat the disease. Various strategies have been postulated for the development of the tuberculosis vaccine viz. improving the current BCG vaccine, over expression of the immunodominant antigens, endosomal escape, recombinant fusion proteins and a hybrid approach which is a multiphase vaccine that can be administered regardless of the infection status of the individual and with activity both in naïve and already infected individuals. The present investigation was aimed to develop liposome based DNA prime-protein boost vaccine regimen against pulmonary tuberculosis. The rationale behind the use of liposomes as delivery systems in intracellular infections such as mycobacteria is selective uptake by the macrophages, following systemic administration and versatility to engineer to target the specific site in the body via binding to specific receptors.

Two types of multilamellar liposomes (MLVs) were prepared, one ligand directed while the other pH sensitive cationic. Liposomes were developed using DRV (dehydration-rehydration vesicles) and film hydration technique using trehalose dibehenate (TDB) as a protein stabilizer. *O*-palmitoyl mannan (OPM) was used to coat the ligand directed liposomes to impart them the desired targetability for the alveolar macrophages. Plasmid DNA encoding genes for Ag85A were adsorbed on the preformed pH sensitive cationic liposomes whereas rAg85A was entrapped in the ligand directed (OPM coated) liposomes.

The optimized formulation was evaluated for various physico-chemical parameters such as vesicle size, shape, entrapment/loading efficiency of the bioactive, their structural integrity by SDS-PAGE followed by confirmation with the western blot and agarose gel electrophoresis and *in vitro release*. *In-vivo* immune responses were obtained in terms of antibody responses, isotype titers as well as cytokine profile.

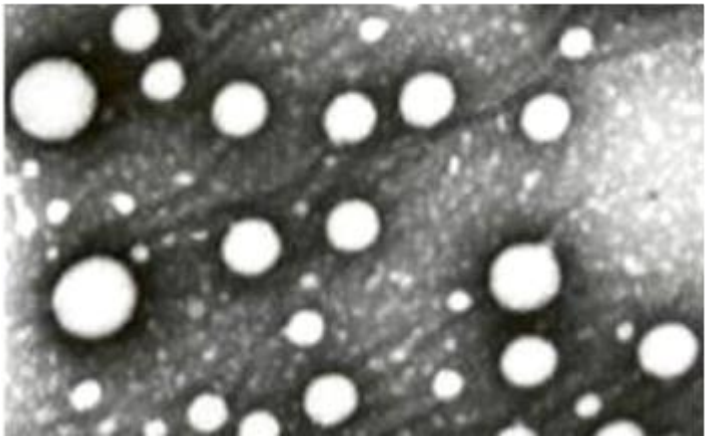

Figure 1: TEM of the liposomal formulations

Biography:

Dr. Abhinav Mehta is currently Associate Professor at R C Patel Institute of Pharmaceutical Education and Research at Shirpur, Maharashtra, India. He has 26 publications in peer reviewed journals. He has h-index of 13 and an i10-index of 16 with more than 570 citations. He has supervised 12 M. Pharm students and co-supervised 1 PhD student. He has to his credit 1 Govt. sponsored project on Drug delivery system and Tuberculosis. He has 1 year postdoctoral experience. His current recent research interest is on the development of stimuli responsive drug delivery system

Speaker Publications:

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2. Abhinav Mehta, Neha Jain, Anne Grobler, Vandana Bharti. Role of Novel Drug Delivery Systems in Bioavailability Enhancement: At A Glance. 2016 6 (1) 7-26.
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