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Towards the development of oral vaccine delivery systems for lipid core peptide-based vaccines using novel multi-layer engineered nanoliposomes against Group *A streptococcus*

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The aim of our project is to develop a novel oral nano-vaccine delivery system against group A streptococcus (GAS) by encapsulating lipid core peptide (LCP) antigens into the liposomes. We synthesized the LCP construct by attaching C-16 lipoamino acids (Toll-like receptor-2 agonist) with J-14 (B-cell epitope derived from GAS M-protein) and P25(universal CD4+ T-helper epitope) using microwave assisted solid-phase peptide synthesis. The optimized LCP-loaded liposome formulations were prepared and their surface were coated with oppositely charged polyelectrolytes [negatively charged sodium alginate and positively charged trimethyl chitosan (TMC) and characterized by dynamic light scattering (DLS) and transmission electron microscopy (TEM). Loading efficiency of the LCP-loaded formulations was approximately 80%. DLS and TEM measurements showed spherical monodisperse particles before and after three layers coating with alginate-chitosan-alginate with final size of ~165 nm and ~195 nm, respectively. Positively-charged formulations (LCP-loaded liposomes and double-layered TMC-coated liposomes) had a significant uptake by dendritic cells and macrophages compared to negatively-charged single and triple-layered liposomes. Developed formulations showed an enhanced colloidal stability of liposomes in simulated gastric and intestinal fluid. In vivo oral immunization studies in Swiss outbred mice with double-layered TMC-alginate chitosan-coated liposomes showed higher J-14 specific mucosal IgA and systemic IgG production in the mucosal fluids and serum, respectively as compared to positive controls. Our findings are an important step to towards overcoming the hurdles associated with the development of oral peptide-based vaccines. Taken together, our results suggest that layer-by-layer engineered nano-architecture formulations as a promising novel strategy for oral delivery of lipopeptide-based vaccines.

Biography

Mr Nirmal Marsini received his Bachelor's degree in pharmacy from Tribhuvan University, (2009) and Master's degree in pharmaceutical sciences (2012) from Yeungnam University, South Korea under Korean government scholarship specializing in formulation development. Currently, he is a 3rd year PhD student at The University of Queensland in Professor Istvan Toth's group under IPRS and APA scholarships. His PhD project is focused on developing oral vaccine delivery system for peptide-based antigens. He was a He has also published 19 original papers in reputed pharmaceutical journals including 5 first author papers.

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