DEVELOPMENT OF LIPOSOME BASED VACCINE FORMULATION AGAINST LEISHMANIASIS

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ABSTRACT

Vaccination remains one of the most efficient strategies in preventing infectious diseases, such as leishmaniasis. However, the development of vaccines against intracellular pathogen infections, that require the induction of efficient T cell immune responses, has proven a rather difficult task. Subunit proteins provide a safe source of antigens for vaccine development especially for intracellular infections. However, they are often limited by their low immunogenicity. In order to achieve effective immune responses, they should be encapsulated into a stable antigen delivery system combined with an appropriate adjuvant. In this respect, the present study focuses on the development of a cationic liposomal platform for the co-delivery of antigens and adjuvants that can elicit strong antigen-specific immune responses. More specifically, liposomes comprising the cationic lipid dimethyl dioctadecylammonium bromide (DDAB), cholesterol (CHOL) and oleic acid (OA), and encapsulating the anti-leishmanial antigen LiChimera and/or the adjuvant imiquimod (IMQ) were prepared using the hydration/extrusion method. The developed liposomes were characterized with respect to particle size, zeta potential, antigen/adjuvant loading, antigen release and storage stability. They were found to have an average diameter of 250 nm, positive zeta potential values of 13.8-34.0 mV, and LiChimera and IMQ loadings equal to 2.5-4.6 wt% and 7.9-13.3 wt% respectively. They were also shown to exhibit sustained LiChimera release in PBS and FBS, and stability for 4 weeks in water for injection (WFI) at 4^{o}C. In vitro testing of blank and adjuvanted liposomes indicated an effective uptake by bone marrow dendritic cells (BMDCs) and promotion of BMDCs maturation and activation. In vivo intramuscular administration of the developed formulation showed active drainage of liposomes to lymph nodes (LNs) mediated by dendritic cells (DCs), B cells and macrophages. Thus, mice immunization with liposomes encapsulating LiChimera and IMQ was shown to elicit infiltration of CD11b^{low} DCs populations in draining LNs followed by increased antigen-specific IgG, IgG2a and IgG1 levels production as well as induction of antigen-specific CD4^{+} and CD8^{+} T cells. Conclusively, the developed IMQ-adjuvanted cationic liposomes were shown to provide a promising delivery platform for protein antigens capable to induce strong adaptive immune responses via DCs targeting and induction of maturation[1].

KEYWORDS: Liposomes, subunit chimeric vaccine, adjuvant, antigen, innate response

REFERENCES

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