

Extended Abstract

Design and Synthesis of Immunostimulating Mannosylated Muropeptide Analogs Containing 2-Aminoadamantane-2-carboxylic Acid [†]

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Abstract: Muramyl dipeptide (MDP, *N*-acetylmuramyl-L-alanyl-D-isoglutamine) is known as the smallest synthetic adjuvant molecule capable of replacing whole *Mycobacteria* in Freund's adjuvant. Numerous MDP derivatives were synthesized with the aim to avoid MDP unwanted side-effects. Many of them have therapeutic potential, including clinical use. A very important parameter in the improvement of pharmacological properties of MDP is lipophilicity, e.g., it eliminates drawbacks caused by poor macrophage penetration and rapid elimination. On the other side, mannose receptors (MR), present on immunocompetent cells (such as macrophages and dendritic cells), are considered to be pattern-recognition receptors and responsible for the binding, among others, of mannosylated antigens or relevant biologically active molecules containing mannose, thus affecting the immune reactions. Up to now, our research was directed towards desmuramyl peptides which contain adamantylglycine and mannosylated adamantylglycine moieties bound to the essential part of MDP, L-Ala-D-isoGln. Here, we present the design and synthesis of novel mannosylated muropeptide analogs containing 2-aminoadamantane-2-carboxylic acid. Prepared desmuramyl peptides have lipophilic 2-aminoadamantane-2-carboxylic acid attached at the N-terminus of desmuramyl dipeptide core and mannose connected to the tripeptide over a glycolyl linker. Immunostimulating activities of prepared compounds will be evaluated in the mice model using ovalbumin as an antigen and compared with previously prepared derivatives.

Keywords: adamantane; adjuvant; mannose; muramyl dipeptide



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