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Short communication

New conjugates of muramyl dipeptide and nor-muramyl dipeptide linked to tuftsin and retro-tuftsin derivatives significantly influence their biological activity

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Abstract:
The synthesis and biological activity of new conjugates of muramyl dipeptide (MDP) and nor-muramyl dipeptide (nor-MDP) with tuftsin and retro-tuftsin derivatives containing isopeptide bond between ε-amino group of lysine and carboxyl group of simple amino acids such as Ala, Gly and Val are presented. We presumed, based on the cytokine profile, that the examined conjugates of tuftsin and MDP were capable of activating antibacterial mechanisms by switching on Th1 immune response. The most active were compounds **11**, **14** and **19**–**23**.

Key words:
muramyl dipeptide, nor-muramyl dipeptide, tuftsin derivatives, synthesis, immunomodulator

Introduction

Muramyl dipeptide (Mur*N*Ac-L-Ala-D-isoGln; MDP) **1** (Fig. 1), a component of peptidoglycan, stimulates various functions of macrophages and increases non-specific resistance of the host against numerous microorganisms [1, 4, 7, 15–17]. Another immunomodulator, tuftsin, is a natural tetrapeptide, H-Thr-Lys-Pro-Arg-OH (TKPR) **2**, present in the peripheral blood of humans and other mammals, where it stimulates monocytes, macrophages, and neutrophils [14, 20]. We have previously reported the synthesis of the conjugates of MDP and nor-muramyl dipeptide (nor-MDP) with tuftsin [2, 3, 6, 18, 19]. The most propitious compounds were then further examined *in vivo*. The elaborated animal model of experimentally induced sepsis allowed us to screen them reliably as potential therapeutic agents [18]. Importantly, tested already compounds were found as efficient stimulators of innate immunity, which resulted in slowing down of experimental sepsis. Hence, the examined already conjugates are reckoned rather as adjuvants than separate therapeutic agents [18].