C-terminal Lysine-linked Magainin 2 with Increased Activity against Multidrug-resistant Bacteria

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Introduction: due to the increasing problem of antibiotic-resistant microorganisms, the development of novel antibiotic agents is a very important task. Dimerization of cationic antimicrobial peptides (cAMPs) is a potential strategy for enhancing antimicrobial activity. **Objectives:** we studied the effects of magainin 2 (MG2) dimerization on its structure and biological activity. **Material and Methods:** lysine and glutamic acid were used to synthesize the C- and N-terminal dimers of MG2, respectively, in order to evaluate the impact of linker position used to obtain the dimers. The peptides were manually synthetized by solid phase synthesis and the secondary structure was determined by circular dichroism. Membrane interaction was studied by carboxyfluorescein (CF) release experiments and antimicrobial activity tests were performed using the broth microdilution method. **Results and Discussion:** both MG2 and its dimeric versions showed a random coil structure in aqueous solution. However, in the presence of a structure-inducing solvent or a membrane mimetic, all peptides acquired helical structure. N-terminal dimerization did not affect the biological activity of the peptide. On the other hand, the C-terminal dimer, $(MG2)_2K$, showed antimicrobial activity 8–16 times higher than that of MG2, and the time required to kill *Escherichia coli* was lower. CF release experiments showed that the enhanced antimicrobial activity is related to membrane permeabilization. $(MG2)_2K$ was also more active against multidrug-resistant bacteria of clinical origin. **Conclusions:** the results presented here demonstrate that C-terminal lysine-linked dimerization improve the activity of MG2, and $(MG2)_2K$ can be considered as a potential antimicrobial agent.