

SYNTHETIC LYSINE-RICH AGENTS BASED UPON THE FROG PEPTIDE OCELLATIN 4 PRESENT ENHANCED CYTOLYTIC ACTIVITY

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Ocellatin 4 is a 21-residue-long weakly antibacterial and strongly hemolytic peptide isolated from the skin secretion of the South American frog *Leptodactylus ocellatus*. Based upon substitutions in its sequence, two novel cytolytic agents have been designed. S2328 (MM.= 2328.54 u) presents seven substitutions (K1-K4-K8-A12-K15-A16-A20), a total of six lysines and +6 charge at pH 7.0. S2555 (MM = 2555.65 u) shows five substitutions (K1-R4-K8-R12-K15), five lysines and a charge of +7. Peptides were chemically synthesized according to the protocol of Atherton e Sheppard (1989), purified by RP-HPLC and analyzed by MALDI-TOF MS. To determine biological activity, serial dilutions of the peptides were incubated with red-blood cells and with reference strains of Gram-negative and Gram-positive bacteria. S2328 and S2555 were, respectively, 35-fold and 21-fold more hemolytic than ocellatin 4. Both peptides were 4-fold more active against Gram-negative bacteria and 8-fold more active against Gram-positive bacteria. The strong hemolytic activity is probably related to the presence of several lysines, which may increase molecular amphipathicity, and the enhanced antibacterial activity is associated with the high cationicity of the peptides.