STRUCTURE-ACTIVITY RELATIONSHIP STUDY OF SHEPHERIN I, A NEW GLYCINE AND HISTIDINE-RICH ANTIMICROBIAL PEPTIDE

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Shepherin I, isolated from the roots of *Capsella bursa-pastoris*, has been employed as a wound-healing agent in Korea. This carboxyl-free antimicrobial peptide (AMP) is characterized by high contents of glycine and histidine and six direct repeats of the motif GGH. Recognizing that histidine-rich peptides are potential new antibiotics, that the spread of *Candidas* resistant to amphotericin and azole agents has increased and that the first step to study the structure-activity relationship of an AMP is to find its fully active minimal portion, we synthesized and tested Shepherin I and fragments against *C. albicans.* Since carboxyamidation may enhance the activity of AMPs, we also studied amidated analogs of these peptides. Carboxyl-free and amidated Shepherin I presented identical MICs (6.25-12.50 μM). While the carboxyl-free fragments 3-28, 1-20 and 3-20 were 2-, 4- and 8-fold less active, respectively, 6-20, 9-20, 12-20, 15-20 and 18-20 presented MICs higher than 100.0 μM. The amidated fragments 3-28 and 6-28 showed MICs of 12.5-25.0 and 25.0-50.0 μM, respectively. Therefore, we concluded that: *i)* although Shepherin I has no fully active minimal portion, its two N-terminal amino acids can be deleted without a substantial reduction of the anticandidal activity; *ii)* carboxyamidation does not affect the potencies of Shepherin I and its fragments.

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