Chiroptical Properties of the Antimicrobial Peptide *Lasiocepsin* and of its analogs

Markéta Pazderková;[1,2] Petr Maloň,[1] Václav Profant, [1] Vladimír Baumruk;[1] Lucie Bednárová[2]

[1] *Institute of Physics, Faculty of Mathematics and Physics, Charles University in Prague, Prague 2, Czech Republic*

[2] *Institute of Organic Chemistry and Biochemistry, Prague 6, Czech Republic, bednarova@uochb.cas.cz*

We report chiroptical properties of the novel antimicrobial peptide (AMP) lasiocepsin (LAS, 27As) containing two disulfide bridges [1] and of its three analogs designed to study the influence of heterodetic disulfide-closed rings. The set of peptides included the natural LAS (H-Gly-Leu-Pro-Arg-Lys-Ile-Leu-**Cys**-Ala-Ile-Ala-Lys-Lys-Lys-Gly-Lys-**Cys**- Lys-Gly-Pro-Leu-Lys-Leu-Val-**Cys**-Lys-**Cys**-OH), two analogs with just one disulfide bridge and the remaining two cysteines replaced by alanine residues (Las[Cys17-Cys27, Ala8,25] – LAS 2; Las[Cys8-Cys25, Ala17,27] – LAS 3), and a linear analog having all four cysteines replaced by alanines (Las[Ala8,17,25,27] – LAS 4A). LAS 2 retains reduced activities against common pathogens while LAS 3 and LAS 4A are inactive [1]. The effect of changing the disulfide bridge pattern on secondary structure is investigated by electronic circular dichroism (ECD) and vibrational optical activity (VOA) including Raman optical activity (ROA) and vibrational circular dichroism (VCD). A combination of these techniques helps us to clarify the role of disulfide bridges in stabilization of LAS's conformation. ECD indicates similar conformation of the disulfide bridge for analogs containing one disulfide (LAS 2, LAS 3), while ROA enables us to determine sense of disulfide torsion, even in the more complicated case of natural LAS containing two disulfide groups. The experimental mainly ROA results were compared to theoretical spectral dependences which were based on known NMR structure of natural lasiocepsin [2].

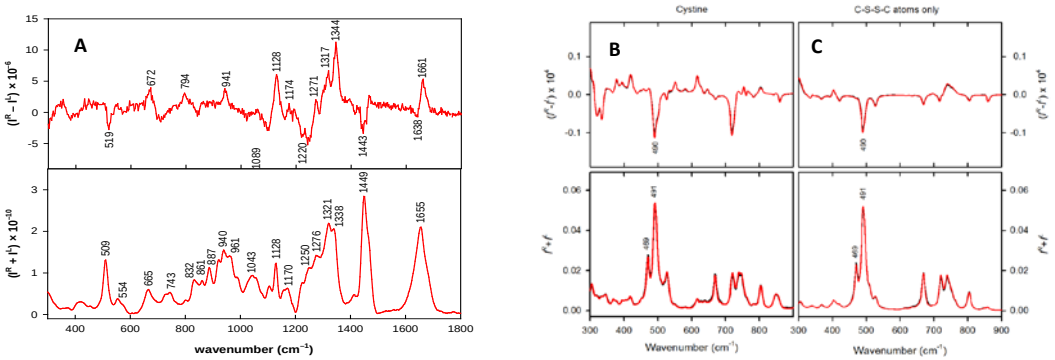

Figure 1: (A) experimental Raman/ROA spectra of lasiocepsin; (B,C) Calculated Raman/ROA signals in disulfide stretching region / for cystin atoms (B), C-S-S-C atoms involves in the calculation (C0

[1] Monincová L, Slaninová J, Fučík V, Hovorka O, Voburka Z, Bednárová L, Maloň P, Štokrová, J, Čeřovský V (2012) Amino Acids. 43(2):751-61

[2] Monincová L, Buděšínský M, Čujová S, Čeřovský V, Veverka V.(2014*) Chembiochem. 15(2):301-8*