A photolabile prodrug of tetrapeptide AAPV bearing 7-methoxycoumarin at the C-terminal

Filipa C. Santos, M. Sameiro T. Gonçalves, Susana P. G. Costa*

Department of Chemistry, University of Minho, Campus of Gualtar, 4710-057 – Braga Portugal *spc@quimica.uminho.pt

The tetrapeptide Ala-Ala-Pro-Val (AAPV) is an elastase inhibitor with potential utility in the management of psoriasis and recent studies have been conducted for the use of AAPV as a therapeutic agent for transdermal delivery [1].

Coumarins are well known fluorophores that have been reported as fluorescent labels and probes, due to their extended spectral range, high fluorescence quantum yields, good photostability and solubility in common solvents [2]. Also, coumarin derivatives have been applied as photocleavable protecting groups in the synthesis of photolabile prodrugs to release the parent drug by UV and visible light irradiation [3, 4].

Considering these facts, the present work describes the evaluation as a photolabile prodrug of a fluorescent conjugate of the tetrapeptide AAPV labeled at the *C*-terminus with 7-methoxycoumarin. This conjugate was submitted to photocleavage studies at different wavelengths of irradiation in different solvents and simulated physiological environment in order to study the release of the peptide. The photolysis process was monitored by HPLC with UV detection and ¹H NMR, with collection of kinetic data.

Acknowledgements: Thanks are due to the *Fundação para a Ciência e Tecnologia* (FCT, Portugal) for financial support to the NMR portuguese network (PTNMR, Bruker Avance III 400-Univ. Minho), FCT and FEDER (European Fund for Regional Development)-COMPETE-QREN-EU for financial support to Research Centre of Chemistry, CQ/UM [PEst-C/QUI/UI0686/2013 (FCOMP-01-0124-FEDER-037302)].

REFERENCES

- [1] Caccetta, R.; Blanchfield, J. T.; Harrison, J.; Toth, I.; Benson, H. A. E. Int. J. Pept. Res. Ther. 2006, 12, 327-333.
- [2] Wagner, B. D. Molecules 2009, 14, 210-237.
- [3] Fonseca, A. S. C.; Gonçalves, M. S. T.; Costa, S. P. G. Amino Acids 2010, 39, 699-712.
- [4] Fonseca, A. S. C.; Soares, A. M. S.; Gonçalves, M. S. T.; Costa, S. P. G. *Tetrahedron* 2012, 68, 7892-7900.

> Química e Saúde