

# NEW IONIC LIQUIDS AND SALTS DERIVED FROM $\beta$ -LACTAM ANTIBIOTICS

**Ricardo Ferraz<sup>1,2</sup>, Luís Branco<sup>2</sup>, Isabel Marrucho<sup>3</sup>, Rúben Fernandes<sup>1,4</sup>, Cristina Prudêncio<sup>1,4</sup>,  
João Paulo Noronha<sup>2</sup>, Zeljko Petrovski<sup>\*,2</sup>**

1 – Escola Superior de Tecnologia da Saúde do Porto - Instituto Politécnico do Porto, Rua Valente Perfeito, nº 322, 4400-330, Vila Nova de Gaia, Portugal;

2 – Departamento de Química/REQUIMTE-CQFB, Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa, 2829-516 Caparica, Portugal.

3 – Instituto de Tecnologia Química e Biológica, ITQB, Universidade Nova de Lisboa,

4 – Centro de Farmacologia e Biopatologia Química, Faculdade de Medicina, Universidade do Porto

Email address: [ricardoferraz@eu.ipp.pt](mailto:ricardoferraz@eu.ipp.pt)

In recent years ionic liquids (ILs) have been increasing the popularity and the number of applications. Ionic liquids were used mainly as solvent in organic synthesis, but in recent years they are also used in analytical chemistry, separation chemistry and material science. Additional to significant developments in their chemical properties and applications, ionic liquids are now bringing unexpected opportunities at the interface of chemistry with the life sciences.

Ionic liquids (ILs) are currently defined as salts that are composed solely of cations and anions which melt below 100°C. Our goal in this work is to explore the dual activity of the ionic liquids, due to the presence of two different ions, an anion with bacterial activity as  $\beta$ -lactam antibiotics and different kinds of cations.

In this work the anions of ILs and salts were derived from three different antibiotics: ampicillin, penicillin and amoxicillin. The cations were derived from substituted ammonium, phosphonium pyridinium and methylimidazolium salts, such as: tetraethyl ammonium, trihexyltetradecylphosphonium, cetylpyridinium, choline (an essential nutrient), 1-ethyl-3-methylimidazolium, and 1-ethanol-3-methylimidazolium structures.

Commercial ammonium and phosphonium halogen salts were first transformed into hydroxides on ionic exchange column (Amberlite IRA-400) in methanol. The prepared hydroxides were then neutralized with  $\beta$ -lactam antibiotics. After crystallization we obtained pure ILs and salts containing  $\beta$ -lactam antibiotics.

This work presents a novel method for preparation of new salts of antibiotics with low melting point and their chemistry and microbiological characterization.

**Acknowledgment:** The author would like to thank Escola Superior de Tecnologia da Saúde do Instituto Politécnico do Porto for financial support.

## References:

- 1) Ionic Liquids in Synthesis (Green Chemistry (Wiley)(2 vol. set). Wiley-VCH: 2007; p 776.
- 2) Fukumoto, K.; Yoshizawa, M.; Ohno, H., Room Temperature Ionic Liquids from 20 Natural Amino Acids. *Journal of the American Chemical Society* 2005, 127 (8), 2398-2399.
- 3) Hough-Troutman, W. L.; Smiglak, M.; Griffin, S.; Reichert, W. M.; Mirska, I.; Jodynis-Liebert, J.; Adamska, T.; Nawrot, J.; Stasiewicz, M.; Rogers, R. D.; Pernak, J., Ionic liquids with dual biological function: sweet and anti-microbial, hydrophobic quaternary ammonium-based salts. *New Journal of Chemistry* 2009, 33 (1), 26-33.
- 4) Jain, N.; Kumar, A.; Chauhan, S.; Chauhan, S. M. S., Chemical and biochemical transformations in ionic liquids. *Tetrahedron* 2005, 61 (5), 1015-1060.
- 5) Pernak, J.; Syguda, A.; Mirska, I.; Pernak, A.; Nawrot, J.; Pradzynska, A.; Griffin, S. T.; Rogers, R. D., Choline-derivative-based ionic liquids. *Chemistry-a European Journal* 2007, 13, 6817-6827