Bioavailability and biological properties of several selected ionic liquids in Testsystem AquaHab®

1. Introduction

Development which meets the demands of human beings living at present without endangering the chances of future generations to satisfy their needs means "sustainable development". Introduction of more sustainability in chemistry is the main message pointed out in chapter 19 of Agenda 21 [1993] - which was a result of the United Nations Conference on Environment and Development held in Rio de Janeiro in 1992 - as well as in the Twelve Principles of Green Chemistry [Anastas, Warner, 1998]. For today's chemists, designing benign industrial chemicals, products and processes is both a vision and a mission [Jastorff *et al.*, 2005]. Therefore a combined research for an acceptable compromise for the economical, social and ecological needs is required.

1.1. The case of ionic liquids

1.1.1. State of the art

Ionic liquids, salts of organic cations with melting points below 100 ºC, are being widely investigated as replacements for volatile organic solvents in industrial and laboratory processes because they are thought to be "environmentally benign" [Masten, 2004]. Ionic liquids have gained popularity in recent years [Welton, 1999; Wasserscheid, Keim, 2000; Sheldon, 2001; Dupont *et al.*, 2002] for their increasing use in the two important fields of chemistry - synthesis and processes - and their concept and history has been well documented [Hurley, Wier, 1951; Robinson, Osteryoung, 1979; Hussey, 1983; Poole *et al.*, 1986; Fuller *et al.*, 1994].

Since the pioneering study of Wilkes and co-workers, ionic liquids have not only become increasingly popular as reaction and extraction media in research and development, they have also widely been promoted as "green solvents", which can easily be verified browsing the contents of a recent issue of "Green Chemistry", or looking through the abstracts of recent conferences on green and/or sustainable chemistry. The rationale for calling them "green" consists of several arguments [Ranke *et al.*, 2006]:

- their vapour pressure is generally negligible, and thus inhalative exposure of workers is reduced as compared to conventional molecular solvents
- they have been shown to be non-flammable, and thus the risk of fast, exothermic oxidations in the case of an accident is strongly reduced
- they are termed relatively non-toxic

1.1.2. Problem outline

Certainly the arguments cited above are very relevant as a basis for terming ionic liquids as "green solvents". Even so, several questions raised [Ranke *et al.*, 2006]:

- What are boundary conditions and exceptions for these arguments?
- What additional aspects have to be taken in account?

Important aspects of the "greenness" of ionic liquids have been incorporated in recent articles by leading authors in the field [Wilkes, 2004; Wasserscheid *et al.*, 2002].

In 2003 within the "*Centre of Environmental Science and Environmental Technology" (UFT)* from Bremen, Germany, based on a fruitful collaboration between academia and industry, a multidisciplinary working group developed a strategy which aims at an environmental risk assessment of chemicals, using a combination of structure-activity relationship (T-SAR), toxicological and eco-toxicological test and modelling [Jastorff *et al.*, 2003]. In short the following tools were proposed:

- interdisciplinary theoretical and work-sharing experimental collaboration
- selection of lead chemicals according to the ‘‘test-kit-concept’’
- ecotoxicological test battery on different levels of complexity (*e.g.* enzymes, cells, organisms, mesocosm studies)
- assessment of the molecular interaction potential, shape and conformational flexibility, chemical and biochemical reactivity of a chemical entity from a systematic algorithm
- evaluation of qualitative and quantitative structure–activity relations (SAR/QSAR)
- theoretical assessment of presumable transformation products due to metabolic reactions based on T-SAR (Thinking in Terms of Structure Activity Relationships)
- multidimensional risk analysis (release, spatiotemporal range, bioaccumulation, biological activity and uncertainty)

Since that time several toxicity and ecotoxicity papers concerning the effect of different types of ionic liquids – especially imidazolium and pyridinium classes of ionic liquids – were published [Ranke *et al.*, 2003; Stock *et al.*, 2004; Skladanowski *et al.*, 2005; Docherty, Kulpa, 2005; Stolte *et al.*, 2006;]. The chemicals were tested basically at the molecular and cellular level. The influence of the structural modifications of the selected classes of ionic liquids on their biological activity was described in detail.

In a publication from 2005 it has been shown that considerable progress has been achieved concerning the assessment of the general biological activity of ionic liquids. This progress has so far focused on screening methods for larger sets of compounds, and on the class of imidazolium based ionic liquids. Some of these have been tested in more complex and resource consuming chronic single-species tests [Bernot *et al.*, 2005a; 2005b], forming the second level of a flexible biological test battery. The last step would consist of multispecies tests for those chemicals which are of high interest with respect to technological, economical and (eco)toxicological aspects [Jastorff *et al.*, 2005].

2. Aim of the proposal

This proposal aims to fulfil several of the research needs concerning the “green solvents”, ionic liquids, pointed out in the most recently existing achievements (*i.e.* multispecies tests for those ionic liquids which are already produced in higher quantities by industry), based on a transdisciplinary and international work. Thus, a closed aquatic multispecies system on laboratory scale (termed AquaHab®) – which consists in a biological unit containing fish, amphipods, snails and plants and a control unit for continuous data (*e.g.* oxygen and carbon dioxide concentration, pH, temperature, illumination) acquisition and storage - will be used for the exposure and effect assessment of the selected ionic liquids. AquaHab® test system was already implemented by the firm *OHB System AG Bremen*. In the same time this research work intents to continue and develop the successful work on a related topic accomplished during the candidates internship within the UFT laboratories. Nevertheless, this project plans to apply within the laboratory from Timisoara an European working model by means of a «know how» transfer.

3. Motivation for the subject selection

Ionic liquids represent a fascinating group of new chemicals with the potential to improve development in organic chemistry and chemical technology [Wasserscheid , Welton, 2002] stimulating a lot of research fields [Jastorff *et al.*, 2003]. At the moment there are still very few research groups focusing their work on studies about the ecotoxicological behaviour of the newly designed compounds in comparison to the available amount of synthesized chemicals. The first steps towards this exciting issue have been already done in Romania, at the West University of Timisoara as well, and the first results were published by Mincea *et al.*, 2004. That is why the working experience of the “Project Team Ionic Liquids” from the Centre of Environmental Research and Technology (UFT), Bremen is to be learned and implemented.

4. The plan of the proposed experiments

First of all a restricted number of ionic liquids (4-6) will be selected according to the T-SAR-concept and to their availability on the market.

The experimental part proposed in this project can be structured in three main sections:

» Adsorption studies between the selected ionic liquids and the surface of the AquaHab® consisting materials (*e.g.* polypropylene, polyurethane, filter stones, polycarbonate etc.)

» Establishing the concentration range for the selected ionic liquids which can be used in the optimised aquatic ecosystem (AquaHab®) by performing toxicity studies on monospecies with increased level of complexity: primary producers (*i.e.* aquatic plants), primary consumers (*i.e.* crustaceans, aquatic snails), secondary consumers (*i.e.* fish)

» AquaHab® type of studies:

- studies concerning the molecular interaction potential of the selected ionic liquids with the closed aquatic ecosystem (in the absence and presence of organisms)
- studies on the bioaccumulation of the selected ionic liquids and their metabolites within the closed aquatic ecosystem
- studies on the transfer of the selected ionic liquids between the aquatic species
- studies to predict the extrapolation of the obtained ecotoxicological results to another species

The required analytical equipment (HPLC, MS, GC) does already exist within the UFT (Centre for Environmental Science and Environmental Technology). The experience of the UFT staff in topics as analytic and environmental chemistry, risk analyses and structure-activity research is to be considered as a valuable support for the successful accomplishment of this project.

5. Outlook

BASF, one of the leading companies in the chemical products and processes, started already to produce on "large-scale" one of the compounds belonging to the ionic liquids class. Other processes including ionic liquids are also in preparation. That is why rises the risk that bigger quantities of ionic liquids are released in the biosphere without possessing enough knowledge about their behaviour and effect in the environment.

The proposed research study is expected to bring new findings about the bioavailability and the biological properties of the selected ionic liquids. The project involves an interdisciplinary collaboration and is based on the candidates working experience within this environment.

The results could provide new ideas for the still open questions like:

- What is the chemical fate of the different types of ionic liquids in aqueous media (association/dissociation/ion pairing)?
- How can this behaviour influence their bioavailability?
- What can be said about their chemical and metabolic stability in an aquatic habitat?

6. Research results revaluation/dissemination

The results gained within the research studies will be imparted as follows:

- participation to at least one international congress with a scientific communication
- to publish them in a paper form within an ISI Journal
- to set up new laboratory courses for the students from the "Environmental chemistry" programme from West University of Timisoara
- to complete a doctoral thesis in an international collaboration

7. Literature

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