IONIC LIQUIDS: TOXICITY ASSAYS IN A CELL MODEL

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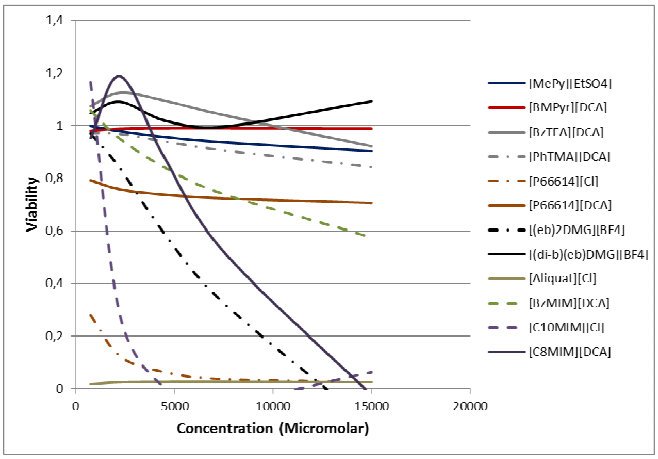
Introduction: Ionic liquids (ILs) are formed by a cation and an anion that can be tuned for generation of different combinations with distinct properties and, several applications have been demonstrated in the literature using ILs. They include their use as thermal fluids, lubricants, and plasticizers and in catalysis as solvent and/or catalyst, for instance [1-3]. The interest about ILs is due to their lower volatility and lower flammability compared to the conventional organic solvents. Therefore, in order to build the most suitable cation-anion combination for the desired application, a great number of ILs, containing several types of cations, have been reported so far. This has prompted their study in terms of toxicological impact on humans and environment since this is a very important information to have in hands in case of their application in a larger scale [4].

Experimental/Analytical/Simulation: As an attempt to predict their effect on humans, toxicological assays have been performed in our laboratory using a human cell line model (CaCo-2). CaCo-2 is a colon adenocarcinoma cell line with a very interesting property for this type of study: it can differentiate in enterocytes, upon reaching a confluent state, resembling human normal intestinal epithelium. Using this model, cells were treated with several concentrations of a large number of different ILs, for a long period, previously to assessment of cellular viability by a tetrazolium dye (MTT). In viable cells, this dye is reduced by mitochondrial reductases into a purple formazan, which can then be quantified spectrometrically.

Results and discussion: Toxicity trends were obtained for a large number of ILs including many different cations as methylimidazolium – [MIM], dimethyl-guanidinium – [DMG], tetra-methyl-ammonium – [TMA], tetra-ethyl-ammonium – [TEA], tri-n-octyl-methyl-ammonium–[Aliquat], tri-n-hexyl-tetra-n-decyl-phosphonium – [P6,6,6,14], 2-methyl-1-ethyl-pyridinium – [2-MEPy] and methyl-pyrrolidinium – [MPyr]. We have clearly seen that the size of the cation alkyl chains are crucial for toxicity and therefore, [P6,6,6,14] and [Aliquat] are in general very toxic as [MIM] and [DMG] when bound to long alkylic chains (Figure 1).[5]. This is possibly due to increasing lipophilicity which favours their cell entrance and bioavailability.

On the other hand, 1-alkyl-3-methylimidazolium (alkyl ≤ C4), [2-MePy] and [MPyr] are involved in less toxic combinations (Figure 1). [5] Additionally, anions also have an important increment for ionic liquid toxicity as bis(trifluoromethanesulfonyl)amide – [NTf2] that seem to enhance mitochondria metabolic activity compared to non-treated cells whereas dicyanoamide – [DCA] that appears to lead to most favourable ILs [5].



Conclusions: Contrary to earlier thoughts, cation and anion have a role in the overall IL toxicity and by tuning these two different ions very different toxicological data can be produced.

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