Study of Benzoic Acid Solubility in Imidazolium Formate as Pure Ionic Liquid and Its Binary Aqueous Mixtures

CLAUDIA SIMONA STEFAN[1]*, ELENA ROXANA CHIRIAC[2], OANA DRAGOSTIN[1], ELENA LACRAMIOARA LISA [1]*, MARIA CIOROI[1]

[1]Dunarea de Jos University of Galati, Faculty of Medicine and Pharmacy, 35 A.I. Cuza Str., 800010, Galati, Romania

[2]University of Medicine and Pharmacy Carol Davila Bucharest, Faculty of Pharmacy, 6 Traian Vuia Str., 020956, Bucharest, Romania

The determination of benzoic acid (BAc) solubility in pure imidazolium formate (ImForm) and their aqueous mixtures of [ImForm/water], was performed by the acid-base titration of the saturated solutions. [ImForm/water] solutions were tested using an ImForm concentration ranging from 1.66-4.33 g/L. The BAc solubility in pure ionic liquid was compared with that of some common organic solvents reported in literature, such as: ethanol, chloroform, cyclohexane. The highest solubility of BAc was for pure ImForm (from 1073 g/L at 293 K up to 2200 g/L at 323 K), the determined values being superior to BAc solubility in organic solvents mentioned. The results confirm that the polar solvents, such as ImForm and ethanol, present the highest BAc solubility values. At 293 K, the mole fraction of BAc in pure ImForm was 2.8 times higher than the mole fraction of BAc in ethanol. The BAc solubility in binary mixtures [ImForm/water] was compared with that determined in [NaCl/water] mixtures. At the same salt concentration, ranging from 1.66 to 4.33 g/L, at a constant working temperature (323 K), the increasing concentration of NaCl lowers the solubility of BAc. In opposite, the increasing of ImForm concentration determines a considerable increase in BAc solubility into the [ImForm/water] mixture. At 277 K, for 1.66 g/L salt concentration in water, the BAc solubility in [salt/water] solvents shows very similar values (~1.3 g/L) for both [ImForm/water] and [NaCl/water]. If the temperature increases to 323 K, the BAc solubility in [ImForm/water] mixture is about 1.5 times higher than that of solubility in distillated water and 2.5 times higher compared to that in [NaCl/water]. It was concluded that the benzoic acid presents a great solubility in pure ImForm and in its [ImForm/water] aqueous mixture.

Keywords: Protic ionic liquid, Imidazolium formate, NaCl aqueous solutions, Benzoic acid, Solubility of benzoic acid

Successfully used in various fields such as organic chemistry synthesis and catalysis [1], electrodeposition [2,3], energy storage [1], separation technologies [4], protein crystallization [1,5,6] the ionic liquids at ambient temperature (RTILs) currently present an increasingly interest especially for the pharmaceutical industry [7-13]. The growing interest for the applications of RTILs in the industrial synthesis of pharmaceutical compounds can be explained by a number of physicochemical properties highly attractive of RTILs [1,14,15], compared with those of organic solvents used routinely. The organic solvents are toxic due their extreme volatility and flammability, and are also responsible for organic contamination of the final drug resulted from the industrial synthesis process. RTILs are ionic compounds composed exclusively of a bulky asymmetric organic cation (e.g. alkyl pyridinium, pyrrolidinium or imidazolium ions) and an inorganic or organic anion (e.g. hexafluorophosphate, tetrafluoroborate, halides, carboxylate, etc). Unlike organic solvents, RTILs show a very good thermal and chemical stability, a low vapour pressure and implicitly a low volatility, indicating they are 'environmentally friendly' [1]. Thanks to the multiple solvation interactions, RTILs currently replace the organic solvents in extraction processes, because their good extractability for various compounds, being used to dissolve a wide of range of both organic or anorganic compounds [7,9,16]. In addition, these 'green organic solvents' show very good properties to preserve a high bio-enzymatic activity and stability [1,5], which revolutionized scientific outlook of the applications of these compounds in pharmaceutical chemistry. In recent years, RTILs are used in the synthesis of antiviral antileishmanial, antiparasitic drugs, anticancer drugs, non-steroidial anti-inflammatory drugs (NSAIDs) or antidepressant drugs [10], to dissolve poorly soluble active pharmaceutical ingredients (APIs) or to control the crystallization media for the APIs [12,13]. As 'green alternatives' of the volatile solvents, RTILs shows a huge advantage: because the physical-chemical properties can be selected and modulated by choosing and combining a certain cation with a particular anion. Thus, there can be modeled physical-chemical parameters such as: density, viscosity, melting point, acidity or basicity, hydrophilicity, hydrophobicity, polarity and water-miscibility, etc. The flexibility of RTILs leads to be named as *designer solvents.*

There are few studies in literature on the solubility of benzoic acid in pure solvents. He and al. [17] report a BAc solubility in room temperatuture ionic liquids based on imidazolium cation and $[NTf_2]^-$ = bis(trifluoromethyl-sulphonyl)imide, $[BF_4]^-$ = tetrafluoroborate, $[PF_6]^-$ = hexafluorophosphate and $[NO_3]^-$ = nitrate anions, using chronoamperometric techniques. To the best of our knowledge, in literature did not find results on the BAc solubility in ionic liquids based on imidazolium cation and formate anion.

In this paper, the solubility of benzoic acid (BAc) will be investigated in a pure protic ionic liquid (PIL) and its aqueous mixtures [PIL/water]. Benzoic acid it is known for its use as food preservative, bacteriostatic and bactericidal agent, antiseptic stimulant, and also ingredient in Whitfield's ointment in the treatment of ringworm. The studied PIL is imidazolium formate (ImForm), constituted by an organic cation such as imidazolium and a carboxylate anion, such as formate. Imidazolium formate is a protic ionic liquid formed by the proton transfer between a Brönsted acid (formic acid) and a Brönsted base

* email: claudia.stefan@ugal.ro; elena.lisa@ugal.ro

(imidazole). Thanks to their "free" available proton present on the heterocyclic cation, the ImForm molecules have the ability to easily establish hydrogen connections with the polar groups presented in their media.

Quantitatively, at a work temperature, the term *solubility* can be expressed by the concentration of the solute in the saturated solvent in which the molecules of the solute are in equilibrium with the solvent molecules. A good solubility requires the existence of spontaneous interactions between the molecules of the solute with the molecules of the solvent (e.g. van der Waals, dipole-dipole interactions or hydrogen bonding, etc).

If the solute presents a polar group (-COOH, -COOR, -OH, -CHO, etc.), which are hydrophilic, this will determine a good solubility of the solute in polar solvents, while the hydrophobic groups (as an alkyle radical, R) will lead to a good solubility in nonpolar solvents.

In this paper, the solubility of BAc in pure ImForm ionic liquid and binary aqueous mixtures of [ImForm/water] are determined, depending on one hand on the ImForm concentration, and on the other hand, by varying the temperature between 277 and 323 K. Also, the results obtained in pure ionic liquid were compared with those reported by other authors in some pure organic solvents such as: ethanol, cyclohexane and chloroform [18] or in salted water [19].

Regarding the influence of the ionic salt nature on the BAc solubility, a comparative study was carried out in [NaCl/water] solutions according to the variation of salt concentration and temperature.

Experimental part

Reagents, equipment and methods

Benzoic acid, BAc (CAS 56750) of 99.5% purity was purchased from Sigma-Aldrich and was used without further purification.

The ionic salts used in this work were: a protic ionic liquid such as imidazolium formate (ImForm) and NaCl salt from ChimReactiv SRL (CAS 7647-14-5).

ImForm was synthesized in our laboratory through a neutralization reaction of the imidazole 100% from Fluka (Brönsted base) with the formic acid 98-100% from Riedel (Brönsted acid) (fig. 1.), according to procedure described elsewhere [14]. The molar ratio of amine/acid was 1:1. The carboxylic acid was added slowly to amine with stirring in a three-necked round-bottom flask immersed into ice bath and equipped with a dropping funnel. The composition was stirred during 4 hours keeping a constant temperature of 20°C. A transparent slightly colored liquid (ImForm) was obtained (ρ = 1.05 g/cm^3 at 20°C and *p*H = 8).

In order to obtain the [salt/water] aqueous solutions, NaCl, ImForm and distilled water were used. Both binary aqueous mixtures were prepared by weighing the preestablished amount of each salt, in the range of 0.05 g; 0.07 g; 0.11 g of either ImForm or NaCl into the 30 mL distillated water, to obtain finally the concentration of 1.66 g/L; 2.33 g/L; 3.66 g/L.

The method of obtaining saturated solutions: Benzoic acid saturation was reached by dissolution a surplus of benzoic acid added to the binary aqueous solutions.

For this purpose, the studied binary solutions were initially thermostated at the working temperature at which an amount in excess of BAc was added under continuous agitation by a magnetic stirrer for 30 min on a heating plate, and then are turned off, to allow the suspended solid phase to settle down for one hour. The temperature was validated by using a digital thermometer. For dosing, each time five samples of 10 mL were taken carefully of clear saturated solution.

Solubility Measurements

The solubility measurements were made in temperature step starting at 4 ° C (277 K), in a range of 277 K up to 323 K (4-50°C). The benzoic acid solubility in the saturated solutions was determined by the acid-base dosage method. For the titration it was used a NaOH solution of 0.05 mol/L concentration, freshly prepared (the titer of the solution was determined just before the use, using a standard solution of oxalic acid). The phenolphthalein was used as indicator in the titration.

Results and discussions

The influence of salt concentration on the BAc solubility

In figure 3 are shown the results obtained on BAc solubility in the [ImForm/water] and [NaCl/water], at a work temperature of 323 K, for ionic salt concentration ranging between 1.66-4.33 g/L. As can be seen, in the case of [ImForm/water] mixtures, the BAc solubility parameter increases when the ImForm concentration increases. In the opposite case, for the [NaCl/water], the BAc solubility decreases with the increasing of NaCl concentration. This indicates that the nature and the size of these ionic species

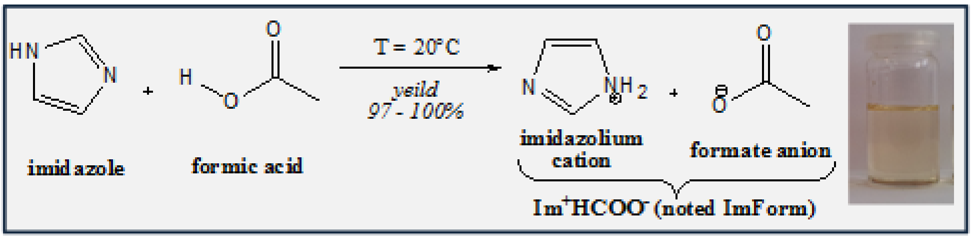

Fig. 1.Synthesis of ImForm (a transparent slightly colored of ImForm in the beaker can be observed)

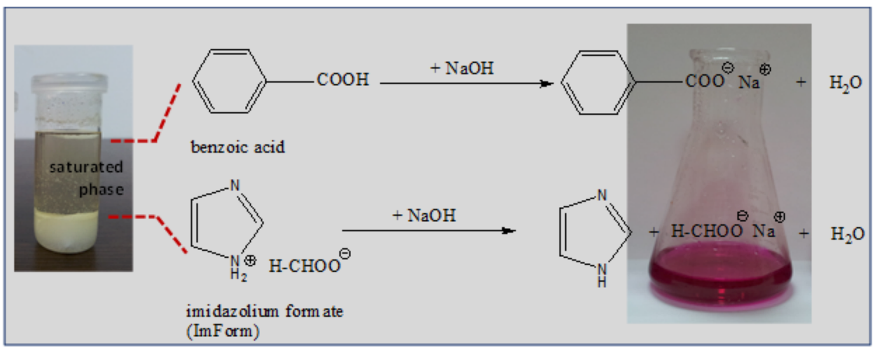

Fig. 2. The titration reactions, in order to determine the BAc solubility of saturated [ImForm/water/BAc] and [ImForm/BAc] solutions

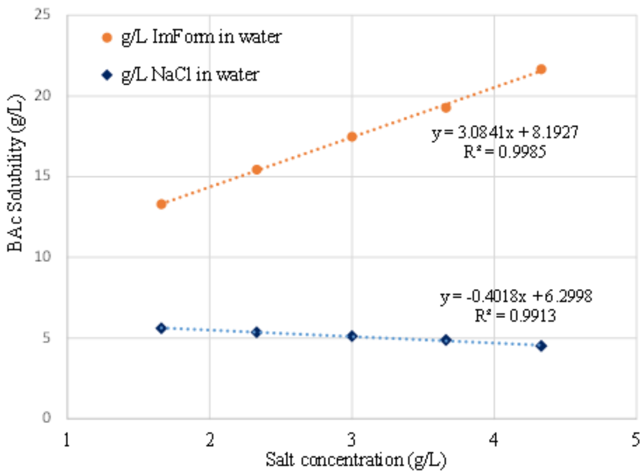

Fig. 3. Dependences of solubility parameter (g/L) of BAc in [salt/water] aqueous mixtures with various concentrations at 323 K

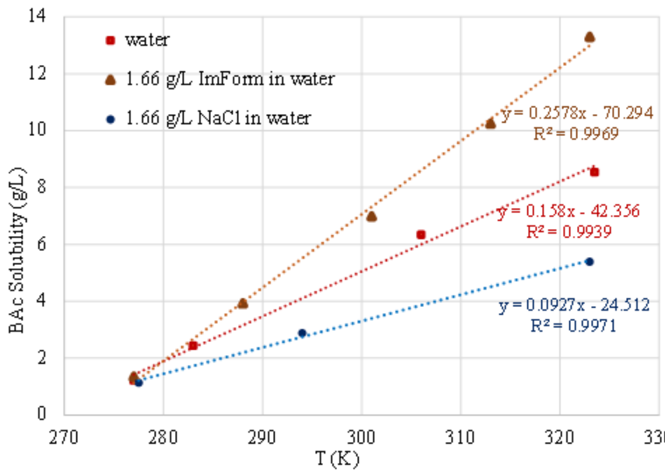

Fig. 4. Benzoic acid solubility (g/L) in water and in [salt/water] solutions, at temperatures between 277 and 323 K

are important factors that are involved in the phenomenon of solvation of BAc molecules.

NaCl is an ionic inorganic salt very soluble in water. The NaCl molecules are solvated very easy, the Na_{aq}^{+} and Cl_{aq}^{-} ions setting the electrostatic ion-dipole interactions with the water dipoles. In the [NaCl/water] solution, the increasing of NaCl concentration determines a 'competition' between the NaCl and the BAc molecules in the solvation process. The benzoic acid is a weak acid that partially dissociates, showing a low solubility in cold water, because of the non-polar character of the benzene cycle. The water molecules will be primarily involved for the solvation of ionic Na_{aq}^{+} and Cl_{aq}^{-} species, and only later, in partial salvation C_6H_5-COO^- ionic species. Consequently, the increasing the concentration of the NaCl molecules in water, increases the participation of the water molecules in the ion solvation, and this therefore lowers the BAc solubility in the studied mixtures.

The increasing of BAc solubility in [ImForm/water] mixtures can be explained by the participation of both water and ImForm, to the BAc solvation phenomenon. As a protic ionic liquid, ImForm is very ionizing, having a 'free' available proton on the heterocyclic core. Due to this structural peculiarity, ImForm is able to easily form hydrogen bonds or to protonate the anions that may be presents in the solution. In addition, the basic pH of ImForm facilitates the existence of benzoate anions, C_6H_5-COO^- in pure ImForm or in the aqueous solutions, which promotes the BAc solubility. The results show that the presence of the protic ionic liquid in water determines a considerable increase of BAc solubility.

The influence of the temperature on the benzoic acid solubility

It is expected that high temperature favors kinetically the dissolution phenomenon. In order to determine the influence of the temperature on the benzoic acid solubility in [salt/water] two aqueous solutions presenting the same salt concentration, 1.66 g/L NaCl and 1.66 g/L ImForm respectively, were tested.

Figure 4 presents the values of BAc solubility in [NaCl/water] and [ImForm/water], compared to that in distilled water, in a temperature range 277-323 K. The results confirm the increasing of BAc solubility with the increasing temperature, in all solvents. It also observed that the BAc solubility is the highest in the [ImForm/water] mixture, and the lowest for the [NaCl/water] solution.

However, at low temperature of work (277 K) the BAc solubility in the studied solvents shows similar values (~1.3 g/L). At the maximum temperature of work (323K), the BAc solubility in the [ImForm/water] mixture is 1.5 times higher than that in distilled water and 2.5 times higher in [NaCl/water] solution. It can be stated therefore that the presence of the protic ionic liquid in water determine a considerable increase of the BAc solubility in the studied temperature range.

The variation of the BAc solubility with ImForm concentration

The temperature dependence of the solubility can be well-correlated by a linear equation (obtained by integrating van't Hoff equation applied for equillibrium reactions):

$$\ln(x) = \frac{-\Delta_r H^{\circ}}{RT} + C \qquad (1)$$

where *x* is the mole fraction solubility, T is the absolute temperature, R is the ideal gas constant and ΔrH^{o} is the standard enthalpy of dissolution of BAc in the solvents considered. Figure 5 presents the BAc solubility in [ImForm/water] and in distilled water, in a temperature range of 277-323 K. As can be seen from this Figure, the van't Hoff equation is confirmed by the linearity of the variation for all studied mixtures.

The lower the mole fraction solubility, the higer is the temperature dependence. These results confirm that BAc solubility in water depends to a great extent by the temperature: if the temperature increases, the BAc solubility increases in distilled water. In case of [ImForm/water] mixtures, the dependence of BAc solubility upon temperature is lower. As shown in figure 5, for the mixtures with the highest content of ionic liquid (3.66 g/L ImForm) the slightest variation of BAc solubility with the temperature is noticed.

The ln (x) = f (1/T) dependences allow the determination of the standard enthalpies of dissolution of BAc in the studied solvents. From the values shown in table 1 it can be seen that the highest value of the enthalpy of dissolution was determined in the case of the distilled water.

As the electrostatic interactions between ions are stronger, the energies are greater. In case of [ImForm/water] binary systems, with the increasing of the ImForm concentration the number of hydrogen bonds that are established between the ionic liquid and the benzoate ions

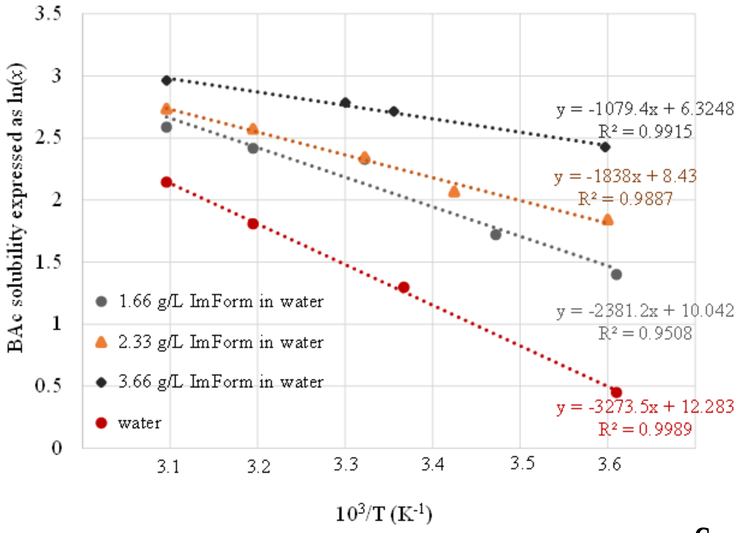

Fig. 5. Solubility (in moles of solute / moles total) of BAc in [ImForm/water] and distilled water at temperature between 277 and 323K. The straight lines are calculated using eq.1

Table 1
THE OBTAINED STANDARD ENTHALPIES OF DISSOLUTION OF BAC IN [IMFORM/WATER]

[ImForm](g/L)	3.66	2.33	1.66	0
$\Delta_r H^{\circ}$ (kJ/mol)	9	15	20	27

is increased, thereby increasing the solubility of the BAc in the studied mixtures.

The solubility of benzoic acid in protic pure ionic liquid

The BAc solubility in pure ImForm was investigated at two operating temperatures: 293 K and 323 K. The obtained results show an increase of the BAc solubility with the increasing work temperature, from 1073 g/L (at 293 K) up to 2200 g/L (at 323 K). At the temperature of 293K, the molar fraction of BAc in pure ImForm is 2.84 times bigger than the molar fraction of BAc in ethanol (x_{ImForm} / $x_{ethanol}$ = 2.8), while at the 323K the ratio is x_{ImForm} / $x_{ethanol}$ = 2.4. These values were compared to those reported in literature for the other common organic solvents, such as: ethanol, chloroform, cyclohexane. Thati and al. [18] report a BAc solubility that closely varies with the polarity of the solvent molecules. Thus, the solubility in some the nonpolar solvents (cyclohexane, chloroform) are much lower than in polar solvents (ethanol). In figure 6 is represented the variation of BAc solubility in the organic solvents, according to Thati, depending on the inverse of temperature, by converting the experimental data into mole fraction solubility, x_i. ImForm being a solvent which has a high polarity, in the graph it can be seen a highest BAc solubility in pure ionic liquid. The order of the variation of BAc solubility in the solvents is the following: cyclohexane <chloroform <ethanol <ImForm.

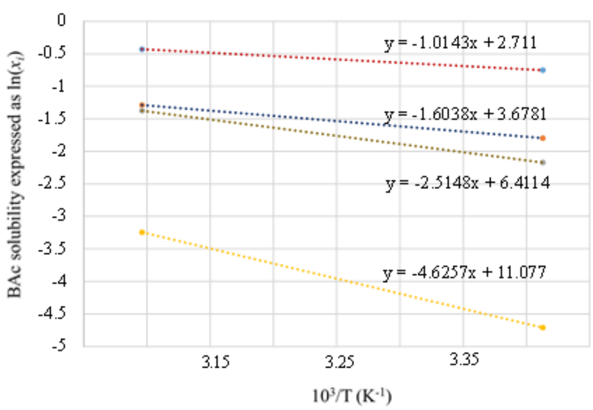

Fig. 6. Comparison on solubility (mole of solute / total moles) of benzoic acid in pure ImForm and in some pure organic solvents, between 293-323 K *(*values reported Thati [18])*

Conclusions

ImForm is a protic ionic liquid with a basic pH, completely miscible with water, allowing a great BAc solubilization. Being an exclusively ionic liquid salt at ambient temperature, ImForm presents a very ionizing character. In the basic medium of ImForm, the benzoic acid molecules exist as benzoate anions. The structural compatibility between the organic molecules determines a considerable increase of BAc solubility in pure ImForm and also in the [ImForm/water] mixtures, with the increasing of ionic liquid concentration. The BAc solubility in pure ImForm was compared with that of some common organic solvents (ethanol, chloroform, cyclohexane etc). The results show that the BAc solubility in pure ImForm is superior to the values reported in the literature for the common organic solvents (polar solvents present the highest value of BAc solubility). In [NaCl/water] solutions the increasing of NaCl concentration causes a decrease of the BAc solubility. The phenomenon is explained by the competition between the ionic species of inorganic salt molecules and the benzoic acid molecules in the solvation process.

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