Effect of the Density and the Refractive Index on the Toxicity of Imidazolium Ionic Liquids: A study of Ionic Interactions

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Abstract. Ionic Liquids (ILs) has got a significant attraction in the academia as well as in industries because of the salient characteristics and flexibility in tune-ability. The ionic nature and a huge number of possible combinations of cations, anions and functional groups make ILs potential candidates for industrially suitable materials. However, the toxic nature of ILs is still a big challenge. To overcome this problem, knowledge of the interactive mechanism of the ionic species of ILs is desired. In current work, we have investigated the ionic interaction of ILs by studying the effect of intensive properties of ILs “density” and “refractive index” of imidazolium NTf² and PF₆ ILs. Result produced in the current provided relationship of toxicity of ILs to their refractive indices and densities. The findings of current work are helpful to understand the mechanism of the toxic behavior of ILs.

1. Introduction

Ionic liquids (ILs) were thought to be green chemicals in the start of their invention because of their noticeable properties, for example, low vapor pressure, very less volatility, ionic nature, nonflammability, high stability[1]. The low vapor pressure of ILs makes them feasible for much industrial application where energy is considered as an economical barrier [2]. Nonflammability of ILs is a very important property particularly, from the safety perspective. Stability of ILs is related to the optimization and performance of the chemicals and the stability is considered as one of the major factors in the selection of chemicals for the adsorption, absorption and catalysis. However, the investigation of their toxicological properties demonstrated that ILs cannot be placed into the category of green chemicals[3]. To understand the roots of the toxic behavior of ILs is a challenging task or the researchers.

In the past, the focus was on the synthesis of ILs to replace conventional organic and inorganic chemical in their respective application [4]. In recent years, the focus of the research is shifted towards the investigations of the properties responsible for their detrimental nature towards the environment.

An extensive research has already been done on an exploration of physicochemical properties of ILs[5]. Then properties of ILs provide a brief information about the interaction of the component of ILs with other compounds and with the components of itself. Cation-anion interaction determines the properties of ILs [6]. Different combination of cation and anion lead to synthesize of a large
number of ILs. Hence, the properties of ILs are totally depending on the structure of ions. The physical, chemical properties, as well as toxic properties, are governed by ionic interactions.

The molecular interactions between the components of ILs define its physical and chemical properties as well as toxicological properties. Detailed study of the ionic interaction of molecules provides structural information which postulates different features of the ILs[7]. A schematic diagram is shown below in Figure 1 which explains the mechanism of toxicity of ILs.

![Figure 1 Interactions within the ILs](image-url)

The discrete knowledge of the mechanism of combining components of ILs for example cations, anions, functional groups, alkyl chain, can define the toxic characteristics. A number of physical properties had been investigated in experimental studies by the researchers[8]. Some of the physical properties which are considered important are density, polarity, refractive index important where the applications of ILs are conferenced [9-11].

2. Methodology

2.1. Materials

In the current research, we have selected on two parameters i.e. the density and the refractive index of imidazolium bis(trifluoromethylsulfonyl)imide (NTf2) and hexafluorophosphate(PF6) ILs. The density and refractive index data were taken from a published work by Tariq et al.[11]. The toxicity data of the ILs are taken from the work done by Ventura et al, Ghanem et al, and Luis et al, [12-14] presented in Table 1.
Table 1. Toxicity of Imidazolium NTf₂ ILS towards different Bacterial species

| Ionic Liquids     | Density | Refractive index | EC50(mmol/L) |
|-------------------|---------|------------------|--------------|
| [EMIM][NTf₂]      | 1.5147  | 1.42251          | 0.844        |
| [BIMI][NTf₂]      | 1.436   | 1.42653          | 0.339        |
| [HMIM][NTf₂]      | 1.371   | 1.42954          | 0.051        |
| [OMIM][NTf₂]      | 1.3189  | 1.43256          | 0.016        |
| [BMIM][PF6]       | 1.3637  | 1.40844          | 1.174898     |
| [HMIM][PF6]       | 1.2924  | 1.41648          | 0.138038     |
| [OMIM][PF6]       | 1.234   | 1.42351          | 0.006761     |

The data presented in Table 1 is used in current method to understand and validate the ionic interactions of ILS to observe the effects of intensive properties of ILS to the toxicity.

2.2. Procedures
The current research work was carried out based on the interaction behavior of the intensive properties of ILS and their relevance was formed with the toxicity of ILS. Toxicity is the function of intensive properties of ILS, especially density and refractive index. To explain this dependency, the flow of the methodology is presented in Figure 2.

![Figure 2 Methodological flow of interaction of intensive properties of IL with toxicity.](image)

3. Results and Discussions
From the intensive properties of ILS especially refractive index and the density, the toxic behavior of ILS was studied. It was observed that with an increase in the refractive index, the density was reduced and the toxicity was increased. It was also noticeable the as the alkyl chain of ILS increased, the toxicity increased which was in line with previous studies done by many researchers [15]. Hence the increase in toxicity of ILS with altering refractive index and density helped to explore the ionic interaction in ILS.
3.1. Effect of the density on the toxicity of ILs
The length of alkyl chain of ILs is one of the major structural property of ILs which had been proved to affect their toxic behavior [16]. In current work, we noticed that with increased alkyl chain length, the reported toxicity was also increased. However, we found that increasing the alkyl chain actually alters the interaction amongst the constituents of imidazolium ILs. For example, when the density of imidazolium ILs was increased, we noticed that toxicity was decreased. Graphical illustration of results of toxicity of imidazolium ILs is presented in Figure 3.

![Graph showing the relationship between density and toxicity](image)

**Figure 3.** Toxicity of imidazolium ILs with (a) NTf2 and (b) PF6 Vs Density.

Figure 3 showed that the EC50 of Imidazolium ILs increased linearly with density and EC50 of the ILs towards *Vibrio fischeri*. Increased density indicated that it was difficult for ILs to enter into the living organism because of the steric hindrance which may affect interaction with lipid membrane. Trends of increasing toxicity with increased density for imidazolium NTf2 ILs in Figure 3 (a) were validated and presented in Figure 3(b).

3.2. Effect of the refractive index on the toxicity of ILs
The graph was plotted between refractive indices of imidazolium NTf2 ILs and their toxicity. Figure 4(a) showed an inverse relationship between the refractive index and EC50 of imidazoliumNTf2 ILs, which specifies a linearly increase in toxicity with refractive index. The trends were validated in Figure 4(b). Refractive indices incorporate with molar volumes, which provide insights into the molecular interactions. However, the refractive index may vary at different temperatures but the toxicological investigations are carried out on room temperature ILs.
Figure 4. Toxicity of imidazolium ILs with (a) NTf₂ and (b) PF₆ Vs refractive index

Refractive index is the property of chemicals which can provide solubility properties by free volume analysis. The solubility of ILs in water is one of the major root cause of the toxicity of ILs towards the living organism when exposed. Hence, the refractive index is of great importance in the understand and assessment of the toxicological behavior of ILs.

4. Conclusion

In current work, we have investigated the interactive mechanism of ILs and studied the effects of density and refractive index on the toxicity of ILs. One of the basic root cause of toxic effects of ILs is water solubility property which makes it possible to mix ILs into the water and enter into the living organism through a cell membrane. We have highlighted the effect of density that the toxicity increase with decreasing the density and vice versa. It is difficult for denser ILs to enter into the cell wall of the cell membrane. In addition, the toxicity increased with increase in the refractive index of imidazolium ILs studied in current work. The refractive index incorporates the free volume of ILs which ultimately favor the solubility of ILs into the water. Hence the refractive index is linearly related with the toxicity of ILs. We have studied the interactive mechanism of two parameters which helped to understand the root cause of the toxic behavior of ILs. There are a number of other structural parameters can be studied to find the knowledge of toxicity on border level. In future, QSPR modeling can be done with a huge data on intensive properties and toxicities of ILs to different organisms of ecosystems.

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