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Review article

Applications of ionic liquids in electrochemical sensors

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ABSTRACT

Ionic liquids (ILs) are molten salts with the melting point close to or below room temperature. They are composed of two asymmetrical ions of opposite charges that only loosely fit together (usually bulky organic cations and smaller anions). The good solvating properties, high conductivity, non-volatility, low toxicity, large electrochemical window (i.e. the electrochemical potential range over which the electrolyte is neither reduced nor oxidized on electrodes) and good electrochemical stability, make ILs suitable for many applications. Recently, novel ion selective sensors, gas sensors and biosensors based on ILs have been developed. IL gels were found to have good biocompatibility with enzymes, proteins and even living cells. Besides a brief discussion of the properties of ILs and their general applications based on these properties, this review focuses on the application of ILs in electroanalytical sensors.

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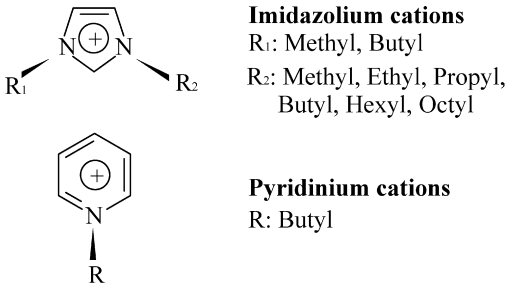
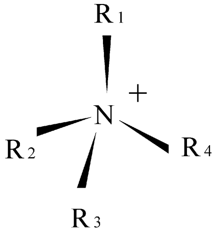


Scheme 1 – Imidazolium and pyridinium cations in ILs.

1. Introduction

One of the key factors in developing new materials is the solvent where the materials are synthesized. Ionic liquids, ILs, belong to a special group of electrolytes consisting only of ions and are free of any molecular solvent. A typical IL that is stable in air and water is based on combination of organic cations (e.g. *N*-alkylpyridinium, *N*,*N*′-dialkylimidazolium) with a variety of anions (e.g. Cl^-, Br^-, I^-, $AlCl_4^-$, NO_3^-, PF_6^-, BF_4^-, $CF_3SO_3^-$, CF_3COO^-, $[(CF_3SO_2)_2N^-{=}Tf_2N^-]$, $[(C_2F_5SO_2)_2N^-{=}Pf_2N^-]$). The big difference in the size of a bulky cation and a small anion does not allow packing of lattice, which happens in many inorganic salts, instead, the ions are disorganized. This results in, that some of these salts remain liquid at the room temperature. The properties of ILs can be tuned to certain extent by varying the combination of anions and cations to find an optimum solvent [1,2]. In addition, special ILs can also be designed by developing novel cations and anions to meet the specific physical properties required for each specific application [3]. For example, selective ion transport, e.g. of Li^+, can be realized either by using liquid imidazole–borane complex [4] or molten salts bearing an anion receptor [5]. Imidazolium and pyridinium are the most common cations in ILs and are shown in Scheme 1.

The IL, ethyl ammonium nitrate was initially mentioned as early as 1914 [6]. Afterwards, one of the first room-temperature ILs based on tetraalkylammonuim cation (Scheme 2) and chloroaluminate anion ($AlCl_4^-$) has extensively been studied by Osteryoung and co-workers [7,8]. Systematic study on the ILs composing of chloroaluminate anions was performed by Hussey and co-workers [9–11], and the first major review of this type of ILs was published in 1983 [12]. However, the ILs based on aluminium halides are extremely reactive towards oxygen and water, and thus have to be handled in anhydrous conditions. It was not until the 1990s that new ILs based on 1-ethyl-3-methylimidazolium cation ($EMIM^+$) and tetrafluoroborate anion (BF_4^-) were reported and found to be resistant to traces of moisture [13]. Since then, different ILs that are not limited to chloroaluminate salts have been synthesized. An increasing number of new ILs have been prepared and used as solvents in synthesis during the last decade [14]. Comprehensive reviews on ILs as electrolytes have also been published recently [15,16]. Although there are some reviews concerning the application of ILs in analytical chemistry [17–19], there are only a few reports on the use of ILs in electrochemical sensors and electroanalytical applications in general. This paper is devoted to review the recent developments in this aspect.

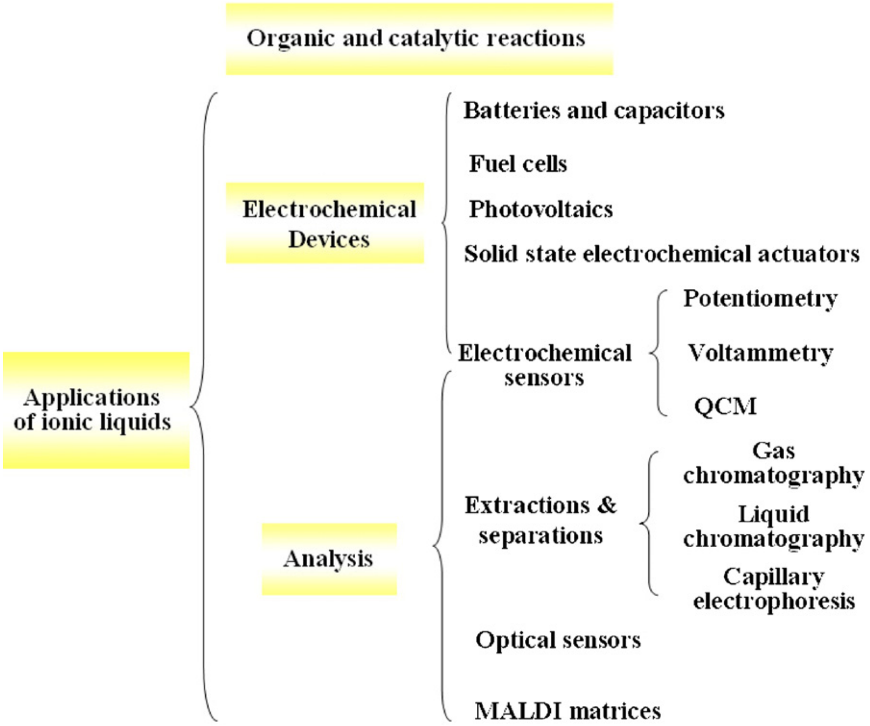


Scheme 2 – Tetraalkylammonium cation.

2. Properties of ILs and their general sensoric applications

The solvent properties of ILs such as melting point, dielectric constant, viscosity, polarity, water-miscibility, etc. can be tailored by combining different cations with suitable anions [14]. Influence of chloride, water and organic solvents on the physical properties of ILs has been investigated [20]. It has been shown that viscosities of the hydrophobic ILs are strongly dependent on the amount of dissolved water [21]. The presence of water and organic solvents will decrease the viscosity of ILs, while the presence of chloride increases the viscosity. Electrochemical studies of the intrinsic properties of ILs have also been reported [20,22–24] and the electrochemical window of ILs can be as wide as 4.5 V compared with 1.2 V in most aqueous electrolytes [25]. Properties such as non-flammability, high ionic conductivity, electrochemical and thermal stability of ILs make them ideal electrolytes in electrochemical devices like in batteries [26–29], capacitors [30–32], fuel cells [33], photovoltaics [34–39], actuators [40], and electrochemical sensors. Only recently, ILs have captured the attention of the analysts to use them in different analytical applications as well. ILs can improve separation of complex mixtures of both polar and non-polar compounds when used either as stationary phase or as additives in gas–liquid chromatography [41–44], liquid chromatography [43], and capillary electrophoresis [45,46]. They are also used in optical sensors [47,48], and to enhance the analytical performance of the matrix-assisted laser desorption ionization mass spectrometry (MALDI-MS) [49]. The use of ILs in different applications is determined by their intrinsic properties. Scheme 3 briefly lists the general applications of ILs.

ILs can generally be divided into two groups according to their solubility in water. The first type, *water-immiscible* (hydrophobic) IL such as 1-butyl-3-methylimidazolium hexafluorophosphate ($[BMIM][PF_6]$) and 1-decyl-3-methylimidazolium bis(trifluoro-methylsulfonyl)imide ($[DMIM][Tf_2N]$) have been used in formation of films on glassy carbon electrode and carbon ceramics [50,51]. Due to hydrolysis of PF_6^- [52] the imidazolium salts with Tf_2N^- are increasingly used as hydrophobic ILs. Water-immiscible ILs form non-polarizable interfaces when in contact with water and they have the advantage to be easily prepared in aqueous solution. They can also be obtained in very dry state and they are especially suitable for applications in electrochemical systems from which moisture should be excluded even over



Scheme 3 – Applications of ILs.

a long period of operation. In contrast, less attention has been paid to the second type, *water-miscible* (hydrophilic) ILs (e.g. [BMIM][BF_4]), because they have so far been considered unstable in aqueous solutions. However, it was recently found that water-miscible ILs can also form films with active electrochemical properties on glassy carbon electrode and can be used in aqueous media [53]. The miscibility of ILs in water is strongly dependent on the anions [20,54]. Cl^-, Br^-, I^-, $NO_3{}^-$, CH_3COO^- and CF_3COO^- are anions that make the ILs miscible with water. ILs composed of anions such as $PF_6{}^-$ and Tf_2N^- are in contrast immiscible with water. Miscibility of water of ILs based on anions such as $BF_4{}^-$ and $CF_3SO_3{}^-$ is dependent on the structure of the cations, even though they in general are miscible with water. The miscibility will decrease with the increase in the cation chain length. Surface and aqueous interfacial tensions have been measured for a series of water-immiscible room-temperature ILs based on 1-alkyl-3-methylimidazolium cations ($C_n$mim, $n = 6$, 8, 10, and 12) and anions of Tf_2N^- and Pf_2N^- [55]. It was found that the surface tensions of the ILs increased with the increasing cation chain length in the similar way as has been found with *n*-alkanes. Interfacial tensions of the ILs with aqueous

Table 1 – The ionic liquids mentioned in this review

Full name	Abbreviation
1-Ethyl-3-methylimidazolium tetrafluoroborate	[EMIM][BF_4]
1-Butyl/hexyl-3-methylimidazolium hexafluorophosphate	[BMIM]/[HMIM][PF_6]
1-Decyl-3-methylimidazolium bis(trifluoro-methylsulfonyl)imide	[DMIM] [Tf_2N]
1-Butyl-3-methylimidazolium tetrafluoroborate	[BMIM][BF_4]
1-Dodecyl-3-methylimidazolium chloride	[DMIM][Cl]
1-Butyl-3-methylimidazolium hexafluorophosphate	[BMIM][PF_6]
1-Butyl-2,3-dimethylimidazolium bis(trifluoro-methylsulfonyl)imide	[BDMIM][Tf_2N]
Dodecylethyldiphenylphosphonium bis(trifluoro-methylsulfonyl)imide	[DEDPP][Tf_2N]
N-Octylpyridinium hexafluorophosphate	[OPy][PF_6]
1-Butyl-3-methylimidazolium bis(trifluoro-methylsulfonyl)imide	[BMIM][Tf_2N]
1-Octyl-3-methylimidazolium hexafluorophosphate	[OMIM][PF_6]
Phosphonium dodecylbenzene-sulfonate	[$P_{6,6,6,14}$][DBS]
1-Ethyl-3-methylimidazolium bis(trifluoro-methylsulfonyl)imide	[EMIM][Tf_2N]
Hexyltriethylammonium bis(trifluoro-methylsulfonyl)imide	[$N_{6,2,2,2}$][Tf_2N]
1-Butyl-3-methylimidazolium chloride	[BMIM][Cl]
1-Decyl-3-methylimidazolium bromide	[DMIM][Br]
N-Butylpyridinium hexafluorophosphate	[BP][PF_6]
1-(2-Hydroxyethyl)-3-methylimidazolium tetrafluoroborate	[HEMIM][BF_4]

solutions, however, were found to decrease with the length of the cation chain. This is due to the increased surface activity of the longer chain cations. Elongation of the alkyl chain also causes pronounced depression of fluidity and ionic conductivity for ILs composed of 1-alkyl-3-methylimidazolium cations with different alkyl chain lengths [56]. Thus, by varying the alkyl chain length or the anion the properties such as hydrophobicity, viscosity and ionic conductivity can be changed in controllable manner. In addition, the surface ordering ability of amphiphilic ILs has also been observed as they always introduce ordered self-organized structures [57].

To use ILs in analytical work has attracted the attention of the researchers in variable branches of chemistry and engineering. Comparing with the relatively thorough studies of ILs in other applications, the use of ILs in electrochemical analysis, however, is still an area under strong development.The ILs mentioned in this review are listed in Table 1.

3. Applications of ILs in electrochemical analysis

3.1. *Ion selective sensors*

All-solid-state miniaturised planar reference electrodes based on ILs have recently been reported [58]. The Ag/AgCl planar microelectrodes were covered with PVC membranes containing the IL, 1-dodecyl-3-methylimidazolium chloride [DMIM][Cl], which provides an internal solid electrolyte. These electrodes showed good potential stability and reproducibility and are big achievements in developing reliable solid-state reference electrodes. Kakiuchi and Yoshimatsu have also reported a concept for a solid-state reference electrode and they thoroughly discussed the thermodynamics of such a device [59].

Potentiometry with ion selective electrodes (ISEs) is an accurate, fast, and inexpensive analytical method [60–64]. ISEs have provided the possibility to detect chemical species with reasonable selectivity and low detection limit. Solid-state ISEs can be realized by applying conducting polymers as the transducing layer in the electrode construction [65]. Poly(3,4-ethylenedioxythiophene) (PEDOT), a frequently used conducting polymer, can be electropolymerized in ILs with bulky organic anions [66]. A PEDOT electrode made in such a way showed linear anionic potentiometric response in 10^{-5} to 10^{-1} M KCl aqueous solutions. Up to now, the reports on the use of ILs directly in ISEs are few [67,68]. However, ILs were found to be excellent materials to prepare membranes for ISEs due to their polymer plasticizing ability and ionic nature. Coll et al. [67] found a remarkable selective response to the highly hydrophilic sulfate anion by using the hydrophobic IL ([BMIM][PF_6]) to prepare the poly(vinyl chloride) (PVC) membranes used in anion selective electrodes. This provides an alternative way to use ILs as ionic additives in conventional ISE membranes. The response to the target sulfate ions was, however, still generated by the ionophore, polyazacycloalkane. Recently, Shvedene et al. [68] have reported a method to use ILs in various polymer membranes both as the plasticizer and the ion-responsive media. The compounds 1-butyl-2,3-dimethylimidazolium bis(trifluoro-methylsulfonyl)imide ([BDMIM][Tf_2N]) and dodecylethyldiphenylphosphonium bis(trifluoro-methylsulfonyl)imide ([DEDPP] [Tf_2N]) were used to plasticize the PVC and poly(methyl methacrylate) (PMMA) membranes and to bring ion-selecting ability to these polymer membranes as well. Good and stable response to (relatively hydrophobic) cations and anions were obtained with these electrodes and they were also found to be suitable to analyze compositions of surfactants [68].

Safavi et al. [69] have constructed a potentiometric ion sensor based on a mixture of graphite powder and the ionic liquids *N*-octylpyridinium hexafluorophosphate [OPy][PF_6] and [BMIM][PF_6]. Because these electrodes do not have any ionophore in the membrane the response of the electrodes is based solely on partition of the ions between the aqueous phase and the electrode membrane. Selectivity of these sensors was not studied but cannot be expected to be high.

3.2. *Voltammetric sensors*

In addition to potentiometric measurements, ILs have more widely been used to detect ions via other electroanalytical methods, particularly by voltammetry. Trace amount of chloride has been determined electrochemically by using linear sweep, square wave and cathodic stripping voltammetry [70]. Low levels of chloride (ppb) in [BMIM][BF_4], [BMIM][Tf_2N] and [BMIM][PF_6] were detected.

IL-type carbon paste electrode has been proposed by Liu et al. [71]. In a recent work the IL imidazolium salt-functionalized polyelectrolyte was used in flow-injection analysis in the electrochemical detector working in the voltammetric mode [72]. All the three electrodes (working, reference and auxiliary) are placed close to each others in the flow channel and are covered with a thin film of the water insoluble IL. In this configuration the electrodes are all the time in contact with the electrolyte although air bubbles in the carrier flow may occur. The electroactive compounds to be determined have, however, to diffuse from the carrier stream into the thin layer of the ionic liquid and to the surface of the working electrode. This may result in a small dead time in the detector signal but in most cases should be negligible.

Maleki et al. have studied the electrocatalytic activity of the ILs [OPy][PF_6] and 1-octyl-3-methylimidazolium hexafluorophosphate [OMIM][PF_6] in carbon paste electrode by using the redox probe $Fe(CN)_6^{3-/4-}$ [73]. Even addition of traces of the ILs increased the electrocatalytic activity of the electrode.

3.3. *Gas sensors*

Due to the entire ionic composition, which eliminates the need to add supporting electrolyte, the intrinsic conductivity and negligible vapor pressure ILs are unique compounds to be used in the development of stable electrochemical sensors for gaseous analytes such as O_2, CO_2, and NH_3 [74–80]. The superoxide radical ($O_2^{\bullet-}$) which is generated in situ by the reduction of O_2 was found to be stable in ILs at glassy carbon, gold (Au) or platinum (Pt) electrodes [74–77]. This makes the amperometric detection of O_2 possible and the reported solid-state O_2 gas sensor based on porous polyethylene supported [EMIM][BF_4] membrane has a wide detection range, high sensitivity and excellent reproducibility [74]. With increasing levels of CO_2 in the sample, cyclic voltammetry shows an increased cathodic peak current from the production of $O_2^{\bullet-}$ radicals together with the decreased peak current from the reverse scan of oxidation. This indicates that the generated $O_2^{\bullet-}$ radical reacts irreversibly with CO_2 to form peroxydicarbonate ion, $C_2O_6^{2-}$ [76]. The kinetics of this reaction has been studied in [EMIM][Tf_2N] and hexyltriethylammonium bis(trifluoro-methylsulfonyl)imide ([$N_{6,2,2,2}$][Tf_2N]). Despite of the significantly different viscosities of these two ILs, the reaction between O_2^- radical and CO_2 was found to proceed in a similar mechanism in both cases [78]. This also provides an amperometric way to detect CO_2.

The electrochemical oxidation of the nitrite ion (NO_2^-) and nitrogen dioxide gas (NO_2) in [EMIM][Tf_2N] have been studied by cyclic voltammetry on Pt electrodes of various sizes [81]. From chronoamperometrical measurements, the following solubility values were calculated: 7.5 mM for NO_2^- and ca. 51 mM for NO_2, indicating that this IL is a potential media for sensing the NO_2 gas.

Determination of ammonia based on the electrooxidation of hydroquinone in dimethylformamide (DMF) and [EMIM][Tf_2N] has also been reported [79]. Ammonia can remove protons from the hydroquinone molecules reversibly and thus facilitate the oxidation process giving a new wave at less positive potentials in the cyclic voltammogram. Similar responses were found both in dimethylformamide and [EMIM][Tf_2N]. The detection limit of ammonia based on this method is 4.2 ppm in DMF.

An amperometric membrane-free gas sensor consisting of a two-electrode cell has been designed [80]. The surface of the working electrodes (gold microelectrodes) is modified with a thin layer of IL which serves as a non-volatile electrolyte, eliminating the need for a gas permeable membrane to separate the sample and the internal electrolyte layer. The viscosity of an IL is generally higher than that of organic solvents (1–2 orders of magnitude higher) inducing a significantly slower mass transport. Although the slow mass transport will cause a longer response time of the gas sensors based on IL, it is still adequate in many practical applications. Such sensors will have potential applications particularly in more extreme operating conditions, such as high temperature and pressure where conventional solvents would evaporate or decompose. The low-volatility and remarkable thermal stability make ILs suitable for gas sensing especially at high temperature.

Solubility and thermodynamic properties of different gases such as CO_2, H_2 and O_2 in [BMIM][PF_6] have been thoroughly studied [82]. ILs are a new class of sensing materials for detection of organic vapors when using the quartz crystal microbalance (QCM) technique [83–85]. QCM is a mass sensor and the working principle of QCM is based on the change in frequency that is measured between a reference state and when the quartz crystal is exposed to a sample vapor. The theoretical sensitivity is in the range of 0.1–1 ng [86]. In an ideal case, the frequency change is only caused by the change in mass loading on the surface of the vibrating crystal. The change in mass can be calculated from the frequency shift by using the Sauerbrey equation [87]. However, Liang et al. [83] showed that changes in viscosity of the IL film upon absorption of organic vapors at room temperature was the main cause for the change in frequency rather than change in the mass of the IL film. The sensing mechanism of a QCM sensor using ILs is based on the fact that the viscosity of the IL membrane decreases rapidly due to solvation of the analytes in the ILs. The change in viscosity, which varies with the chemical species of the vapors and the type of ILs, results in a frequency shift of the quartz crystal. QCM is particularly suitable to detect complex odors, because it allows the deposition of a wide range of selective interfaces on the surface of the crystal. An IL piezoelectric gas sensor using phosphonium dodecylbenzene-sulfonate [$P_{6,6,6,14}$][DBS] as sensing materials coated on QCM transducers was demonstrated to be able to detect both polar (ethanol or dichloromethane) and non-polar (heptane or benzene) organic vapors at high temperature [88]. The sensor gives linear, fast and reversible response even at temperatures up to 200 °C. In the same study it was also shown that there is a big change in viscosity of the ILs upon absorption of organic vapors at room temperature. However, the change of viscosity caused by the gas absorption becomes very small at high temperature and the frequency changes are then mainly due to changes in mass of the IL film.

ILs offer many options for chemical modifications and hence a huge flexibility in tailoring molecular recognition sites in their structures by controlled organic synthesis and surface design. These possibilities provide exciting opportunities to explore the applications of ILs not only in high temperature gas sensing but also in high sensitive and selective determination of trace analytes using ILs in sensor arrays. For example, a task specific IL with an amine group on the cation has been designed to capture CO_2 and was reported to enhance significantly the solubility of CO_2 in that particular IL [89]. A set of diverse ILs showed selective responses to different organic vapors due to structural differences in the used ILs. Therefore, a sensor array of ILs would be able to effectively differentiate different vapors in using pattern recognition methods, and having increased selectivity to organic vapors both at room and high temperatures [84]. For complex odors, artificial olfactory systems ideally consist of series of different sensors and often with different sensor principles. The feasibility of using [BMIM][PF_6] as the selective layer on QCM for artificial olfactory systems has been studied [90]. Since the physicochemical properties of ILs can be tuned to fit in particular applications the ILs can provide high solubility of analytes and hence short response and desorption times, as well as an excellent baseline recovery after exposure to sample vapors. Such sensors can therefore make significant contribution to sensor arrays of artificial olfactory systems which rely on employing a multitude of sensor principles and selective materials. However, it should also be noted that since the frequency change apparently depends on both the mass load as well as the change in viscosity of the IL, it would be necessary to understand in detail to what extent the change in sensor signal is due to viscosity changes and to what degree it is due to chances in mass load when such a system is used in quantitative determinations. A straightforward interpretation of the sensor response might be demanding, in particular when the sensor is exposed to multi-component mixtures. Nevertheless, gas sensors relying on QCM with ILs may serve as alternative or complementary sensors. The use of trapped ILs in alumina nanopores was reported to avoid all the problems in signal interpretation connected with dewetting and viscoelasticity

[85]. Pure gravimetric sensors using ILs as transducing layers was constructed based on these porous alumina layers.

Understanding the interference of different factors on the liquid phase behavior of ILs with other liquids is useful in developing ILs as designer solvents. A systematic study of the influence of different factors on the phase behavior of imidazolium-based ILs with alcohols has been presented [91]. An IL ethanol chronoamperometric sensor with nickel electrodes proves to be highly sensitive (detection limit of 0.13% (v/v)) based on the redox reaction between the $Ni(OH)_2/NiOOH$ couple in ILs [92].

3.4. *Gelation of ILs and their use in biosensors*

ILs have shown good compatibility with biomolecules and enzymes, and even whole cells are active in various ILs. [BMIM][Cl] was found miscible with silk, which is an attractive biomaterial with excellent mechanical properties and biocompatibility. The patterned films cast from this silk–IL solution supported normal cell proliferation and differentiation [93]. Recently, some authors have reported increased stability of enzymes in ILs compared with stability in some organic solvents [94–96]. ILs were also found to act as agents to stabilize proteins effectively at elevated temperatures [97]. Laszlo and Compton have also reported the catalysis of hemin activated by an electron acceptor in IL solutions and it was found that the activity of hemin increased with the enhanced amount of IL in the methanol–IL system [94]. Elaboration of biosensors incorporating ILs is a particularly fertile area for exploration. It is assumed that the hydrogen bond and the electrostatic interaction between the IL and the enzyme result in a high kinetic barrier for unfolding of the enzyme. Therefore, the rigid structure of the enzyme can be protected from being destroyed [96]. Further work should be carried out to investigate thoroughly the mechanism for the high activity and good thermal stability of enzymes immobilized in IL based matrices. However, it should also be pointed out that some ILs can, unfortunately, also inactivate enzymes [98,99]. The choice of the best IL always depends on the specific application.

Addition of water to either 1-decyl-3-methylimidazolium bromide ([DMIM][Br]) or its nitrate analog has shown to trigger self-assembly of IL and formation of ionogels [100]. These ionogels can be tuned to have special properties simply by careful selection of the anion and adjustment of the water concentration. This provides a versatile platform for preparation of nano- and mesoporous materials. Several different gelation methods for ILs have been reported to produce matrices for biosensors [101–106].

Dramatically enhanced activity and thermal stability of horseradish peroxide (HRP) were obtained when it was immobilized it in the [BMIM][BF_4] based sol–gel matrix [107]. The IL was used as a template solvent for the silica gel matrix via a simple sol–gel method via hydrolysis of tetraethyl orthosilicate in [BMIM][BF_4]. This particular HRP immobilized sol–gel matrix was further used in amperometric biosensors [108]. The novel amperometric hydrogen peroxide biosensor based on this ionogel exhibited excellent stability and sensitivity. The detection limit for hydrogen peroxide is reported to be 1.1 μM.

Direct electrochemical reduction of hemin has been studied by cyclic voltammetry and chronocoulometry in the ILs, [BMIM][PF_6] and [OMIM][PF_6] [109]. *N*-Methylimidazole (NMI)-ligated hemin had a lower $E_{1/2}$ than pyridine-ligated hemin in both ILs, which is consistent with the stronger electron donor characteristic of NMI. It was further discovered that while hemin is electrochemically active in IL, its behavior is modified by the ligand field strength and surface adsorption phenomena at the working electrode. Electrochemistry and electrocatalysis of a number of heme proteins entrapped in agarose hydrogel films in [BMIM][PF_6] have also been investigated [50]. UV–vis and FTIR spectroscopy show that the heme proteins retain their native structure in agarose film. Cyclic voltammogram shows that the direct electron transfer between the heme proteins and glassy carbon electrode is quasi-reversible in [BMIM][PF_6]. The redox potentials for hemoglobin (Hb), myoglobin, HRP, cytochrome *c*, and catalase were found to be lower than those in aqueous solution, indicating the catalytic effect in the IL matrix. The heme proteins can catalyze electroreduction of trichloroacetic acid and *tert*-butyl hydroperoxide in [BMIM][PF_6] [50]. Direct electrochemical response of HRP [108], myoglobin [111] and Hb [112] have been observed on IL modified electrodes. Nafion was used as a binder to form a Nafion–IL composite film and to help [BMIM][PF_6] to adhere on the glassy carbon electrode effectively. The composite film can readily be used as an immobilization matrix to entrap HRP, which can still retain its bioactivity [110]. [BMIM][PF_6] can also replace paraffin as binder in carbon paste electrode where the immobilized Hb showed excellent electrocatalytic activity in reduction of H_2O_2 and nitrite [112]. *N*-Butylpyridinium hexafluorophosphate ([BP][PF_6]) can also be used as binder to immobilize Hb in the Nafion/nano-$CaCO_3$ film, which shows electrocatalytic behavior in reduction of H_2O_2, trichloroacetic acid and nitrite [113]. Myoglobin can be adsorbed tightly on the surface of the basal plane graphite electrode in the presence of 1-(2-hydroxyethyl)-3-methylimidazolium tetrafluoroborate [HEMIM][BF_4] [111]. Promotion for the direct electron transfer between myoglobin and basal plane graphite electrode was observed. [BMIM][BF_4] based sol–gel modified electrode was prepared by immobilizing [BMIM][BF_4] into silica sol–gel matrix on the surface of Au electrode via a simple sol–gel method [114].

It has also been reported that the water-miscible imidazolium-based ILs can interact with glassy carbon electrode and form molecular films on the electrode surface [53]. These molecular films are found to possess striking electrochemical properties such as electrocatalysis in oxidation of ascorbic acid and the capability to facilitate direct electron transfer in HRP.

3.5. *Biosensors based on carbon–ILs composites*

Carbon nanotube (CNT) modified glassy carbon electrodes show enhanced sensitivity and stability in oxidation of phenolic compounds [115]. The CNT modified electrodes were also found to show good electrocatalytic ability to biomolecules such as dopamine (DA), ascorbic acid (AA) and dihydronicotinamide adenine dinucleotide (NADH) [116–119]. CNTs usually exist as tangled bundles that are difficult to dissolve in both aqueous and organic media. However, they can be well individualized in ILs due to 'cation–π' interactions and a CNTs–IL gel can easily be prepared using IL as the binder [120], where the CNTs greatly enhances the conductivity of the system. Electrochemical functionalization of single wall carbon nanotubes in [BMIM][PF_6] was used to make a glucose sensor by covalently binding glucose oxidase (GOD) to the modified nanotube [121].

Gels of acid treated multiwall CNTs with water-miscible IL, [BMIM][BF_4] were made by grinding them together [122]. Glassy carbon electrode modified by this gel was used in direct electrochemical study of heme proteins (Hb and HRP). The heme proteins entrapped in CNTs-[BMIM][BF_4] gel exhibit good biocatalytic activity towards H_2O_2 due to the biocompatibility of [BMIM][BF_4]. This composite material has shown to keep the bioactivity and to facilitate direct electron transfer of heme proteins. Carbon fiber microelectrode has also been modified by CNTs–IL gel and used in bioelectrochemical studies [123]. The carbon fiber microelectrode modified by CNTs–IL gel promotes greatly the direct electron transfer of glucose oxidase and exhibits effective catalytic activity to biomolecules, such as DA, AA, and NADH. IL has also been used as binder to modify electrode surface of multiwall carbon nanotubes. This construction has better electrochemical properties than by chitosan or Nafion modified electrodes. The GOD adsorbed at this modified electrode shows good stability and has good electrocatalytic activity to glucose with a broad linear concentration range up to 20 mM [124].

At a conventional solid electrode such as glassy carbon, the oxidation potentials of AA and uric acid (UA) are close to that of DA, resulting in an overlapping voltammetric response [125]. Nevertheless, selective detection of DA in presence of AA and UA on a glassy carbon electrode modified by multiwall CNTs–IL ([OMIM][PF_6]) gel has been reported [126]. The anodic peaks of AA, UA and DA can be well separated in the mixture since the peak potential of AA is shifted to a more negative value, while that of UA is shifted to a more positive value. The detection limit of DA by using differential pulse voltammetric technique is ca. 1.0×10^{-7} M in the presence of a large excess (more than 100 times excess) of AA in neutral pH solutions. An effective, quick and sensitive sensor was developed to determine DA in the presence of UA and of AA.

Safavi et al. [127] have also observed the anodic peak separation of DA from AA and UA on the carbon composite electrode, which is made of mixing *N*-octylpyridinium hexafluorophosphate [OPy][PF_6] with graphite powder. The IL [OPy][PF_6] is used as the pasting binder in place of non-conductive organic materials in conventional carbon paste electrodes. It was possible to simultaneously determine DA, AA, and UA by using this electrode composition. The carbon composite electrodes using IL as the binder were reported to combine the advantages of CNTs, pyrolytic graphite and carbon paste electrodes [128]. The high performance carbon composite electrodes based on IL can provide high-rate electron transfer with resistance towards fouling caused the biomolecules. Fouling is usually caused by the adhesive film formed by oxidation products of phenolic compounds passivating the electrode surface [129].

Surface of a glassy carbon electrode was modified by applying on it a gel containing multi-wall carbon nanotubes and [BMIM][PF_6] [130]. The surface of this electrode was further modified by adsorption of Hb on it. The eletrochemical response of that modified electrode was found to be stable. The enzyme catalase kept its activity to hydrogen peroxide even after adsorption to the gel modified electrode. A modified carbon electrode has also been made by mixing [OPy][PF_6] and graphite powder [131]. That electrode was used in voltammetric determination of L-cysteine in neutral aqueous media. The electrode shows electrocatalytic activity in oxidation of L-cysteine and no deactivation of the electrode was found during the studies.

Nitric oxide (NO) is released by many cells in mammalian systems and play a number of important role in biological systems. From the biochemical as well as from the medical point of view it is important to differentiate the NO generated in abnormal and normal tissues. However, NO reacts rapidly with hemoglobin, O_2, and other biological oxidative species in vivo and/or in vitro. Voltammetric detection of NO by microelectrodes can be used in situ measurements of NO in single cells near the source of the NO synthesis. A novel gel microelectrode based on the hydrophobic IL, 1-hexyl-3-methylimidazolium hexafluorophosphate ([HMIM][PF_6]) has been reported [132]. A cavity is first etched at the tip of a electrode, and then it is filled with a conductive gel composite containing single wall CNTs and the IL. This microelectrode is then coated with a Nafion membrane, which can eliminate interferences from nitrite and some biomolecules. The sensing reaction involving NO is proposed to follow an electrochemical–chemical (EC) oxidation mechanism and it has a linear response range from 100 nM to 100 μM.

3.6. *Other applications*

Use of microwave activated electrochemistry has been proposed for electroanalysis [133]. It was discovered that the microwave activation also induces high temperature–high speed electrochemical processes in ILs [134]. The high viscosity of ILs, which is sometimes a drawback in electroanalysis, can be overcomed by thermal activation.

Au nanoparticles and nanorods have widely been used in assay of biological samples by means of electroanalytical and/or optical methods [135,136]. Synthesis of Au nanoparticles modified ILs based on the imidazolium cation has been reported [137]. Combining the specific property of biocompatibility of some ILs and the physical and electrochemical properties of Au nanoparticles would make a unique matrix for electrochemical detection in biological samples. Palladium nanoparticles have been dispersed in a carbon electrode modified with [OPy][PF_6] [138]. The electrode showed electrocatalytic activity to reduction of dissolved oxygen in basic, acidic and neutral aqueous solutions.

4. Conclusions

ILs are solvents that can be designed for special applications either by synthesizing new ILs or by paring different cations and anions to fine-tune the properties of a particular IL.

Electrochemical methods such as potentiometry, voltammetry and QCM have been used in ILs to develop new generation of ion selective sensors, voltammetric devices, gas sensors and biosensors. The good catalytic ability together with the simple preparation procedure will greatly promote the development and application of CNT–IL based microelectrodes to be used in biosensors and other bioelectrochemical devices. ILs with the appropriate properties should be selected for each particular application.

Synthesis of ILs with built-in functionalities such as cations or anions incorporating polymerizable moieties and ion-recognizing groups is a promising direction of development. It can be predicted that the use of ILs in electrochemical sensing is a promising and exciting area of research and definitely needs further exploration. Combination of ILs with electrochemical sensors has the potential to broaden or even revolutionize the range of analytical methods.

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