Critical Reviews in Analytical Chemistry

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/batc20

Room Temperature Ionic Liquids-Based Electrochemical Sensors: An Overview on Paracetamol Detection

R. Rama, S. Meenakshi, K. Pandian & S. C. B. Gopinath

To cite this article: R. Rama, S. Meenakshi, K. Pandian & S. C. B. Gopinath (2021): Room Temperature Ionic Liquids-Based Electrochemical Sensors: An Overview on Paracetamol Detection, Critical Reviews in Analytical Chemistry, DOI: 10.1080/10408347.2021.1882834

To link to this article: https://doi.org/10.1080/10408347.2021.1882834

Published online: 23 Feb 2021.

CRITICAL REVIEWS IN ANALYTICAL CHEMISTRY
https://doi.org/10.1080/10408347.2021.1882834

Taylor & Francis
Taylor & Francis Group

Room Temperature Ionic Liquids-Based Electrochemical Sensors: An Overview on Paracetamol Detection

R. Rama[a], S. Meenakshi[a], K. Pandian[b], and S. C. B. Gopinath[c,d]

[a]Department of Chemistry, School of Basic Sciences, VELS Institute of Science, Technology and Advanced Studies (VISTAS), Chennai, Tamil Nadu, India; [b]Department of Inorganic Chemistry, University of Madras, Guindy Campus, Chennai, Tamil Nadu, India; [c]Institute of Nanoelectronic Engineering, Universiti Malaysia Perlis (UniMAP), Perlis, Malaysia; [d]Faculty of Chemical Engineering Technology, Universiti Malaysia Perlis (UniMAP), Perlis, Malaysia

ABSTRACT

Paracetamol (PAR) is an effective antipyretic and analgesic drug utilized worldwide, safer at therapeutic levels but over-dosing and the chronic usage of PAR results in accumulation of toxic metabolites, which leads to kidney and liver damages. Hence, a simple, rapid, cost-effective, and sensitive analytical technique is needed for the accurate determination of PAR in pharmaceutical and biological samples. Though numerous techniques have been reported for PAR detection, electrochemical methods are being receiving more interest due to their advantages. Moreover, in the past few decades, room temperature ionic liquids (RTILs) have been utilized in electrochemical sensors due to their attractive properties. In this present review, authors gathered research findings available for the determination of PAR using RTIL-based electrochemical sensors and discussed. The advantages and limitations in these systems as well as the future research directions are summarized.

KEYWORDS

Carbon-ceramic electrode; carbon paste electrodes; glassy carbon electrodes; ionic liquids; modified electrodes; paracetamol detection

Introduction

Paracetamol (Acetaminophene or *N*-acetyl-*p*-aminophenol, PAR) which contains acetylated aromatic amide is being utilized worldwide due to its antipyretic and analgesic action and it is the main alternative of acetyl salicylic acid (aspirin). PAR is safe with very few side effects at therapeutic levels and generally used for the relief from pains, minor aches, neuralgia, arthritis, and fever. But it was reported that overdose of PAR will result in the build-up of toxic metabolite known as *N*-acetyl *p*-benzoquinoneimine (NAPQI) which will damage liver and kidneys in human body and finally it can lead to death.[1–4] Hence, the development of analytical methods and techniques for rapid, selective, and accurate determination of PAR present in pharmaceutical formulations and various types of biological samples such as urine, blood, and plasma are highly essential for the drug quality control and clinical analysis. In this context, numerous research findings have been reported worldwide.[5,6] Actually, various methods such as Fourier-transform infrared (FTIR) spectroscopy, high performance liquid chromatography (HPLC), spectrophotometry, titrimetry, liquid chromatography with tandem mass spectroscopy (LC-MS-MS), and capillary electrophoretic methods were explored for the determination of PAR.[7–14]

Among the various techniques, electrochemical methods are advantageous due to low cost, portability, easy operation, accurate detection, etc.[15–20] Numerous types of electrochemical sensors for the detection of PAR are being reported worldwide. For example, glassy carbon electrode (GCE) modified with nanocomposites based on nitrogen-rich porous carbon (P-NC),[21] cerium oxide (CeO_2/CNT),[22] bismuth oxide (Bi_2O_3/MWCNT),[23] graphene-platinum (GrPtNPs),[24] lanthanum doped copper oxide (La^{3+}-CuO/MWCNT),[25] etc., have been explored for the detection of PAR. Similarly, carbon paste electrodes (CPEs) based on zeolitic imidazolate frameworks/cobalt and tannic acid nanocomposite (ZIF-8@Co-TA/CPE),[26] grapheneoxide-Y_2O_3 nanomaterial,[27] aluminum oxide/palladium NPs (PdNP@Al_2O_3),[28] and poly (naphthol green B) film,[29] etc., were also studied. Moreover, PAR detection at various modified graphite,[30–32] gold,[33,34] and diamond[35–37] electrodes have been also examined.

In the recent past, room temperature ionic liquids (RTILs) are receiving great attention due to their fascinating properties such as high thermal stability, negligible vapor pressure, high solubility for organic species, wide liquid range and electrochemical window, electrical conductivity, and tunable properties.[38–40] Various RTIL-based detection methods for PAR have been reported in literature. For example, Vázquez et al. reported the determination of PAR using ultrasound-assisted ionic liquid dispersive liquid–liquid microextraction (US-IL-DLLME) coupled with high-performance liquid chromatography (HPLC) with a hybrid triple quadrupole-linear ion trap-mass spectrometer (LC-

CONTACT R. Rama rama.ragu10@gmail.com Department of Chemistry, School of Basic Sciences, VELS Institute of Science, Technology and Advanced Studies (VISTAS), Chennai, Tamil Nadu, India

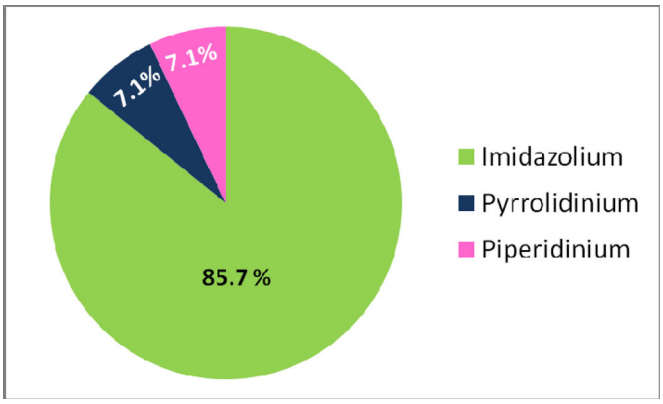

Figure 1. Percentage of different types of RTIL cations used in electrochemical detection of PAR.

QqLIT-MS). But the volatile organic solvents such as methanol and acetonitrile are used.[41] Similarly, Yu et al. explored DLLME coupled HPLC method using magnetic ionic liquids (MILs) for the PAR determination and during the HPLC analysis, acetonitrile was used. Moreover, the LOD of 1 µg/L was reported which is high as compared to the values reported by RTIL-based electrochemical method.[42] Among the various techniques, RTIL- based electrochemical methods for PAR detection are advantageous due to low cost, portability, easy operation, simplistic miniaturization, free of organic solvents, rapid, sensitive, and accurate detection with lower detection limit, etc.[43–47] Figure 1 depicts the % of various types of IL cations used in electrochemical detection of PAR.

Moreover, glassy carbon electrodes (GCEs), carbon-ceramic electrode (CCE), and carbon paste electrodes (CPEs) designed with nanomaterials and RTILs have been reported for the electrochemical detection of PAR. In this review article, these research findings are gathered and discussed in detail. The structure of ionic liquids used in these studies is shown in Figure 2.

Electrochemical behavior of PAR

Roston et al. reported the electrochemical behavior of PAR at carbon paste electrode and proposed mechanism for the electrochemical oxidation of PAR in aqueous solution (Figure 3). It was reported that PAR undergoes electrochemical oxidation by pH-dependent exchange of two electrons & two protons and forms *N*-acetyl-*p*-benzoquinone-imine (NAPQI) (step I). At pH $\geq$ 6, NAPQI exists in the stable unprotonated form and if the medium is more acidic, NAPQI undergoes protonation (step II) and yield electrochemically active fewer stable species. Then it forms immediately a electrochemically inactive hydrated form (step III) which converts into benzoquinone (BQ) at highly acidic condition (step IV).[48] Similarly, Nematollahi et al. reported electrochemical behavior of PAR at glassy carbon electrode in acidic and alkaline pH solutions. It was reported that NAPQI involves in hydroxylation, dimerization or hydrolysis reactions based on pH of the solution.[49]

RTIL-based GCEs and CCE in the detection of PAR

Various types of modified glassy carbon electrodes based on RTILs have been explored for the determination of paracetamol (PAR). For example, Kianipour et al. reported GCE modified with 1-ethyl-3-methyl-imidazolium tetrafluoroborate ($[C_2mim]^+[BF_4]^-$), multiwall carbon nanotubes (MWCNTs) and chitosan (CHIT) (RTIL-MWCNTs-CHIT/GCE) to determine PAR along with ascorbic acid (ASC), uric acid (URI), and mefenamic acid (MEF) simultaneously. Electrochemical behavior of these compounds was examined using cyclic voltammetry (CV), differential pulse voltammetry (DPV), and chrono amperometry (CA) techniques. It was noted that as compared to the bare GCE, RTIL-MWCNTs-CHIT/GCE resulted significant current response for the oxidation of all analytes tested due to the improved electron transfer occurred by the presence of RTIL and MWCNTs. Moreover, the electrochemical response was also studied as a function of pH (4 to 10) of the electrolyte. Up to the pH 7, the oxidation peak current of PAR increased and after that it was found to be decreased. The reason for this was explained based on the enhanced deprotonation of CHIT at high pH and reduced adsorption attitude of PAR toward highly charged electrode surface. Limit of detection (LOD) was found to be 0.240 μmol L^{-1} and 0.555 μmol L^{-1} (S/N = 3) at the modified electrode from the DPV and CA responses of PAR, respectively. In addition, RTIL-MWCNTs-CHIT/GCE was found to show significant repeatability and it was explained based on antifouling property of chitosan. The modified electrode resulted greater stability since CNTs-interspersed chitosan has more mechanical strength and stability toward water. There were no interferences in obtaining the data using MWCNTs-CHIT/GCE for the simultaneous detection of ASC, URI, PAR, and MEF present in human urine (PAR recovery: 96.8–99 %) and blood (PAR recovery: 99 – 101.5 %) at optimum conditions.[50]

Babaei et al. explored GCE modified using single-walled carbon nanotubes (SWCNTs), $[C_2mim]^+[BF_4]^-$ and CHIT (SWCNT-CHIT-IL/GCE) to determine adrenalin (AD) and PAR simultaneously. The electrochemical behavior AD and PAR were investigated using CV, DPV, and CA methods. In CV, at pH 7 there were two stable and distinct redox peaks for PAR with high peak current at RTIL-based modified GCE and it was explained based on the higher conductivity of RTIL. Moreover, higher value obtained for electron transfer rate constant revealed that SWCNT-CHIT-IL system has the capacity in supporting the electron transfer between PAR and surface of the electrode. The voltammetric behavior of AD and PAR were found be good in the pH range of 4 and 7. The LOD of PAR was found to be 0.06 μM and 0.54 μM from DPV and CA, respectively. SWCNT-CHIT-IL/GCE was reported as a suitable electrochemical sensor for the determination of PAR in human blood (PAR recovery: 96 – 102%) and urine samples (PAR recovery: 98 – 102%) with higher sensitivity, repeatability, stability, and reproducibility as well as without any interferences.[51]

Similarly, GCE modified by MWCNTs, amine functionalized magnetite nanoparticles and $[C_2mim]^+[BF_4]^-$ (IL–NH_2-Fe_3O_4NP–MWCNT-GCE) was studied by

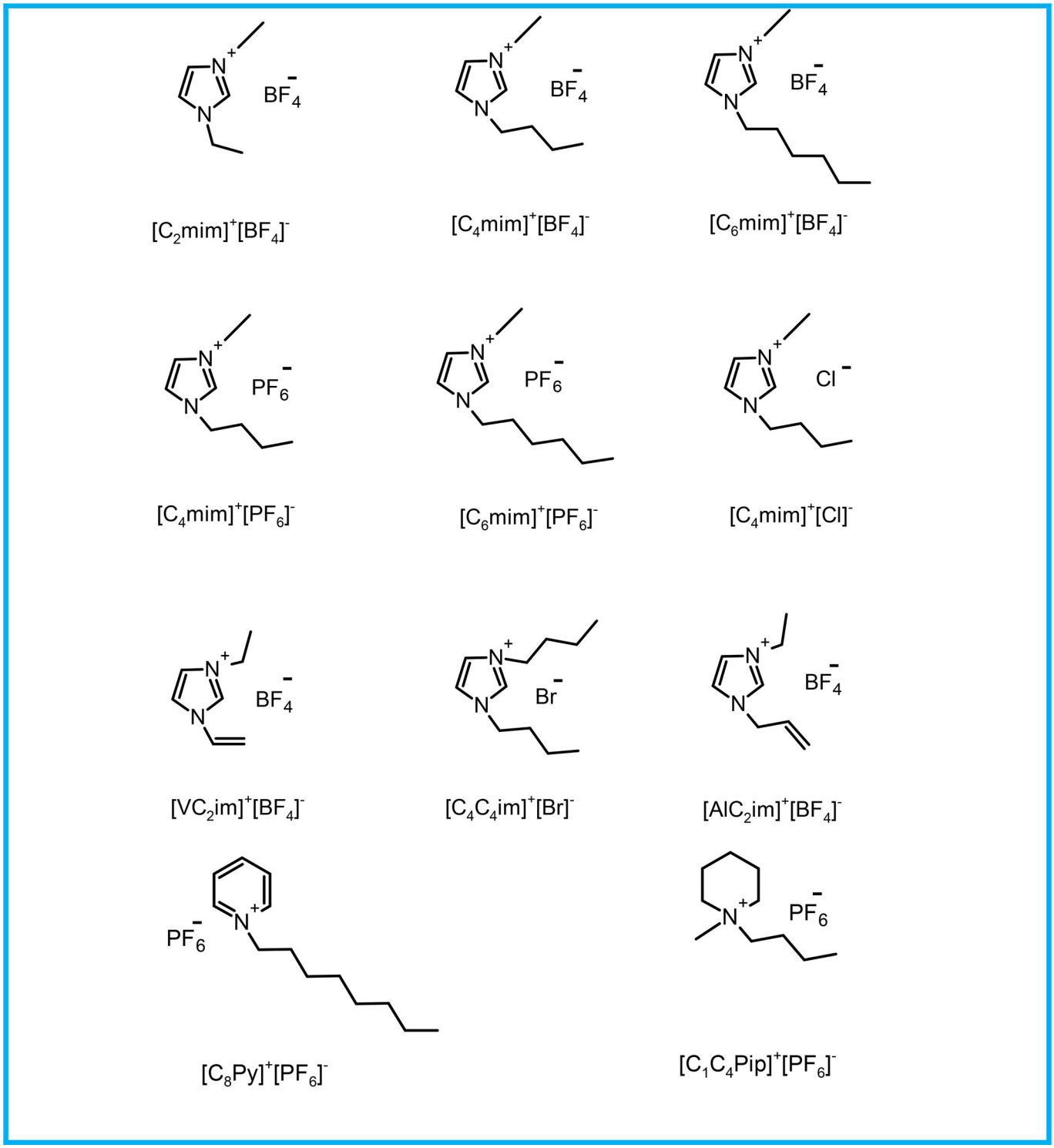

Figure 2. RTILs used for electrochemical determination of PAR. Varied chemical structures are shown.

Rajasekhar et al.[52] for the detection of PAR. This RTIL modified electrode gave interesting results as compared to bare and MWCNT modified GCE. The electrochemical activity of PAR at the RTIL modified GCE was also studied as a function of pH (6 to 12) (Figure 4). The peak current corresponds to the oxidation of PAR increased until the pH 9.5 and then it diminished. Moreover, adsorption-controlled progression was proposed for the oxidation of PAR at IL–NH_2-Fe_3O_4NP–MWCNT-GCE with a lower LOD of 0.04 µM in a reasonable linearity range. Selective detection of PAR with free from interference using DPV technique was reported by standard addition process. The electrochemical mechanism for the PAR oxidation at the IL–NH_2-Fe_3O_4NP–MWCNT-GCE modified electrode was similar to that reported in literature.

The performance of the modified electrode was evaluated using commercial PAR tablets such as Grandpa, Panado, and Paramol. The recovery percentage of PAR was found to be in the range of 98.0 to 99.7% at IL-NH_2-Fe_3O_4NP–MWCNT-GCE without any interference.

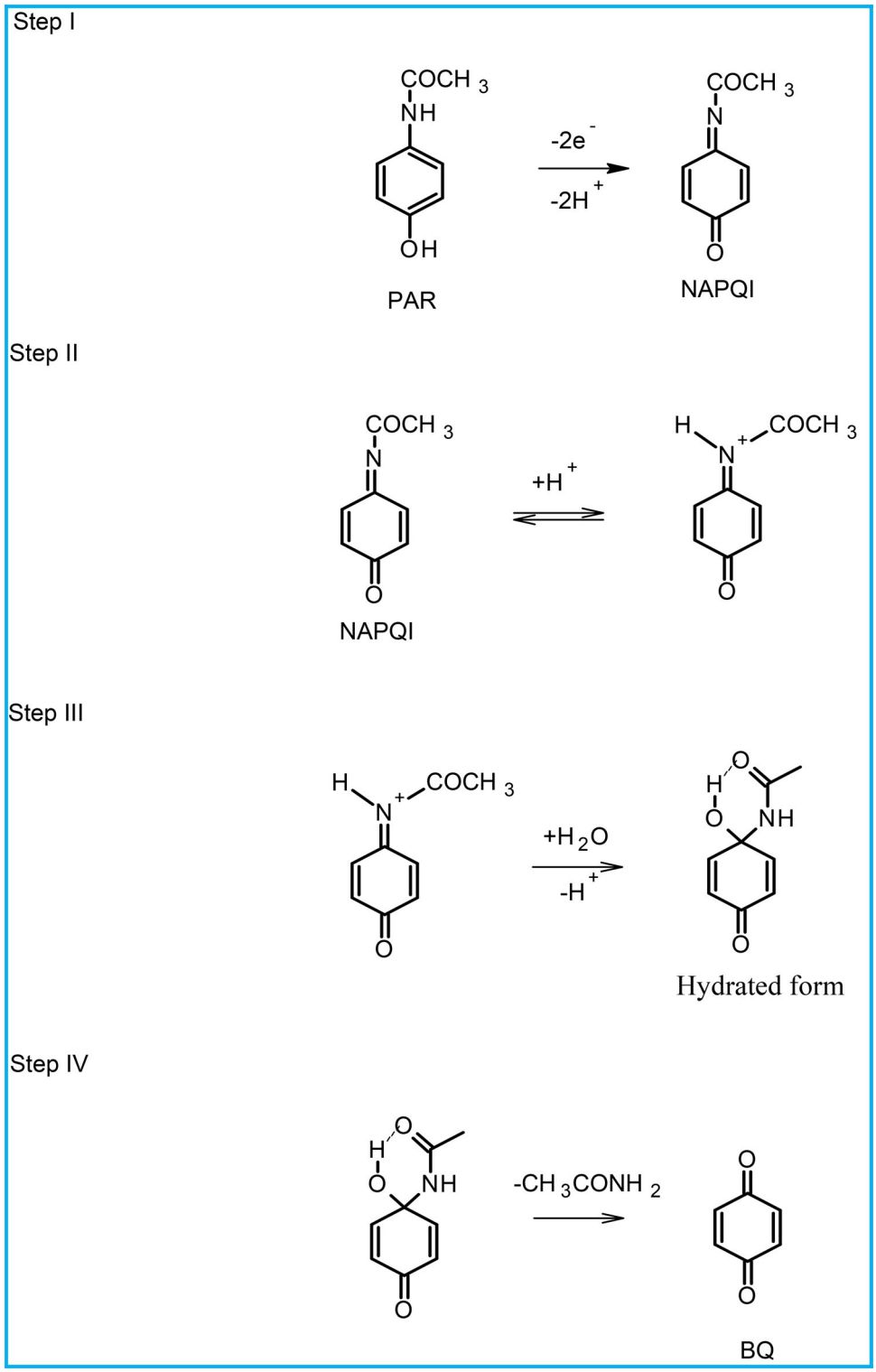

Figure 3. Electrochemical oxidative mechanism of PAR.[48] The steps involved are displayed.

Likewise, functionalized MWCNTs and 1-butyl-3-methylimidazolium hexafluorophosphate ($[C_4mim]^+[PF_6]^-$) modified GCE (GCE/*f*-MWCNT-IL) was investigated by Gomes et al.[53] and significant current response was obtained due to the presence of RTIL. Based on molecular dynamics calculations, it was suggested that van der Waals force (Lennard Jones) is more substantial between PAR and RTIL due to attractive coulombic contact between PAR and $[PF_6]^-$ as well as a pi-type interaction between PAR and $[C_4mim]^+$. The adsorption behavior of PAR in neutral as well as oxidized states was also investigated. Oxidation and desorption behavior of PAR depended on the presence of suitable quantities of RTIL. Moreover, they have also reported[54] the electrochemical behavior of PAR present in the tablets namely, Tylenol® 500 and Tylenol®DC at GCE modified with different ratios of *f*MWCNT and $[C_4mim]^+[PF_6]^-$. At the GCE modified with *f*MWCNT and RTIL, the current response was higher than that obtained at

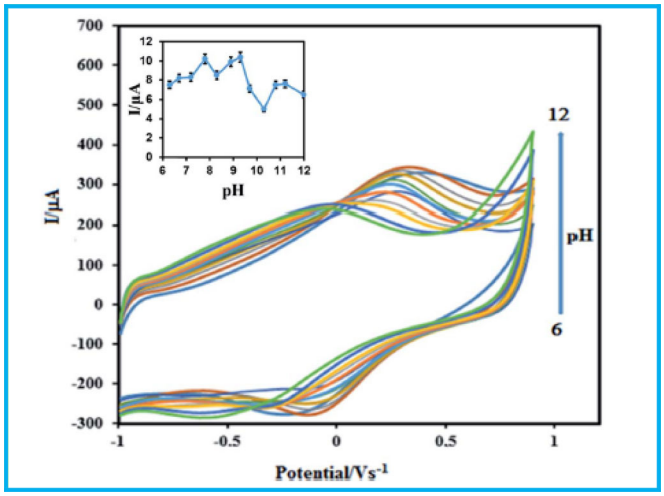

Figure 4. Cyclic voltammograms of 0.1 mM PAR at IL-NH_2-Fe_3O_4NP–MWCNT-GCE as a function of pH (6 to 12).[52]

$[C_4mim]^+[PF_6]^-$/GCE and fMWCNT/GCE. Recovery of PAR in tablets was found to be 82.84–94.75% at *f*MWCNT/$[C_4mim]^+[PF_6]^-$/GCE. Electrooxidation of PAR at the modified electrode was adsorption-controlled process and occurred by the exchange of two electrons and two protons. There was a significant electron transfer, stability, apposite linear range, LOQ of 224 nM and less LOD of 67.3 nM at *f*MWCNT/$[C_4mim]^+[PF_6]^-$/GCE. It was reported that dispersion of *f*MWCNT in the presence of RTIL was due to the shear force and at high concentration of RTIL, *f*MWCNT could be enfolded by the RTIL and it reduces the benefits of *f*MWCNT.

Wang et al. explored a modified GCE with 1-butyl-3-methylimidazolium tetrafluoroborate ($[C_4mim]^+[BF_4]^-$) incorporated into TiO_2 NPs (nano-TiO_2/ $[C_4mim]^+BF_4]^-$/GCE) and it resulted high peak current with lower over potential at the PAR detection as compared to the bare electrode. This modified electrode was effectively utilized for the analysis of PAR in urine samples and the LOD was found to be 0.01 μM. Moreover, PAR recovery at nano-TiO_2/$[C_4mim]^+BF_4]^-$/GCE was in the range of 100.7–103.1%.[55] Carbon-ceramic electrode (CCE) modified with RTIL, 1-allyl-3-ethylimidazolium tetrafluoroborate ($[AlC_2im]^+[BF_4]^-$) have been examined by Majidi et al. for the simultaneous determination of dopamine (DA) and PAR. LODs of 63 mM and 68 nM were reported for PAR and DA, respectively. Pharmaceutical, blood and urine samples were analyzed and excellent recoveries (96.3 – 102.5% in urine sample), repeatability, reproducibility along with stability was noted for the $[AlC_2im]^+[BF_4]^-$ modified electrode.[56]

Moreover, GCE modified with poly(ionic liquid) (PIL), mesoporous carbon nanospheres (MCNs), and CHIT (PIL-MCNs/CHIT/GCE) was examined for PAR detection by Yingying et al. The PIL based on 1-vinyl-3-ethylimidazolium tetrafluoroborate ($[VC_2im]^+[BF_4]^-$) was used in this study. Redox peak current was found to be increasing up to pH 5 and a pair of well-distinct redox peaks obtained at PIL-MCNs/CHIT/GCE as compared to the bare electrode. The electrochemical behavior of PAR at PIL-MCNs/CHIT/GCE was found to be diffusion-controlled process with a detection limit of 0.164 μM. This PIL-based sensor was applied for the detection of PAR in commercial tablets and 99.6 – 106.5% of recovery was reported.[57] The above discussed RTIL-based GCE systems in the determination of PAR are briefly summarized in Table 1.

RTIL-based CPEs for the determination of PAR

Simultaneous determination PAR and morphine by CdO NPs and 1,3-dipropylimidazolium bromide ($[C_4C_4im]^+[Br]^-$)-based electrochemical sensor (CdO/NPs/ILs/CPE) with good stability, sensitivity, and reproducibility was reported by Cheraghi et al. Pharmaceutical and urine samples were analyzed in this study using CdO/NPs/ILs/CPE. The current response corresponds to oxidation of PAR was found to be increasing from pH 5 until 8 and then it diminished. It was observed that RTIL and the CdO NPs provided active electron transfer between the modified CPE electrode and PAR. As compared to bare electrode, CdO/NPs/ILs/CPE resulted high oxidation peak current with less over-potential and LOD of 0.07 μM. The 2 electron 2 proton process of PAR oxidation was reported at CdO/NPs/ILs/CPE.[58]

Similarly, Safavi et al.[59] studied *1*-octyl pyridinium hexafluorophosphate ($[C_8py]^+[PF_6]^+$)-based CPE for the simultaneous detection of PAR and *p*-aminophenol (PAP) in pharmaceutical samples. It was reported that electrochemical activity of PAR and PAP was improved effectively and the peak currents also increased at RTIL-based electrode as compared to the bare electrode. Due to the efficient electro catalytical activity, $[C_8py]^+[PF_6]^-$ was proposed as a suitable binder for the determination of PAR and the LOD was found to be 5.0×10^{-7} M with the relative standard deviations of $< 2\%$. Significant recoveries in the range of 97.2 – 108.3% was also reported for PAR at $[C_8py]^+[PF_6]^+$/CPE. Moreover, it was reported that PAR oxidation is a 2-electron 2-proton process as reported in literature.

Tajik et al. have examined CPE prepared with *1*-(*4*-bromobenzyl)-*4*-ferrocenyl-1H- [1–3]-triazole (1,4-BBFT), graphene nano-sheets and the binder, *1*-hexyl-*3*-methylimidazolium hexafluoro phosphate ($[C_6mim]^+[PF_6]^-$) (1,4-BBFT/IL/GPE), and explored for the simultaneous determination of PAR, isoproterenol and theophylline present in the tea, blood, and urine samples. Recovery of 97.3 – 103.3 % was reported for PAR at 1,4-BBFT/IL/GPE. A well-defined anodic peak potential for these analytes were observed. The LOD obtained was 8.1×10^{-6} mol L^{-1} for PAR and there was a high selectivity.[60] Shang Guan et al. used *1*-butyl-*3*-methylimidazolium hexafluorophosphate ($[C_4mim]^+[PF_6]^-$) as a binder for the preparation of a CPE and it was explored for the PAR detection. As compared to the non-conductive organic binders, $[C_4mim]^+[PF_6]^-$ provided an improved reversibility and better current response for the electrochemical reaction of PAR. The detection limit for the determination of PAR at the RTIL modified CPE was found to be 0.3 μM (S/N = 3) and the average % of recovery for PAR was 98.5% in tablet samples and 99.3% in

Table 1. Determination of PAR using RTIL modified CCE and GCEs.

Material	Electrode	Method	pH	Linear range, μM	Detection limit, μM	**Sensitivity μA μM^{-1}**	RSD (%)	Sample analysis	Ref
$[C_2mim]^+[BF_4]^-$, MWCNTs & CHIT	GCE	DPV CA	7.0	1–400 3–650	0.240–0.555	–	0.96	Human serum and urine	[50]
$[C_2mim]^+[BF_4]^-$, SWCNT & CHIT	GCE	DPV CA	7.0	0.5–400	0.06–0.54	0.847 – 0.7108	1.8	Human urine and blood	[51]
$[C_2mim]^+[BF_4]^-$, NH_2-Fe_3O_4NP and MWCNT	GCE	DPV	9.5	0.01–0.7	0.04	–	1.2	Pharmaceutical samples	[52]
f-MWCNT & $[C_4mim]^+[PF_6]^-$	GCE	CV	5.0	–	–	–	–	–	[53]
f-MWCNT & $[C_4mim]^+[PF_6]^-$	GCE	SWV	5.0	0.3 to 3.0	0.0673.	–	2.56	Tablet	[54]
Nano-TiO_2 & $[C_4mim]^+[BF_4]^-$	GCE	SWV	5.9	0.05–50.0	0.01	–	4.8	Human urine	[55]
$[AlC_2im]^+[BF_4]^-$	CCE	DPV	7.0	0.1–20	0.063	–	1.4	Human urine, serum and blood	[56]
$[VC_2im]^+[BF_4]^-$ & MCNs/CS	GCE	DPV	5.0	1–300	0.164	–	3.49	Paracetamol tablets	[57]

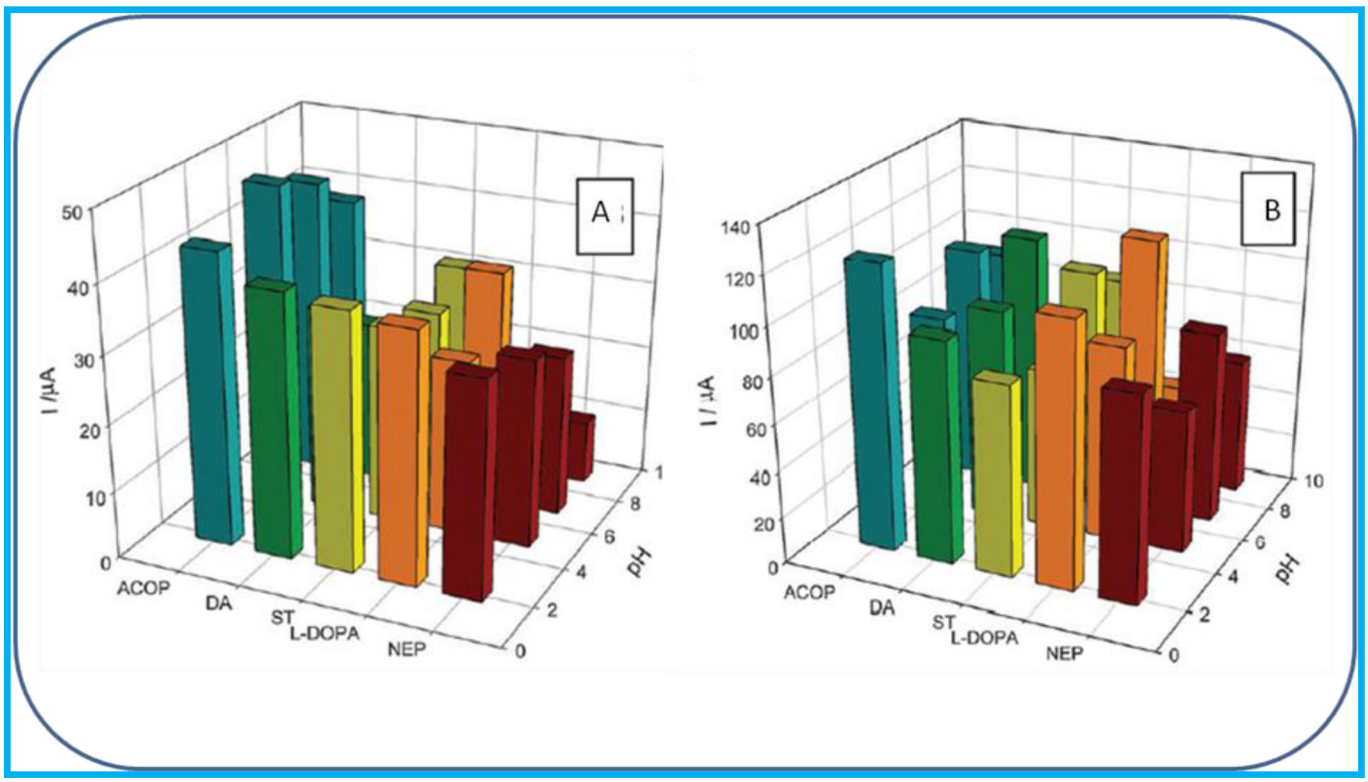

Figure 5. Current response of neurotransmitters and PAR at various pH conditions, (A) at the bare CPE, (B) NiONps/ILMCPE … SDS.[63]

urine samples. The number of electrons and protons involved in the PAR oxidation at the $[C_4mim]^+[PF_6]^-$ modified electrode was found to be two.[61]

Zinc oxide NPs and 1-methyl-3-butylimidazolium chloride ($[C_4mim]^+[Cl]^-$)-based CPE (IL/ZnO/NPs/CPE) was proposed by Raoof et al.[62] for the determination of PAR in drug, urine and serum samples. Electrochemical behavior of PAR at the modified electrode was investigated using CV, CA, and electrochemical impedance spectroscopy (EIS) techniques. The oxidation of PAR at the $[C_4mim]^+[Cl]^-$ modified electrode was found to be pH dependent and number of electrons and protons involved were equal to two. Detection limit of 0.07 μmol L^{-1} for the detection of PAR with superior stability and reproducibility was observed at IL/ZnO/NPs/CPE. The sensitivity of modified electrode toward the oxidation of PAR in the presence of dihydronicotinamide adenine dinucleotide (NADH) was 0.115 μA μM^{-1}. Similarly, Atta et al. examined electrochemical sensor, NiONps/ILMCPE … SDS-based on RTILs (*1*-butyl-*1*-methyl piperidinium hexafluorophosphate ($[C_4mpip]^+[PF_6]^-$)/*1*-hexyl-*3*-methyl imidazolium tetrafluoroborate ($[C_6mim]^+[BF_4]^-$), NiONPs, and sodium dodecyl sulfate for the simultaneous determination of PAR and neurotransmitters (dopamine (DA), norepinephrine (NEP), levodopa (L-DOPA), serotonin (ST)). A graph for current response of neurotransmitters and PAR as a function of pH values, at the bare CPE and NiONps/ILMCPE … SDS was reported and it is shown in Figure 5.

Table 2. Determination of PAR using various RTIL modified CPEs.

Material	Method	pH	Linear range, μM	Detection limit, μM	Sensitivity $\mu A\ \mu M^{-1}$	RSD (%)	Sample analysis	Ref
CdO NPs and $[C_4C_4im]^+[Br]^-$	SWV	8.0	0.1 – 600	0.07	0.151	1.6	Pharmaceutical and human urine samples	[58]
$[C_8py]^+[PF_6]^+$	DPV	7.0	2 – 2200	0.5	–	1.97	Tablets	[59]
1,4-BBFT and $[C_6mim]^+[PF_6]^-$	SWV	7.0	10 – 1000	8.1	0.731	–	Pharmaceutical, tea, blood and urine samples	[60]
$[C_4mim]^+[PF_6]^-$	DPV	4.6	2 – 2000	0.3	–	2.1	Tablets	[61]
ZnO-NPs and $[C_4mim]^+[Cl]^-$	SWV	7.0	0.1 – 550	0.07	0.115	1.6	Human urine, serum and pharmaceutical samples	[62]
$[C_4mpip]^+[PF_6]^-$ or $[C_6mim]^+[BF_4]^-$ and NiO-NPs and SDS	DPV	7.4	4.44 – 33.3	0.00861	–	–	Tablets and human urine	[63]

The limit of detection for PAR at the modified electrode was found to be 8.61 nM which is significantly low as compared to the LODs reported for the other RTIL-based sensors discussed here. Commercial tablets and urine samples were examined using the modified electrode and the recovery % was in the range of 100.24 – 101.78 and 99.6 – 102.5 in drug and urine samples, respectively. LOD value of 1.11×10^{-8} M and LOQ value of 3.67×10^{-8} M for small dynamic ranges were reported. For the large dynamic ranges, LOQ and LOD values were 6.72×10^{-7} M and 2.02×10^{-7} M, respectively. The LOQ values represent the lowest concentration of PAR which can be measured with acceptable level of repeatability, precision and trueness. LOQ values reported for PAR determination at RTIL-based electrodes are 3.3 times higher than LOD values which can decide the presence of analyte.[63] Some of the data obtained for the above discussed RTIL-based CPE systems for the detection of PAR are summarized in Table 2.

Conclusion

In this article, electrochemical detection of paracetamol (PAR) using RTIL-based electrochemical sensors has been discussed. Electrochemical techniques such as DPV, SWV, and CV were used in these studies. Several types of RTILs-based GCEs, CCE, and CPEs were explored for the electrochemical detection of PAR. GCEs modified with RTILs and various types of materials such as MWCNTs, SWCNTs, chitosan, amino group functionalized magnetite NPs, mesoporous carbon nanospheres and TiO_2 NPs have been examined. Similarly, CCE modified with $[Almim]^+[BF_4]^-$ IL and also CPEs based on RTILs together with different types of materials such as CdO, NiO, and ZnO NPs, 1,4-BBFT and sodium dodecyl sulfate were also reported in PAR detection.

Several advantages such as easy fabrication procedure, reproducibility, low LOD, free from interferences and wide dynamic range, etc., were observed in the most of the RTIL-based electrochemical sensors discussed in this article as compared to the bare electrodes. The LOD was found be generally less at RTIL-based GCEs as compared to CPEs modified with RTILs and the sensor based on nano-TiO_2/$[C_4mim]^+[BF_4]^-$/GCE has shown a very good LOD of 0.01 μM. In the case of CPEs, NiONps/ILMCPE … SDS resulted excellent LOD of 0.00867 μM. Determination of PAR was carried out at neutral pH condition mostly and there were no interferences in obtaining the data in most of the studies. Relative standard deviation (RSD) values of 0.96 to 4.8% for RTIL modified GCEs, 1.4% for RTIL modified CCEs and 1.6 to 2.1% for RTIL modified CPEs revealed that RTIL-based sensors have good reproducibility.

Despite of many advantages, there are few drawbacks in some of these RTILs-based electrochemical sensors reported for PAR detection. That is, only a few of RTIL-based sensors were examined for a wide range of PAR concentrations. For example, $[C_8py]^+[PF_6]^+$/CPE, 1,4-BBFT/IL/GPE, and $[C_4mim]^+[PF_6]^-$/CPE were explored for a wide range of PAR concentrations 2 – 2200 μM, 10 – 1000 μM, and 2 – 2000 μM, respectively. Detection limits were in the range of 0.00861 – 0. 555 μM at RTIL modified electrodes and in some systems, it needs to be improved.

Moreover, reports on sensitivity of RTIL-based PAR sensors is limited and simultaneous determination of PAR with many types of structural analogues need to be focused. In order to know about sensitivity and selectivity of a proposed sensor toward paracetamol (PAR), it is essential to study in the presence of structural analogues which may interfere with the results obtained for PAR. Some of the RTIL-based sensors have been explored for the simultaneous determination of PAR with some analogues such as ascorbic acid, uric acid, mefenamic acid, adrenalin, dopamine, hydroquinone, catechol, morphine, p-aminophenol, isoproterenol, theophylline, and adenine dinucleotide (NADH). But determination of PAR in the presence of some more compounds such as methocarbamol, chlorpheniramine, ibuprofen and paracetamol-glucuronide, etc., are yet to be studied.

Actually, in these studies, imidazolium, pyridinium, and piperidinium cations-based RTILs were explored and among them imidazolium cation-based RTILs have been used mostly and hence various other types of suitable cations have to be explored for the electrochemical detection of PAR. The development of biocompatible ILs (Bio-ILs)-based electrochemical sensors is being a focus of intensive research in the recent past for many applications in biomedical field as well as in electrochemistry as sensors due to their biodegradable and non-cytotoxic properties. In order to avoid the environmental impact, biocompatible sensors are generally proposed. Hence in this direction, research works need be carried out to achieve the biocompatible RTIL-based electrochemical sensors for the detection of PAR present in the pharmaceutical and biological samples.

In addition, there is a growing research interest on poly(-ionic liquid)s (PILs)-based materials due to combined advantages of both ionic liquid and polymer network which offer interesting properties such as enhanced stability, flexibility, improved control over its meso- to nano-structure, improved process ability, etc., and also they are able to interact with other molecules via ion exchange, hydrophobic and hydrophilic interactions, hydrogen bonds, p–p stacking and electrostatic interactions. But only one PIL-based electrochemical system have been reported for the determination of PAR and hence studies on various other PILs-based sensors in PAR detection need to be considered in detail. Very few studies on determination of PAR using of RTIL-based electrochemical sensors have been reported in literature. Some more development and commercialization of RTIL-based electrochemical sensor systems for PAR detection have also to be focused for different types of real samples.

Funding

SCBG was supported by a special grant (9001-00596) from Universiti Malaysia Perlis.

ORCID

S. Meenakshi http://orcid.org/0000-0002-2247-3760

References

[1] Ashoka, N.; Swamy, B. K.; Jayadevappa, H.; Sharma, S. Simultaneous Electroanalysis of Dopamine, Paracetamol and Folic Acid Using TiO2-WO3 Nanoparticle Modified Carbon Paste Electrode. *J. Electroanal. Chem.* **2020**, *859*, 113819. DOI: 10.1016/j.jelechem.2020.113819.

[2] Doğan, B.; Elik, A.; Altunay, N. Determination of Paracetamol in Synthetic Urea and Pharmaceutical Samples by Shaker-Assisted Deep Eutectic Solvent Microextraction and Spectrophotometry. *Microchem. J.* **2020**, *154*, 104645. DOI: 10.1016/j.microc.2020.104645.

[3] Kushwaha, C. S.; Shukla, S. K. Electrochemical Sensing of Paracetamol Using Iron Oxide Encapsulated in Chitosan-Grafted-Polyaniline. *ACS Appl. Polym. Mater.* **2020**, *2*, 2252–2259. DOI: 10.1021/acsapm.0c00239.

[4] Palanna, M.; Mohammed, I.; Aralekallu, S.; Nemakal, M.; Sannegowda, L. K. Simultaneous Detection of Paracetamol and 4-Aminophenol at Nanomolar Levels Using Biocompatible Cysteine-Substituted Phthalocyanine. *New J. Chem.* **2020**, *44*, 1294–1306. DOI: 10.1039/C9NJ05252F.

[5] Abbasi, S.; Haeri, S. A.; Sajjadifar, S. Bio-Dispersive Liquid Liquid Microextraction Based on Nano Rhamnolipid Aggregates Combined with Molecularly Imprinted-Solid Phase Extraction for Selective Determination of Paracetamol in Human Urine Samples Followed by HPLC. *Microchem. J.* **2019**, *146*, 106–114. DOI: 10.1016/j.microc.2018.12.065.

[6] Wang, J.; Zhang, H.; Zhao, J.; Zhang, R.; Zhao, N.; Ren, H.; Li, Y. Simultaneous Determination of Paracetamol and p-Aminophenol Using Glassy Carbon Electrode Modified with Nitrogen- And Sulfur-Co-Doped Carbon Dots. *Mikrochim. Acta* **2019**, *186*, 733. DOI: 10.1007/s00604-019-3870-2.

[7] Katseli, V.; Economou, A.; Kokkinos, C. A Novel All-3D-Printed Cell-on-a-Chip Device as a Useful Electroanalytical Tool: Application to the Simultaneous Voltammetric Determination of Caffeine and Paracetamol. *Talanta* **2020**, *208*, 120388. DOI: 10.1016/j.talanta.2019.120388.

[8] Kumar, K. G.; Letha, R. Determination of Paracetamol in Pure Form and in Dosage Forms Using N, N-Dibromo Dimethylhydantoin. *J. Pharm. Biomed. Anal.* **1997**, *15*, 1725–1728. DOI: 10.1016/S0731-7085(96)01976-0.

[9] Mohamed, D.; Hegazy, M. A.; Elshahed, M. S.; Toubar, S. S.; Helmy, M. I. Liquid Chromatography-Tandem MS/MS Method for Simultaneous Quantification of Paracetamol, Chlorzoxazone and Aceclofenac in Human Plasma: An Application to a Clinical Pharmacokinetic Study. *Biomed. Chromatogr.* **2018**, *32*, e4232. DOI: 10.1002/bmc.4232.

[10] Nugrahani, I.; Manosa, E. Y.; Chintya, L. FTIR-Derivative as a Green Method for Simultaneous Content Determination of Caffeine, Paracetamol, and Acetosal in a Tablet Compared to HPLC. *Vib. Spectrosc.* **2019**, *104*, 102941. DOI: 10.1016/j.vibspec.2019.102941.

[11] Borahan, T.; Unutkan, T.; Şahin, A.; Bakırdere, S. A Rapid and Sensitive Reversed Phase-HPLC Method for Simultaneous Determination of Ibuprofen and Paracetamol in Drug Samples and Their Behaviors in Simulated Gastric Conditions. *J. Sep. Sci.* **2019**, *42*, 678–683. DOI: 10.1002/jssc.201801002.

[12] Glavanović, S.; Glavanović, M.; Tomišić, V. Simultaneous Quantitative Determination of Paracetamol and Tramadol in Tablet Formulation Using UV Spectrophotometry and Chemometric Methods. *Spectrochim. Acta A Mol. Biomol. Spectrosc.* **2016**, *157*, 258–264. DOI: 10.1016/j.saa.2015.12.020.

[13] Montaseri, H.; Forbes, P. B. Analytical Techniques for the Determination of Acetaminophen: A Review. *TrAC, Trends Anal. Chem.* **2018**, *108*, 122–134. DOI: 10.1016/j.trac.2018.08.023.

[14] Lecoeur, M.; Rabenirina, G.; Schifano, N.; Odou, P.; Ethgen, S.; Lebuffe, G.; Foulon, C. Determination of Acetaminophen and Its Main Metabolites in Urine by Capillary Electrophoresis Hyphenated to Mass Spectrometry. *Talanta* **2019**, *205*, 120108. DOI: 10.1016/j.talanta.2019.07.003.

[15] Fu, L.; Lai, G.; Yu, A. Preparation of *β*-Cyclodextrin Functionalized Reduced Graphene Oxide: Application for Electrochemical Determination of Paracetamol. *RSC Adv.* **2015**, *5*, 76973–76978. DOI: 10.1039/C5RA12520K.

[16] Li, Z.-Y.; Gao, D.-Y.; Wu, Z.-Y.; Zhao, S. Simultaneous Electrochemical Detection of Levodapa, Paracetamol and l-Tyrosine Based on Multi-Walled Carbon Nanotubes. *RSC Adv.* **2020**, *10*, 14218–14224. DOI: 10.1039/D0RA00290A.

[17] Kumar, Y.; Pramanik, P.; Das, D. K. Electrochemical Detection of Paracetamol and Dopamine Molecules Using Nano-Particles of Cobalt Ferrite and Manganese Ferrite Modified with Graphite. *Heliyon* **2019**, *5*, e02031. DOI: 10.1016/j.heliyon.2019.e02031.

[18] Pereira, A. C. S.; Nunes da Silva, D.; Porto, L. S.; Pereira, A. C. Development of Electrochemical Biosensor Based on Nanostructured Carbon Materials for Paracetamol Determination. *Electroanalysis* **2020**, *32*, 1905–1913. DOI: 10.1002/elan.201900117.

[19] Shetti, N. P.; Malode, S. J.; Nayak, D. S.; Reddy, K. R.; Reddy, C. V.; Ravindranadh, K. Silica Gel-Modified Electrode as an Electrochemical Sensor for the Detection of Acetaminophen. *Microchem. J.* **2019**, *150*, 104206. DOI: 10.1016/j.microc.2019.104206.

[20] Camargo, J. R.; Andreotti, I. A.; Kalinke, C.; Henrique, J. M.; Bonacin, J. A.; Janegitz, B. C. Waterproof Paper as a New Substrate to Construct a Disposable Sensor for the Electrochemical Determination of Paracetamol and Melatonin. *Talanta* **2020**, *208*, 120458. DOI: 10.1016/j.talanta.2019.120458.

[21] Liang, W.; Liu, L.; Li, Y.; Ren, H.; Zhu, T.; Xu, Y.; Ye, B.-C. Nitrogen-Rich Porous Carbon Modified Electrochemical Sensor for the Detection of Acetaminophen. *J. Electroanal. Chem.* **2019**, *855*, 113496. DOI: 10.1016/j.jelechem.2019.113496.

[22] Iranmanesh, T.; Foroughi, M. M.; Jahani, S.; Zandi, M. S.; Nadiki, H. H. Green and Facile Microwave Solvent-Free

Synthesis of CeO2 Nanoparticle-Decorated CNTs as a Quadruplet Electrochemical Platform for Ultrasensitive and Simultaneous Detection of Ascorbic Acid, Dopamine, Uric Acid and Acetaminophen. *Talanta* **2020**, *207*, 120318. DOI: 10.1016/j.talanta.2019.120318.

[23] Chipeture, A. T.; Apath, D.; Moyo, M.; Shumba, M. Multiwalled Carbon Nanotubes Decorated with Bismuth (III) Oxide for Electrochemical Detection of an Antipyretic and Analgesic Drug Paracetamol in Biological Samples. *J. Anal. Sci. Technol.* **2019**, *10*, 22. DOI: 10.1186/s40543-019-0181-5.

[24] Kumar, M. A.; Lakshminarayanan, V.; Ramamurthy, S. S. Platinum Nanoparticles–Decorated Graphene-Modified Glassy Carbon Electrode toward the Electrochemical Determination of Ascorbic Acid, Dopamine, and Paracetamol. *CR. Chim.* **2019**, *22*, 58–72. DOI: 10.1016/j.crci.2018.09.015.

[25] Foroughi, M. M.; Jahani, S.; Nadiki, H. H. Lanthanum Doped Fern-like CuO Nanoleaves/MWCNTs Modified Glassy Carbon Electrode for Simultaneous Determination of Tramadol and Acetaminophen. *Sensors Actuators B: Chem.* **2019**, *285*, 562–570. DOI: 10.1016/j.snb.2019.01.069.

[26] Setoudeh, N.; Jahani, S.; Kazemipour, M.; Foroughi, M. M.; Nadiki, H. H. Zeolitic Imidazolate Frameworks and Cobalt-Tannic Acid Nanocomposite Modified Carbon Paste Electrode for Simultaneous Determination of Dopamine, Uric Acid, Acetaminophen and Tryptophan: Investigation of Kinetic Parameters of Surface Electrode and Its Analytical Performance. *J. Electroanal. Chem.* **2020**, *863*, 114045. DOI: 10.1016/j.jelechem.2020.114045.

[27] Martínez-Sánchez, C.; Montiel-González, F.; Rodríguez-González, V. Electrochemical Sensing of Acetaminophen Using a Practical Carbon Paste Electrode Modified with a Graphene oxide-Y2O3 Nanocomposite. *J. Taiwan Inst. Chem. Eng.* **2019**, *96*, 382–389. DOI: 10.1016/j.jtice.2018.12.004.

[28] Soltani, N.; Tavakkoli, N.; Shahdost-Fard, F.; Salavati, H.; Abdoli, F. A Carbon Paste Electrode Modified with Al2O3-Supported Palladium Nanoparticles for Simultaneous Voltammetric Determination of Melatonin, Dopamine, and Acetaminophen. *Mikrochim. Acta* **2019**, *186*, 540. DOI: 10.1007/s00604-019-3541-3.

[29] Kuskur, C. M.; Swamy, B. K.; Jayadevappa, H. Poly (Naphthol Green B) Modified Carbon Paste Electrode for the Analysis of Paracetamol and Norepinephrine. *Ionics* **2019**, *25*, 1845–1855. DOI: 10.1007/s11581-018-2606-3.

[30] Saciloto, T. R.; Cervini, P.; Gomes Cavalheiro, E. T. New Screen Printed Electrode Based on Graphite and Polyurethane Composite for the Determination of Acetaminophen. *Anal. Lett.* **2013**, *46*, 312–322. DOI: 10.1080/00032719.2012.718829.

[31] Özcan, A.; Sahin, Y. A Novel Approach for the Determination of Paracetamol Based on the Reduction of N-Acetyl-p-Benzoquinoneimine Formed on the Electrochemically Treated Pencil Graphite Electrode. *Anal. Chim. Acta* **2011**, *685*, 9–14. DOI: 10.1016/j.aca.2010.11.004.

[32] Kachoosangi, R. T.; Wildgoose, G. G.; Compton, R. G. Sensitive Adsorptive Stripping Voltammetric Determination of Paracetamol at Multiwalled Carbon Nanotube Modified Basal Plane Pyrolytic Graphite Electrode. *Anal. Chim. Acta* **2008**, *618*, 54–60. DOI: 10.1016/j.aca.2008.04.053.

[33] Pedrosa, V. A.; Lowinsohn, D.; Bertotti, M. FIA Determination of Paracetamol in Pharmaceutical Drugs by Using Gold Electrodes Modified with a 3-Mercaptopropionic Acid Monolayer. *Electroanalysis* **2006**, *18*, 931–934. DOI: 10.1002/elan.200503483.

[34] Menon, S.; Jesny, S.; Kumar, K. G. A Voltammetric Sensor for Acetaminophen Based on Electropolymerized-Molecularly Imprinted Poly(o-aminophenol) Modified Gold Electrode. *Talanta* **2018**, *179*, 668–675. DOI: 10.1016/j.talanta.2017.11.074.

[35] Sadok, I.; Tyszczuk-Rotko, K.; Nosal-Wiercińska, A. Bismuth Particles Nafion Covered Boron-Doped Diamond Electrode for Simultaneous and Individual Voltammetric Assays of Paracetamol and Caffeine. *Sensors Actuators B: Chem.* **2016**, *235*, 263–272. DOI: 10.1016/j.snb.2016.05.087.

[36] Tyszczuk-Rotko, K.; Bęczkowska, I.; Wójciak-Kosior, M.; Sowa, I. Simultaneous Voltammetric Determination of Paracetamol and Ascorbic Acid Using a Boron-Doped Diamond Electrode Modified with Nafion and Lead Films. *Talanta* **2014**, *129*, 384–391. DOI: 10.1016/j.talanta.2014.06.023.

[37] Lourenção, B. C.; Medeiros, R. A.; Rocha-Filho, R. C.; Mazo, L. H.; Fatibello-Filho, O. Simultaneous Voltammetric Determination of Paracetamol and Caffeine in Pharmaceutical Formulations Using a Boron-Doped Diamond Electrode. *Talanta* **2009**, *78*, 748–752. DOI: 10.1016/j.talanta.2008.12.040.

[38] Lei, Z.; Chen, B.; Koo, Y.-M.; MacFarlane, D. R. Introduction: Ionic Liquids. *Chem. Rev.* **2017**, *117*, 6633–6635. DOI: 10.1021/acs.chemrev.7b00246.

[39] Javed, F.; Ullah, F.; Zakaria, M. R.; Akil, H. M. An Approach to Classification and Hi-Tech Applications of Room-Temperature Ionic Liquids (RTILs): A Review. *J. Mol. Liq.* **2018**, *271*, 403–420. DOI: 10.1016/j.molliq.2018.09.005.

[40] Vekariya, R. L. A Review of Ionic Liquids: Applications towards Catalytic Organic Transformations. *J. Mol. Liq.* **2017**, *227*, 44–60. DOI: 10.1016/j.molliq.2016.11.123.

[41] Vázquez, M. P.; Vázquez, P. P.; Galera, M. M.; García, M. G.; Uclés, A. Ultrasound-Assisted Ionic Liquid Dispersive Liquid-Liquid Microextraction Coupled with Liquid Chromatography-Quadrupole-Linear Ion Trap-Mass Spectrometry for Simultaneous Analysis of Pharmaceuticals in Wastewaters. *J. Chromatogr. A* **2013**, *1291*, 19–26. DOI: 10.1016/j.chroma.2013.03.066.

[42] Yu, H.; Merib, J.; Anderson, J. L. Faster Dispersive Liquid-Liquid Microextraction Methods Using Magnetic Ionic Liquids as Solvents. *J. Chromatogr. A* **2016**, *1463*, 11–19. DOI: 10.1016/j.chroma.2016.08.007.

[43] Silvester, D. S. Recent Advances in the Use of Ionic Liquids for Electrochemical Sensing. *Analyst* **2011**, *136*, 4871–4882. DOI: 10.1039/c1an15699c.

[44] Wang, X.; Hao, J. Recent Advances in Ionic Liquid-Based Electrochemical Biosensors. *Sci. Bull.* **2016**, *61*, 1281–1295. DOI: 10.1007/s11434-016-1151-6.

[45] Wei, D.; Ivaska, A. Applications of Ionic Liquids in Electrochemical Sensors. *Anal. Chim. Acta* **2008**, *607*, 126–135. DOI: 10.1016/j.aca.2007.12.011.

[46] Abo-Hamad, A.; AlSaadi, M. A.; Hayyan, M.; Juneidi, I.; Hashim, M. A. Ionic Liquid-Carbon Nanomaterial Hybrids for Electrochemical Sensor Applications: A Review. *Electrochim. Acta* **2016**, *193*, 321–343. DOI: 10.1016/j.electacta.2016.02.044.

[47] Shiddiky, M. J.; Torriero, A. A. Application of Ionic Liquids in Electrochemical Sensing Systems. *Biosens. Bioelectron.* **2011**, *26*, 1775–1787. DOI: 10.1016/j.bios.2010.08.064.

[48] Van Benschoten, J. J.; Lewis, J. Y.; Heineman, W. R.; Roston, D. A.; Kissinger, P. T. Cyclic Voltammetry Experiment. *J. Chem. Educ.* **1983**, *60*, 772. DOI: 10.1021/ed060p772.

[49] Nematollahi, D.; Shayani-Jam, H.; Alimoradi, M.; Niroomand, S. Electrochemical Oxidation of Acetaminophen in Aqueous Solutions: Kinetic Evaluation of Hydrolysis, Hydroxylation and Dimerization Processes. *Electrochim. Acta* **2009**, *54*, 7407–7415. DOI: 10.1016/j.electacta.2009.07.077.

[50] Kianipour, S.; Asghari, A. Room Temperature Ionic Liquid/Multiwalled Carbon Nanotube/Chitosan-Modified Glassy Carbon Electrode as a Sensor for Simultaneous Determination of Ascorbic Acid, Uric Acid, Acetaminophen, and Mefenamic Acid. *IEEE Sensors J.* **2013**, *13*, 2690–2698. DOI: 10.1109/JSEN.2013.2259588.

[51] Babaei, A.; Babazadeh, M.; Afrasiabi, M. A Sensitive Simultaneous Determination of Adrenalin and Paracetamol on a Glassy Carbon Electrode Coated with a Film of Chitosan/Room Temperature Ionic Liquid/Single-Walled Carbon Nanotubes Nanocomposite. *Chin. J. Chem.* **2011**, *29*, 2157–2164. DOI: 10.1002/cjoc.201180374.

[52] Chokkareddy, R.; Thondavada, N.; Bhajanthri, N. K.; Redhi, G. G. An Amino Functionalized Magnetite Nanoparticle and Ionic Liquid Based Electrochemical Sensor for the Detection of Acetaminophen. *Anal. Methods* **2019**, *11*, 6204–6212. DOI: 10.1039/C9AY01743G.

[53] Salvador, M. A.; Sousa, C. P.; Maciel, C. D.; Gomes, R. N.; Morais, S.; de Lima-Neto, P.; Coutinho-Neto, M. D.; Correia, A. N.; Homem-de-Mello, P. Experimental and Computational Studies of the Interactions between Carbon Nanotubes and Ionic Liquids Used for Detection of Acetaminophen. *Sensors Actuators B: Chem.* **2018**, *277*, 640–646. DOI: 10.1016/j.snb.2018.09.017.

[54] Gomes, R. N.; Sousa, C. P.; Casciano, P. N.; Ribeiro, F. W. P.; Morais, S.; de Lima-Neto, P.; Correia, A. N. Dispersion of Multi-Walled Carbon Nanotubes in [BMIM] PF6 for Electrochemical Sensing of Acetaminophen. *Mater. Sci. Eng.: C* **2018**, *88*, 148–156. DOI: 10.1016/j.msec.2018.03.016.

[55] Wang, B.; Li, Y.; Qin, X.; Zhan, G.; Ma, M.; Li, C. Electrochemical Fabrication of TiO2 Nanoparticles/[BMIM] BF4 Ionic Liquid Hybrid Film Electrode and Its Application in Determination of p-Acetaminophen. *Mater. Sci. Eng.: C* **2012**, *32*, 2280–2285. DOI: 10.1016/j.msec.2012.06.015.

[56] Majidi, M. R.; Pournaghi-Azar, M. H.; Baj, R. F. B. Graphene Nanoplatelets like Structures Formed on Ionic Liquid Modified Carbon-Ceramic Electrode: As a Sensing Platform for Simultaneous Determination of Dopamine and Acetaminophen. *J. Mol. Liq.* **2016**, *220*, 778–787. DOI: 10.1016/j.molliq.2016.05.034.

[57] Song, Y.; Zhang, Y.; Li, J.; Tan, C.; Li, Y. Preparation of Poly Ionic Liquid-Mesoporous Carbon Nanospheres and Its Application in Simultaneous Determination of Hydroquinone and Catechol, and Detection of Paracetamol. *J. Electroanal. Chem.* **2020**, *865*, 114157. DOI: 10.1016/j.jelechem.2020.114157.

[58] Cheraghi, S.; Taher, M. A.; Maleh, H. K. A Novel Strategy for Determination of Paracetamol in the Presence of Morphine Using a Carbon Paste Electrode Modified with CdO Nanoparticles and Ionic Liquids. *Electroanalysis* **2016**, *28*, 366–371. DOI: 10.1002/elan.201500357.

[59] Safavi, A.; Maleki, N.; Moradlou, O. A Selective and Sensitive Method for Simultaneous Determination of Traces of Paracetamol and p-Aminophenol in Pharmaceuticals Using Carbon Ionic Liquid Electrode. *Electroanalysis* **2008**, *20*, 2158–2162. DOI: 10.1002/elan.200804292.

[60] Tajik, S.; Taher, M. A.; Beitollahi, H. Application of a New Ferrocene-Derivative Modified-Graphene Paste Electrode for Simultaneous Determination of Isoproterenol, Acetaminophen and Theophylline. *Sensors Actuators B: Chem.* **2014**, *197*, 228–236. DOI: 10.1016/j.snb.2014.02.096.

[61] ShangGuan, X.; Zhang, H.; Zheng, J. Electrochemical Behavior and Differential Pulse Voltammetric Determination of Paracetamol at a Carbon Ionic Liquid Electrode. *Anal. Bioanal. Chem.* **2008**, *391*, 1049–1055. DOI: 10.1007/s00216-008-2096-7.

[62] Raoof, J. B.; Teymoori, N.; Khalilzadeh, M. A.; Ojani, R. Synergistic Signal Amplification Based on Ionic liquid-ZnO Nanoparticle Carbon Paste Electrode for Sensitive Voltammetric Determination of Acetaminophen in the Presence of NADH. *J. Mol. Liq.* **2016**, *219*, 15–20. DOI: 10.1016/j.molliq.2016.02.075.

[63] Atta, N. F.; Ibrahim, A. H.; Galal, A. Nickel Oxide Nanoparticles/Ionic Liquid Crystal Modified Carbon Composite Electrode for Determination of Neurotransmitters and Paracetamol. *New J. Chem.* **2016**, *40*, 662–673. DOI: 10.1039/C5NJ01804H.