

A critical review on electro-analysis of clinically important drug Paracetamol

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Abstract

Paracetamol have been extensively used in both the human and veterinary clinics due to its antipyretic and analgesic properties. It is considered as a well-tolerated drug in patients suffering from aspirin intolerance, ulcers, or difficulty in blood clotting. It is very important to monitor the doses of paracetamol in the patient's body under examination since the overdose results in accumulation of toxic metabolites which may cause severe adverse effects. Due to a wide use of paracetamol and the adverse effects of its over dose, it is always being an interesting issue to develop suitable techniques for its quantitative as well as qualitative analysis. The development of simple, convenient, highly sensitive, versatile, fast and economic techniques is very necessary to control the over uses of this drug causing many side effects. Various techniques used for the determination and detection of paracetamol have been reviewed in this paper predominantly focusing on electro-analytical methods.

Keywords: Paracetamol, drug, electro-analysis, electro-catalytic oxidation, sensor.

1 Introduction

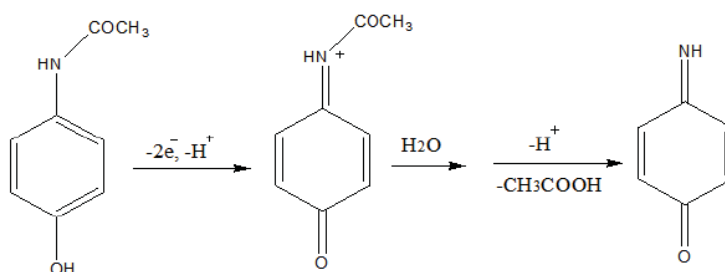
Paracetamol is an acylated aromatic amide known by several names viz. acetaminophen, 4-acetamidophenol, *N*-acetyl-*p*-aminophenol, 4'-hydroxyacetanilide and tylenol. Paracetamol is a very commonly used antipyretic and analgesic drug. It is commonly used for relieving headaches and other minor pains. It is a major ingredient in numerous cold and flu remedies. In combination with opioid analgesics, paracetamol can also be used in the management of more severe pain such as post-surgical pain. The over dose of paracetamol causes highly objectionable side effects such as liver disorder, skin rashes and inflammation of the pancreas. These are some serious side effects of paracetamol overusage which can sometimes prove to be irreversible [1]. Sometimes its overdose may cause fatal hepatotoxicity and nephrotoxicity [2-4]. Therefore, detection of paracetamol is an important issue.

Due to a wide use of paracetamol and the adverse effects of its over dose, it always has been an interesting issue to develop suitable techniques for its quantitative as well as qualitative analysis. The development of simple, convenient, highly sensitive, versatile, fast and economic techniques is very necessary to control the over uses of this drug causing many side effects. Many methods have been described for the determination of paracetamol such as spectrophotometry [5, 6], titrimetry [7, 8], HPLC [9], liquid chromatography [10, 11],

chemiluminescence [12, 13], spot test [14]. All of these methods were associated with one or the other drawback like tedious procedure, time consuming, high cost, excessive use of solvents etc. However, electroanalytical techniques have been found to be elegant, economic and highly sensitive techniques. Researchers are working for the identification of different electroanalytical methods for the detection of different drugs [15, 16]. Therefore, the electrochemical methods may be considered as the alternative methods to overcome the drawbacks of existing analytical methods which are time consuming and expensive.

2 Electro-analysis of paracetamol

Few electroanalytical methods have been identified by researchers for the determination of paracetamol. The mechanism of electrochemical oxidation of paracetamol has been reported by Shang Guan and Zhang [17] which is shown in Scheme 1. The electroanalytical methods include amperometry, differential pulse voltammetry, square wave voltammetry and cyclic voltammetry. These methods have been critically reviewed in this paper.



Scheme 1: Electrochemical oxidation of paracetamol [17]

2.1 Amperometry

In this electroanalytical method, a constant reducing or oxidizing potential is applied to an indicator (working electrode) and the resulting steady-state current is measured. Commonly, the magnitude of the measured current depends on the concentration of the reduced or oxidized substance, and hence this method can be used for detection of electroactive substances in the solution. It has been applied by few researchers for determining paracetamol in spiked/real samples. Zen and Ting [18] demonstrated the Nafion/ruthenium oxide pyrochlore chemical modified electrode applied for the simultaneous detection of caffeine and paracetamol. A biosensor based on vaseline/graphite modified with avocado tissue (*Persea americana*) as the source of *polyphenol oxidase* has been developed and used for the chronoamperometric determination of paracetamol in pharmaceutical formulations [19]. This enzyme catalysed the oxidation of paracetamol to *N*-acetyl-*p*-benzoquinoneimine whose electrochemical reduction back to paracetamol was found to take place at a certain potential. Kubota and co-workers have studied the use of EDTA in the medium to avoid the passivation of solid electrode during electrochemical analysis of paracetamol [20].

Cobalt hexacyanoferrate modified wax composite electrode has been reported as an excellent amperometric sensor for the determination of paracetamol [1]. Reports show the synthesis of a novel thio-bridged cysteine ligand and its respective cobalt phthalocyanine complex (CoTATPAPc) for the modification of glassy carbon electrode. The modified electrode (CoTATPAPc/GCE) displayed remarkable electrocatalytic efficiency for the simultaneous sensing of paracetamol (PA) and 4-aminophenol (4-AP). The amperometric sensor successfully exhibited a linear response in the 20 to 360 nM concentration range, with LOD values of 4.2 and 4.1 nM for 4-AP and PA, respectively [21].

2.2 Differential pulse voltammetry

In differential pulse voltammetry, short pulses with limited amplitude are superimposed upon a staircase waveform. This method can provide improved selectivity for observing different redox processes than other voltammetric methods. A C₆₀-modified glassy carbon electrode has been introduced by Goyal and Singh [22] for the voltammetric determination of paracetamol which showed a high stability and sensitivity. A stable and high sensitive electrochemical sensor for paracetamol using carbon-coated nickel nanoparticles modified glassy carbon electrodes have been reported by Wang *et al.* [23]. A simple method determining paracetamol and few other drugs in model solutions and spiked human urine samples using a differential pulse voltammetry technique has also been reported [24]. All the investigated analytes from the biological endogenous components in human urine were successfully separated by this method. Differential pulse voltammetry technique has also been used by other researchers for the determination of paracetamol using different electrodes [25-27].

Carbon spherical shells (CSS) were synthesized with diameter 400 to 500 nm using 79% carbon and 21% oxygen, and their surface was functionalized with carbonyl and hydroxyl groups. These CSS were then used to modify glassy carbon electrode (GCE) forming GC/CSS modified electrode for sensitive detection of paracetamol in sweat, saliva and urine using differential pulse voltammetry. Sensitivity was found to increase with the decrease in size of CSS and it was also competitive with conventional HPLC method [28]. The electrochemical behavior of paracetamol has been studied at nanoclay modified graphite electrode in pH 5 phosphate buffer solution of 0.02 M ionic strength. The results showed a probable electrochemical mechanism to perform analytical applications using differential pulse voltammetric method [29]. Raymundo-Pereira *et al.* have proposed a simple and cost effective method for real-time monitoring of possible contamination in the water supply network using differential pulse voltammetry. They have used carbon screen-printed electrodes to determine simultaneously the presence of emerging pollutants hydroquinone (HQ), paracetamol (PARA) and estradiol (E2) in tap water, with detection limits of 185, 218 and 888 nmol L⁻¹, respectively, within a linear range between 0.5 and 10.0 μmol L⁻¹. These results were found to be competitive with high-performance liquid chromatography (HPLC), which is the gold-standard methodology for water analysis [30]. Some electrodes for efficient detection of paracetamol have been developed from nanoparticles of cobalt ferrite (CoFe₂O₄) and manganese ferrite (MnFe₂O₄). These particles were used for electrode modification with graphite for simultaneous detection of

paracetamol and dopamine and was found to be superior to reported literatures [31]. A differential pulse adsorptive stripping voltammetry method has been reported recently using a screen-printed sensor with a carbon/carbon nanofibers working electrode (SPCE/CNFs) for the direct determination of low concentrations of paracetamol in environmental water samples [32].

Wang and coworkers utilized DPV to detect paracetamol with its varying concentrations. This method showed high sensitivity and good resolution [33]. Under optimized experimental conditions, the anodic peak current was directly proportional to the concentration of paracetamol from 5 to 190 μM as shown in Fig. 1.

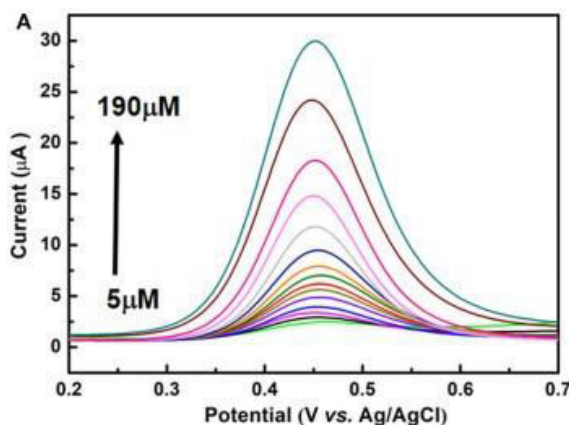


Fig. 1. Differential Pulse Voltammogram for different paracetamol concentrations [33].

2.3 Square wave voltammetry

Squarewave voltammetry is a form of linear potential sweep voltammetry that uses a combined square wave and staircase potential applied to a stationary electrode. A sensitive electroanalytical method using a multiwalled CNT modified basal plane pyrolytic graphite electrode for the determination of paracetamol has been used by Kachoosangi *et al.* [34]. Adsorptive stripping voltammetry technique was applied in this study and the limit of detection for paracetamol was found to be the lowest as compared with previous studies. A voltammetric method for the determination of paracetamol using square wave voltammetry has also been introduced using a boron-doped diamond electrode substrate in aqueous media [35]. A glassy carbon electrode modified with a composite of carbon nanotubes, samarium oxide (Sm_2O_3) and zirconium oxide (ZrO_2) nanoparticles ($\text{Sm}_2\text{O}_3@ZrO_2/\text{CNT}$) has also detected as an electrochemical platform that can be utilized for the determination of paracetamol. The proposed method used square wave voltammetry (SWV) technique that enabled a linear plot over a concentration range of 3.7×10^{-9} – 2.2×10^{-6} M with a detection limit of 3.4×10^{-10} M. This novel platform was successfully applied to pharmaceutical preparation and blood sample for the determination of paracetamol. Such a sensitive determination method for paracetamol is of great interest for the public health [36].

2.4 Cyclic voltammetry

Cyclic Voltammetry (CV) is a widely employed potentiodynamic electrochemical technique that can be used to gain qualitative and quantitative information about electrochemical reactions. During CV measurement, the potential of the working electrode is measured in system under study with respect to the reference electrode, and the potential is scanned back and forth between specific upper and lower limits. At the same time, the current passing between the working electrode and the counter electrode is recorded. Cyclic voltammetry has been used by several researchers for determination of paracetamol using modified electrodes [37, 38]. Zidan *et al.* used zinc oxide microparticles for the mechanical modification of glassy carbon electrode and found that the modified electrode acted as good electrochemical sensor for the detection of paracetamol [39]. Later, they used bismuth oxide nanoparticles modified glassy carbon electrode for the electrochemical detection of paracetamol [40]. The results of their study were found to be superior to those of HPLC methods. The electrocatalytic response for the oxidation of paracetamol on the copper poly-terthiophene carboxylic acid modified electrode has also reported [41].

Due to their excellent redox mediator properties, some metal hexacyanoferrates have been used for the development of electroanalytical methods for detection of paracetamol. The carbon paste electrode modified with copper hexacyanoferrate has been prepared and applied in the voltammetric determination of paracetamol in pharmaceutical preparations with good sensitivity and selectivity. The modified electrode was found to be simple and easy to prepare quickly [42]. In above cases, the cyclic voltammograms of the modified electrode showed the presence of a well-defined redox peaks. The voltammetric response was also found to be affected by using different ionic species and their different concentrations in the supporting electrolyte. Copper hexacyanoferrate-poly(3,4-ethylenedioxythiophene) film modified electrode has been used in determining paracetamol [43]. Electrochemically reduced graphene oxide/neodymium hexacyanoferrate film has been fabricated on the glassy carbon electrode and the fabricated film modified GCE was successfully employed for the detection of paracetamol drug [44]. Researchers have also used 1-ethyl-3-methylimidazolium tetrafluoroborate-nickel hexacyanoferrate nanoparticles modified graphite electrode for quantitative determination of paracetamol [45].

Printex 6L Carbon nanoballs of diameters between 20 and 25 has been reported as electrode material for electrochemical detection of paracetamol. These balls were found to form homogeneous films on glassy carbon electrodes. The limit of detection for these glassy carbon decorated carbon nanoball(GC/CNB) sensors was $8.0 \times 10^{-9} \text{ mol L}^{-1}$ for paracetamol, being competitive with other devices made with carbonaceous materials. In spite of their simplicity, the sensor was also stable, reproducible and robust against typical interferents in biological fluids such as nitrite, sulfite, the antibiotic amoxicillin, sodium dodecyl sulfate and humic substances [46].

A novel paracetamol sensor has been developed which is based on Pd nanoparticles deposited on carboxylated graphene oxide (GO-COOH) and nafion (Nf) modified glassy carbon electrode (GCE). Excellent electrocatalytic responses has been observed for the oxidation of

paracetamol in the linear range 0.04–800 μM with detection limit of 0.012 μM and excellent sensitivity of 232.89 $\mu\text{A mM}^{-1} \text{cm}^{-2}$ [47]. Recently, a polymeric ionic liquid incorporated carbon nanospheres (PIL-MCNs) modified glassy carbon electrode has been reported to sensitively detect paracetamol with good detection limits [48]. Few more electrochemical methods using cyclic voltammetry technique have been reported using the modified electrodes for the detection of paracetamol [49, 50]. Wang and coworkers reported an electrochemical sensor for the detection of paracetamol using NiCu-CAT modified GCE which showed a detection Limit of about 5 μM for paracetamol through a wide concentration range (5–190 μM). The NiCu-CAT/GCE exhibits excellent reproducibility, stability, and interference for paracetamol. The voltammogram of their study has been shown in Fig 2 [33].

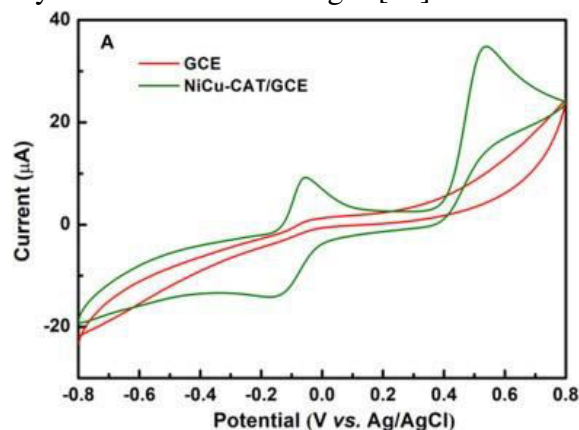


Fig. 2. Cyclic Voltammogram of bare GCE and modified GCE in presence of 40 μM paracetamol [33]

The efforts are being made by researchers to develop a simple, sensitive, economic and accurate electroanalytical method for the determination of paracetamol which can be used for pharmaceutical and clinical applications.

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References:

1. Prabakar SJR, Narayanan SS (2007) Amperometric determination of paracetamol by a surface modified cobalt hexacyanoferrate graphite wax composite electrode. *Talanta* 72:1818-1827.
2. Martin FL, McLean AE (1998) Comparison of paracetamol-induced hepatotoxicity in the rat in vivo with progression of cell injury in vitro in rat liver slices. *Drug Chem Toxicol* 21:477-494.
3. Muqford CA, Tarloff JB (1997) The contribution of oxidation and deacetylation to acetaminophen nephrotoxicity in female Sprague-Dawley rats. *Toxicol Lett* 93:15-22.

4. Nagasawa HT, Shoeman DW, Cohen, JF, Rathbun, WB (1996) Protection against acetaminophen-induced hepatotoxicity by L-CySSME and its N-acetyl and ethyl ester derivatives. *J Biochem Toxicol* 11:289-295.
5. Dinç E, Yucesoy C, Onur F (2002) Simultaneous spectrophotometric determination of mefenamic acid and paracetamol in a pharmaceutical preparation using ratio spectra derivative spectrophotometry and chemometric methods. *J Pharm Biomed Anal* 28:1091-1100.
6. Moreira AB, Oliveira HPM, Atvars TDZ, Dias ILT, Neto GO, Zagatto EAG, Kubota LT (2005) Direct determination of paracetamol in powdered pharmaceutical samples by fluorescence spectroscopy. *Anal Chim Acta* 539:257–261.
7. Srivastava MK, Ahmad S, Singh D, Shukla IC (1985) Titrimetric determination of dipyrone and paracetamol with potassium hexacyanoferrate(III) in an acidic medium. *Analyst* 110:735-737.
8. Burgot G, Auffret F, Burgot JL (1997) Determination of acetaminophen by thermometric titrimetry. *Anal Chim Acta* 343:125–128.
9. Grosa G, Del Grosso E, Russo R, Allegrone G (2006) Simultaneous, stability indicating, HPLC-DAD determination of guaifenesin and methyl and propyl-parabens in cough syrup. *J Pharm Biomed Anal* 41:798-803.
10. Peng W, Li T, Li H, Wang E (1994) Direct injection of urine and determination of acetaminophen by micellar liquid chromatography with a wall-jet cell/carbon fibre microelectrode. *Anal Chim Acta* 298:415–421.
11. Dinç E, Ozdemir A, Aksoy H, Baleanu DJ (2006) Chemometric approach to simultaneous chromatographic determination of paracetamol and chlorzoxazone in tablets and spiked human plasma. *J Liq Chromatogr Relat Technol* 29:1803-1822.
12. Galvez AM, Mateo JVG, Martínez-Calatayud J (1999) Study of various indicating redox systems on the indirect flow-injection biamperometric determination of pharmaceuticals. *Anal Chim Acta* 396:161-170.
13. Huang YM, Zhang C, Zhang XR, Zhang ZJ (1999) Cerium (IV) based chemiluminescence analysis of analgin. *Anal Lett* 32:933-943.
14. Pezza L, Tubino M, Melios CB, Pezza HR (2003) Rapid qualitative spot-test analysis for the detection of dipyrone in pharmaceutical preparations. *Anal Sci* 16:313-315.
15. Ali SR, Chandra P, Latwal M, Jain SK, Bansal VK (2011) Growth of Cadmium Hexacyanidoferrate(III) Nanocubes and Its Application in Voltammetric Determination of Morphine, *Bull Chem Soc Jpn* 84:1355-1361.
16. Latwal M, Chandra P, Ali SR (2014) Synthesis of nanostructured copper hexacyanidoferrate and its application in voltammetric detection of salbutamol, *J App Electrochem* 44:1127-1134.
17. ShangGuan X, Zhang H (2008) Sensor for acetaminophen in a blood medium using a Cu(II)-conducting polymer complex modified electrode. *Anal Bioanal Chem* 391:1049–1055.

18. Zen JM, Ting YS (1997) Simultaneous determination of caffeine and acetaminophen in drug formulations by square-wave voltammetry using a chemically modified electrode. *Anal Chim Acta* 342:175–180.
19. Fatibello-Filho O, Lupetti KO, Vieira IC (2001) Chronoamperometric determination of paracetamol using an avocado tissue (*Persea americana*) biosensor. *Talanta* 55:685–692.
20. de Carvalho RM, Freire RS, Rath S, Kubota LT (2004) Effects of EDTA on signal stability during electrochemical detection of acetaminophen. *J Pharm Biomed Anal* 34:871–878.
21. Palanna M, MohammedI, Aralekallu S, Nemakal M, Sannegowda LK (2020) Simultaneous detection of paracetamol and 4-aminophenol at nanomolar levels using biocompatible cysteine-substituted phthalocyanine. *New J Chem* 44:1294–1306.
22. Goyal RN, Singh SP (2006) Voltammetric determination of paracetamol at C60-modified glassy carbon electrode. *Electrochim Acta* 51:3008–3012.
23. Wang S, Xie F, Hu R (2007) Carbon-coated nickel magnetic nanoparticles modified electrodes as a sensor for determination of acetaminophen. *Sens Actuators B chem* 123:495–500.
24. Baranowska I, Markowski P, Gerle A, Baranowski J (2008) Determination of selected drugs in human urine by differential pulse voltammetry technique. *Bioelectrochem* 73:5–10.
25. Ni Y, Wang Y, Kokot S (2004) Differential pulse stripping voltammetric determination of paracetamol and phenobarbital in pharmaceuticals assisted by chemometrics. *Anal Lett* 37:3219 – 3235.
26. Goyal RN, Gupta VK, Oyama M, Bachheti N (2005) Differential pulse voltammetric determination of paracetamol at nanogold modified indium tin oxide electrode. *Electrochem Commun* 7:803–807.
27. ShangGuan X, Zhang H, Zheng J (2008) Electrochemical behavior and differential pulse voltammetric determination of paracetamol at a carbon ionic liquid electrode. *Anal Bioanal Chem* 391:1049–1055.
28. Campos AM, Raymundo-Pereira PA, Mendonça CD, Calegari ML, Machado SAS, Oliveira ON (2018) Size Control of Carbon Spherical Shells for Sensitive Detection of Paracetamol in Sweat, Saliva, and Urine. *CS Appl Nano Mater* 1:654–661.
29. Patil MM, Shetti NP, Malode SJ, Nayak DS, Chakklabbi TR (2019) Electroanalysis of paracetamol at nanoclay modified graphite electrode. *Mat Tod Proceed* 18:986-993.
30. Raymundo-Pereira PA, Gomes NO, Machado SAS, Oliveira ON (2019) Simultaneous, ultrasensitive detection of hydroquinone, paracetamol and estradiol for quality control of tap water with a simple electrochemical method. *J Electroanal Chem* 848:113319.
31. Kumar Y, Pramanik P, Das DK (2019) Electrochemical detection of paracetamol and dopamine molecules using nano-particles of cobalt ferrite and manganese ferrite modified with graphite. *Heliyon* 5:e02031.

32. Sasal A, Tyszczyk-Rotko K, Chojecki M, Korona T, Nosal-Wiercińska A (2020) Direct Determination of Paracetamol in Environmental Samples Using Screen-printed Carbon/Carbon Nanofibers Sensor– Experimental and Theoretical Studies. *Electroanal* 32:1618-1628.
33. Wang J, Liu S, Luo J, Hou S, Song H, Niu Y, Zhang C (2020) Conductive Metal-Organic Frameworks for Amperometric Sensing of Paracetamol. *Front Chem* 8:594093.
34. Kachosangi RT, Wildgoose GG, Compton RG (2008) Sensitive adsorptive stripping voltammetric determination of paracetamol at multiwalled carbon nanotube modified basal plane pyrolytic graphite electrode. *Anal Chim Acta* 618:54-60.
35. Lourenc BC, Medeiros RA, Rocha-Filho RC, Mazoa LH, Fatibello-Filho O (2009) Simultaneous voltammetric determination of paracetamol and caffeine in pharmaceutical formulations using a boron-doped diamond electrode. *Talanta* 78:748–752.
36. Teker T, Aslanoglu M (2020) Sensitive and selective determination of paracetamol using a composite of carbon nanotubes and nanoparticles of samarium oxide and zirconium oxide. *Microchem J* 158:105234.
37. Chen T, Huang K (2012) Electrochemical detection and degradation of acetaminophen in aqueous solutions. *Int J Electrochem Sci* 7:6877–6892.
38. Bahramipur H, Jalali F (2012) Sensitive determination of paracetamol using a graphene-modified carbon- paste electrode. *Afr J Pharm Pharmacol* 6:1298-1305.
39. Zidan M, Tee TW, Abdullah AH, Zainal Z, Kheng GJ (2010) Electrochemical oxidation of paracetamol mediated by zinc oxide modified glassy carbon electrode. *Aust J Basic Appl Sci* 4:6025-6030.
40. Zidan M, Tee TW, Abdullah AH, Zainal Z, Kheng GJ (2011) Electrochemical oxidation of paracetamol mediated by nanoparticles bismuth oxide modified glassy carbon electrode. *Int J Electrochem Sci* 6:279 – 288.
41. Boopathi M, Won MS, Shim YB (2004) A sensor for acetaminophen in a blood medium using a Cu(II)-conducting polymer complex modified electrode. *Anal Chim Acta* 512:191–197.
42. Teixeira MFS, Marcolino-junior LH, Fatibello-Filho O, Moraes FC, Nunes RS (2009) Determination of analgesics (dipyron and acetaminophen) in pharmaceutical preparations by cyclic voltammetry at a copper (II) hexacyanoferrate(III) modified carbon paste electrode. *Curr Anal Chem* 5:303-310.
43. Tsai T, Chen T, Chen S, Lin K (2011) A study of copper(II) hexacyanoferrate-PEDOT films and their sensitivity for ascorbic acid and acetaminophen. *Int J Electrochem Sci* 6:2058–2071.
44. Devadas B, Rajkumar M, Chen S, Saraswathi R (2012) Electrochemically reduced graphene oxide/ neodymium hexacyanoferrate modified electrodes for the electrochemical detection of paracetamol. *Int Electrochem Sci* 7:3339–3349.

45. Babu RS, Prabhu P, Anuja S, Narayanan SS (2012) Electrocatalytic oxidation of acetaminophen using 1-ethyl-3-methylimidazolium tetrafluoroborate-nickel hexacyanoferrate nanoparticles gel modified electrode. *J Chem Pharma Res* 4:3592-3600.
46. Raymundo-Pereira PA, Campos AM, Mendonça CD, Calegari ML, Machado SAS, Oliveira ON (2017) Printex 6L Carbon Nanoballs used in Electrochemical Sensors for Simultaneous Detection of Emerging Pollutants Hydroquinone and Paracetamol, *Sens Actuat B Chem* 252:165-174.
47. Saleem SJ, Guler M (2019) Electroanalytical Determination of Paracetamol Using Pd Nanoparticles Deposited on Carboxylated Graphene Oxide Modified Glassy Carbon Electrode. *Electroanal* 31:2187-2198.
48. Song Y, Zhang Y, Li J, Tan C, Li Y (2020) 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* 865:114157.
49. Ashoka NB, Swamy BEK, Jayadevappa H, Sharma SC (2020) Simultaneous electroanalysis of dopamine, paracetamol and folic acid using TiO₂-WO₃ nanoparticle modified carbon paste electrode. *J Electroanal Chem* 859:113819.
50. Fu R, Shen M, Ding Y, Li M, Li L, Ren Z, Wu Q (2020) Electrocatalytic Oxidation and Sensitive Determination of Paracetamol Based on Nanosheets Self-assembled Lindgrenite Microflowers. *Electroanal* 32:978-985.