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A New Coated Wire Selective Electrode for Quetiapine in Biological and Pharmaceutical Analysis

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Fabrication of organic PVC membrane based coated wire electrode for sensitive, fast, precise and simple determination of quetiapine in pharmaceutical formulation and urine samples is demonstrated. The new electrode was constructing using quetiapine : tetraphenyl borate ion pair complex as electro-active material, PVC as supporting matrix, 2-nitrophenyl octyl ether as mediator of solvent and potassium tetrakis (4-chlorophenyl) borate as lipophilic additive. The electrode provides Nernstian response (57 ±0.2 mV/decade) over a wide concentration range of 1×10^{-5} to 1×10^{-2} mol $L^{-1}$of quetiapine with lower limit of detection (3.2×10^{-6} mol L^{-1}), fast response time (less than ten seconds) and relatively long life span (30 days). Stability with verification of the suitability of the electrode to be applied in the analysis of drug quality control in pharmaceutical and biological (urine) samples was assessed. The results obtained revealed a good agreement with those obtained from independent standard method (high performance liquid chromatography). In the pharmaceutical analysis application, the recovery of the quetiapine selective electrode ranging from 98.83 to 103.27 %, the confidence of the two methods is 95% and the standard deviation is 2.49. While in the biological analysis of urine, the recovery of the electrode with respect to the standard method ranging from 96.45 to 97.48 %, the confidence is 95 % and the standard deviation is 1.48.

Keywords: Quetiapine; PVC membrane; coated wire electrode; pharmaceutical analysis; biological applications.

1. INTRODUCTION

Quetiapine (QT), 2-[2-(4-dibenzo [b,f] [1,4] thiazepin-11-yl-1-piperazinyl) ethoxy] ethanol, is an a typical antipsychotic used to treat schizophrenia which is a short-term therapy. The drug is used to

treat symptoms of dementia personal and psychological diseases and disorders as well as to treat post-traumatic stress and the treatment of insomnia and anxiety [1]. Accurate and precise determination of the drug species represent therefore, very interesting challenge for many scientist. Quetiapine was determined using HPLC-MS/ES in human plasma with twice extraction by ether after alkalization of samples [2]. This method require a tedious and sophisticated separation protocol. Quetiapine has been also, detected in biological fluids and human plasma by HPLC with electrochemical detection [3], UV detection [4] and mass detection [5]. Although these techniques are characterized by relatively short time consuming compared to chromatography mass spectrometry (GC–MS) methods, they require sophisticated instruments, tedious and much expensive. However, most of the drug species were recently, analyzed using ion selective electrodes and potentiometric sensors due to their wonderful characteristics namely; high speed, simplicity, sensitivity, selectivity and low cost [6]. These devices have versatile applications, flow injection analysis capability and integration feasibility as well as applicability to use with turbid, untreated and small samples [7,8]. The potentiometric sensor and ion selective electrodes are widely used in the measurements of different cations and anions species in environmental, biological and industrial interest samples [9-18]. An interesting category of these devices are based on PVC membrane due to its simplicity and applicability [19]. Based on these facts, some electrochemical methods have been reported for quetiapine quantification [20-28]. Some of these methods are based on the oxidation of drug molecules at different pH in the glassy carbon electrode (GCE). However, carbon electrodes suffer from fouling and difficulty controlling their surfaces reproducible manner. Few electrodes were also, reported for quetiapine drug based on cyclic voltammetry [23, 26-28] and potentiometric ion selective electrodes [25].

In this paper, sensitive PVC membrane has been prepared and used as a sensetive coating mixture in fabrication of coated wire electrode responsive for quetiapine drug. The electrode assembly has been used in estimation of the sensitivity, detection limit, response time and the proper pH range. Quetiapine electrode has been successfully used in the determination of the drug in some formulations (Seroquel tablets) in aqueous and biological (urine) samples. The results were compared with those obtained with the standard high performance liquid chromatography (HPLC) method. In addition, statistical calculation has been confirmed the validity of the results.

2. EXPERIMENTAL

2.1. Apparatus

A Jenway pH/mV meter (Model 3510) supported with a Metrohm single junction reference electrode (Model 6.0726.100) and Jenway pH glass electrode was used in the potentiometric measurements. During the measurements the test solutions were continuously stirring using Stuart magnetic stirrer (Heat-Stir, SB162). The validation experiments were conducted by HPLC (Model Shimadzu) supported with UV detector (Model SPP20A).

2.2. Materials and Reagents

All chemicals were of analytical reagent grade and double distilled water (DDW) was used throughout. Pure quetiapine grade and its tablets (Seroquel® 200mg / tablet) were supplied from AstraZeneca UK Limited and local pharmaceutical stores, respectively. Tetra hydro furan (THF) (99%), polyvinyl chloride (PVC) high molecular weight (≥2000), were obtained from Riedel-de Haën chemical company (Germany). Acetone (99.5%), 2-nitrophenyloctyl ether (99%), sodium tetra phenyl borate (99.5%) and potassium tetrakis (4-chlorophenyl) borate (98%) were provided by Aldrich chemical company, Germany. Potassium di-hydrogen orthophosphate (99.5%), sodium hydroxide (98%), ortho-phosphoric acid (85%) and nitric acid (69%) were provided by Loba Chemie, India. Urine sample taken from a healthy man volunteer 33 years old.

2.3. Standard quetiapine solution

A stock solution of quetiapine (0.01mol L^{-1}) was freshly prepared by dissolving a quantity of 0.0959 g of the drug in 25 mL DDW and consequently used in the preparation of the calibration curve solutions (1.0×10^{-8} -1.0×10^{-3} mol L^{-1}) by appropriate dilution with DDW.

2.4. Preparation of quetiapine : tetraphenyl borate ion-pair complex

Quetiapine-tetraphenyl borate ion-pair complex was precipitated by mixing equi-molar ratio (25 mL 1.0×10^{-2} mol L^{-1}) of quetiapine and sodium tetra phenyl borate drop by drop with continued stirring. The obtained milky white precipitate was then, left for settling 24 hours at room temperature, decanted and washed by DDW several times. For separation, the precipitate was centrifuged for ten minutes at 1000 rpm. The ion pair complex was dried at room temperature for 24 hours before being characterized using infra-red(IR) spectrometry which was used to prove the formation of ion pair complex [29].

2.5. Quetiapine coated wire electrode fabrication

A sensetive coating mixture was prepared by thoroughly mixing14 mg of quetiapine : tetraphenyl borate ionophore, 6 mg of potassium tetra kis (4-chlorophenyl) borate anion excluder, 114 mg of ortho-nitro phenyl octyle ether (ONPOE) plasticizer, 66 mg of PVC support and 10 ml of THF solvent in a fume hood. The mixture was then poured in small glass tube and used as a coating PVC sensitive membrane. A pure silver wire (5 cm) was mechanically treated using fine sandpaper and chemically by dipping in nitric acid followed by washing with water and THF. The treated silver wire conducting substrate was fixed horizontally inside a fume hood, dipped inside the sensitive coating mixture for few seconds and then left in air for 2 minutes for solvent evaporation. The last two steps were repeated several times until a uniform PVC layer covered one end (3 cm) of the silver wire was

obtained. The prepared assembly was dried at ambient temperature for 24 hours and used as a coated wire based quetiapine selective electrode.

2.6. Electrochemical characterization f Quetiapine electrode

The new coated wire based quetiapine ion selective electrode was calibrated by recording the potential of the pH/mV meter after consecutive dipping of the indicator and reference electrodes in the calibration solutions (1.0×10^{-7} - 1.0×10^{-2} mol L^{-1}). Before, measurements the electrode was soaked in 1.0×10^{-3} mol L^{-1} of the quetiapine solution followed by washing in DDW until steady sate potential was obtained. In order to test the reproducibility of the coated wire electrode response, the calibration was repeated several times for three different electrode assemblies [30].

The dynamic response time of the new quetiapine coated wire based electrode was tested by recording the potential of the cell verses time in seconds after consecutive dipping the cell in quetiapine solutions in the linear range (1.0×10^{-5} -1.0×10^{-2} mol L^{-1}). Moreover, the long term stability and consequently the life span of the electrode were evaluated by monitoring the potentiometric parameters after frequent calibration of the assembly from time to time.

The influence of pH of the quitiapine test solutions (1×10^{-3} and 1×10^{-2} mol L^{-1}) on the electrode response was investigated by changing the pH in the range 2-11. Small aliquots of diluted sodium hydroxide and nitric acids were used in the changing the pH of the test solutions.

The selectivity of the new coated wire electrode towards quitiapine with respect to number of inorganic species was evaluated using separate solution method [31-33]. In this study, the potentials of 1.0×10^{-3} mol $L^{-1}$of both quetiapine and interferents ions solutions were individually measured at the same conditions. Some of monovalent (Ag^{+}, Li^{+}, Na^{+}, K^{+}, NH_4^{+}) , divalent (Ca^{+2}, Pb^{+2}, Cu^{+2}, Mg^{+2}, Cd^{+2}), and trivalent (Cr^{+3}, Fe^{+3}) ions were selected for this study.

The influence of temperature on the quetiapine electrode response was assessed. In this study, the coated wire based electrode was calibrated in the linear range (1.0×10^{-5} - 1.0×10^{-2} mol L^{-1}) at different temperatures ranging from 20 to 60°C. The potentiometric parameters particularly, sensitivity of the electrode were recorded as a function of temperature.

2.7. Application of the electrode

The new quetiapine selective electrode was used in the quantification of the drug in some pharmaceutical formulations and in the human urine by direct potentiometry using the standard calibration curve. In such study, HPLC was used as standard independent method for quetiapine assessment in the same samples, for comparison. The mobile phase used was comprising phosphate buffer solution (pH =3) and acetonitrile solution (6:4 ratio). Standard quetiapine solutions (300, 200, 100 and 50 ppm) were prepared using the mobile phase as solvent and was used for HPLC calibration. Urine solution (5%) was also used as solvent for preparation of (2000, 1000, 500, 200, 100 and 50 ppm) of the quetiapine test solutions. Finally, quetiapine real sample solution (2000 ppm) was prepared using Seroquel tablet (200 mg) by dissolving one tablet in 100 mL DDW, the previous

solution was filtered and then used in the preparation of solutions of (1000, 500, 200, 100 and 50 ppm) by appropriate dilution [34].

The concentrations of quetiapine in real samples of Seroquel tablet solutions as well as in urine samples were determined by direct potentiometry using the quetiapineion selective electrode previously calibrated. These samples gradually measured from diluted solutions to concentrated one and the potential was recorded.

In order to assess the reliability of the new quetiapine electrode the real samples previously determined were also measured using high performance liquid chromatographic (HPLC) as independent standard method. In such chromatographic analysis, acetonitrile and phosphate buffer mixture (40:60) was used as the mobile phase. The applied column was RP-C18 (250mm × 4.6mm, 5µm particle size) and the flow rate was 1 mL/min. Prior to the analysis the column was flushed for one hour by mobile phase without sample for washing. The investigated real samples of the pharmaceutical formulations as well as the human urine were measured using HPLC previously calibrated by injection of 20 µL sample.

3. RESULTS AND DISCUSSIONS

3.1. Electrochemical evaluation of the coated wire quetiapine electrode

The quetiapine : tetraphenyl borate ion pair complex (Figure 1) was prepared and used as sensitive element in the fabrication of new coated wire electrode responsive for quetiapine drug species. The formation and the composition of the ion pair complex were approved using FT-IR analysis (data not presented).

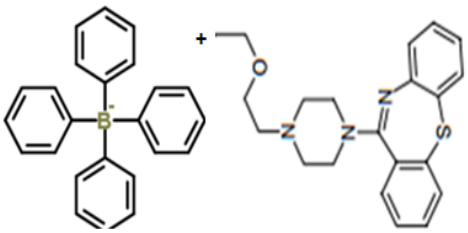

Figure 1. Quetiapine : tetraphenylborate ion pair complex ionophore.

The fabricated coated wire assembly was electrochemically evaluated as quetiapine selective electrode according to IUPAC recommendations. The potentiometric characteristics of the new electrode namely; sensitivity, limit of detection, response time, life span and influence of pH were summarized in Table 1.

Table 1. The potentiometric response properties of coated wire quetiapine electrode.

Parameter	Quetiapine electrode
Slope, mV/decade	57±2
Linear range, mol/L	$1 \times 10^{-2} - 1 \times 10^{-5}$
The correlation coefficient, R	0.994
Detection limit, mol/L	3.2×10^{-6}
Response time, s	<10
Life span, day	30
pH range	3.8-7.9

It is clear from the results obtained that, the fabricated quetiapine electrode offered good potential characteristics. The electrode showed near Nernstian response for quetiapine drug species (slope; 57 ± 2 mV/concentration decade) with a linear behavior covering the concentration range of 1.0 × 10^{-2} - 1.0 × 10^{-5} mol L^{-1} at 25 °C (Fig. 2). The slope of electrode was follow Nernst equation for mono cation with correlation coefficient "R" of 0.994 and detection limit of 3.2 x 10^{-6} mol L^{-1}. The repeated calibration (at least fifteen times) showed that the mean standard deviation was 1.62 and relative standard deviation was 2.18.

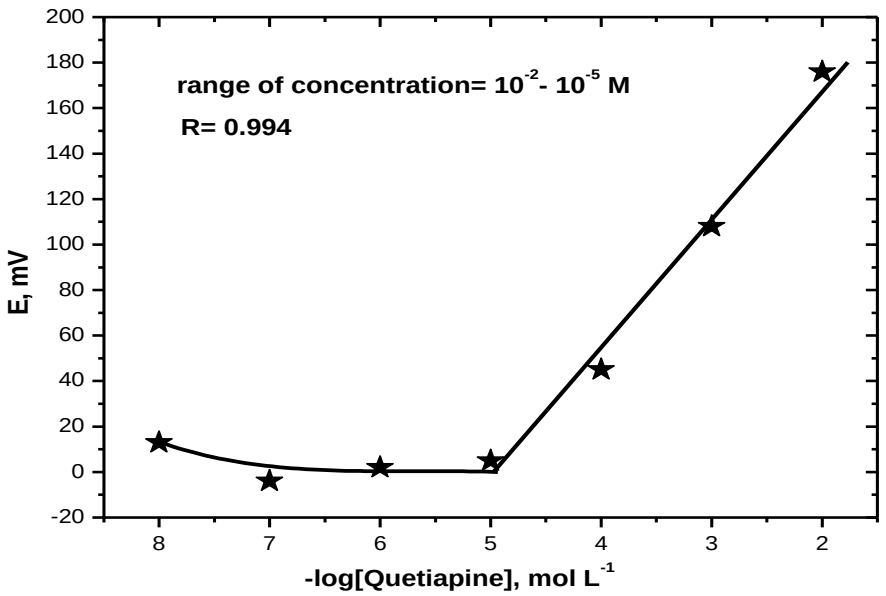

Figure 2. Potentiometric calibration plot of quetiapine coated wire electrode (25 ^{o}C, pH=6).

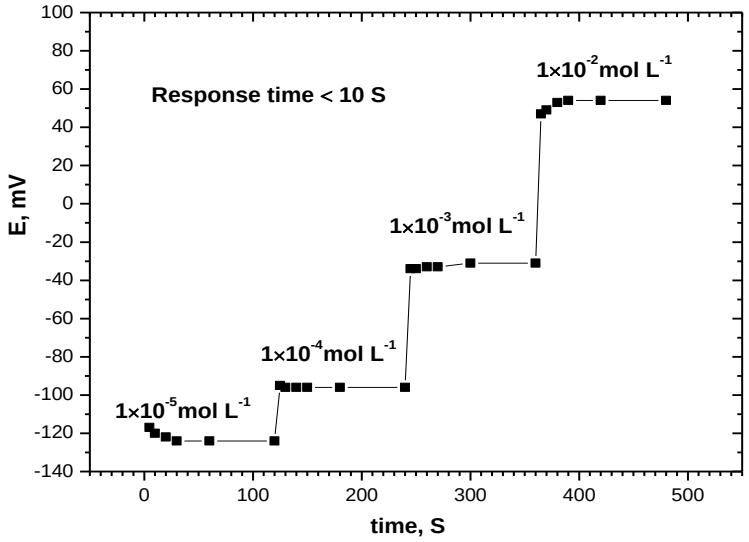

Figure 3. Typical dynamic response time of the quetiapine coated wire electrode (25 ^{o}C, pH=6).

The response time of the new coated wire electrode was measured by immersing the assembly in a series of different quetiapine solutions in which the concentration of the drug is increase tenfold and then the potential readings were recorded versus time in (s). The response time of the electrode which is the time required to reach 95% of its final potential was determined and the data obtained was presented in Figure 3. As can be seen, the response time was somewhere between (5-10) seconds and response time decreases with increases the concentration of quetiapine.

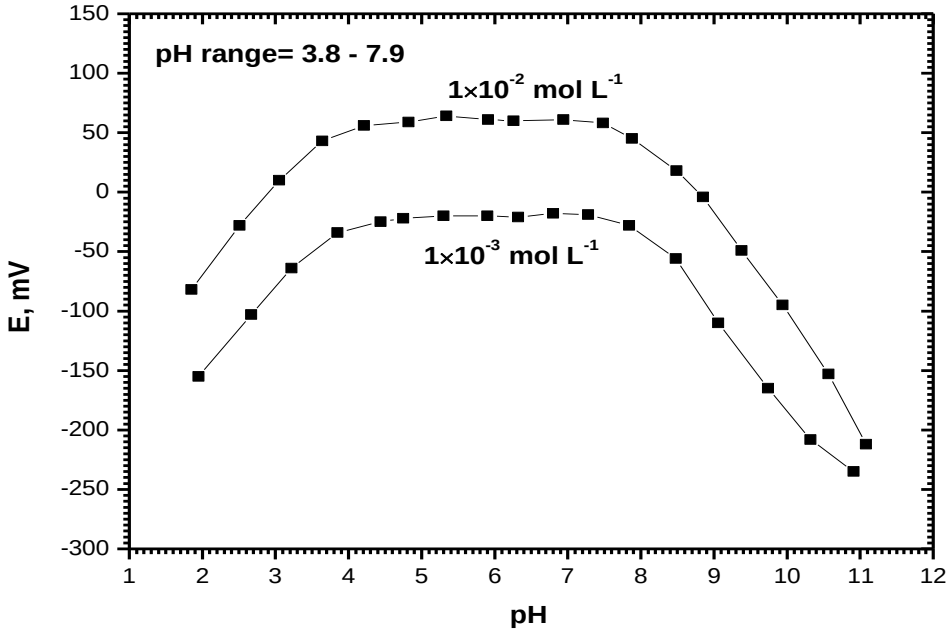

Figure 4. Effect of pH on the potential of the quetiapine coated wire electrode (25 ^{o}C).

The influence of pH on the potential of the electrodes was studies using two quetiapine test solutions of concentrations 1.0×10^{-2} and 1.0×10^{-3} mol L^{-1}. In this study, the pH of each test solution was varies from 2.0 to 11.0 and the potential readings were recorded. The data obtained was presented in figure 4. As can be seen, the quetiapine coated wire ion selective electrodes has stable potential in the pH range 3.8-7.9, and consequently this range was applied in the rest of the experiments. The significant potential changes at pH greater than 7.9 or less than 3.8 may attributed to the damage of the quetiapine selective membrane and change the shape of the drug at too high or too low acidic function, respectively [35].

On the other hand, the separate solutions method was used to determine the potentiometric selectivity coefficient $K_{i,j}^{pot}$ for uni, bi and tri positive interfering ion with respect to the quetiapine drug at concentration of 10^{-3} mol L^{-1} for both quetiapine and the interfering cation, equation (1).

$$\log K_{A,B}^{pot} = \left(\left(\frac{E_B - E_A}{S}\right)\right) + \left(1 - \left(\frac{Z_A}{Z_B}\right)\right)\log a_A \ldots\ldots\ldots\ldots (1)$$

Where $K_{i,j}^{Pot}$ is the selectivity coefficient, E_A is measured quetiapine ion potential (mV) at a given concentration of 10^{-3} mol L^{-1}, E_B is measured potential of ion interference (mV) at the same concentration, S is the calibration slope of the quetiapine ion (57 ± 2), a_A and Z_A is the effectiveness of the concentration of quetiapine ion and its valance, respectively, and Z_B is the valance of interference ion. The data obtained was collected in table (2). The value of the selectivity coefficient for all interferences less than 0.002, which indicates reasonable selectivity of coated wire electrode for a quetiapine drug in comparison with the investigated different ions.

The effect of temperature on the slope of quetiapine selective electrode was determined and the results were presented in Fig. 5. As seen, the potentiometric calibration slope of the quetiapine coated wire electrode is independent on temperature below 30 °C due to the stability of the ion pair sensitive material within this range of temperature. While at high temperatures (40-60 °C), a gradual decrease in slope of quetiapine electrode was observed which may be attributed to the lack of stability of quetiapine drug and the degradation of ion pair sensitive material at high temperatures.

Table 2. Selectivity coefficient values of the quetiapine electrode.

Interferant, B	K_{ij}^{pot}
Quetiapine	1.0
Ag^{+}	2.0×10^{-3}
Li^{+}	1.0×10^{-3}
Na^{+}	2.0×10^{-4}
K^{+}	3.0×10^{-4}
NH_4^{+}	3.0×10^{-4}
Cd^{2+}	1.0×10^{-4}
Ca^{2+}	3.0×10^{-5}
Cu^{2+}	8.0×10^{-5}
Mg^{2+}	6.0×10^{-5}
Pb^{2+}	8.0×10^{-5}
Cr^{3+}	6.0×10^{-5}
Fe^{3+}	2.0×10^{-5}

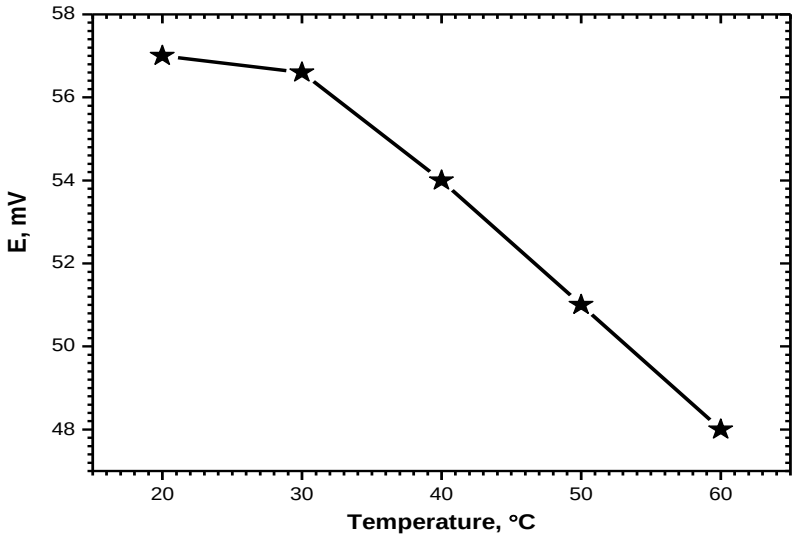

Figure 5. The effect of temperature on the slope of quetiapine coated wire electrode (pH=6).

The long term stability of the quetiapine coated wire electrode was assessed by frequent calibration for 3 months. The potentiometric properties of the electrode were stable for a period of 30 days which assigned as life span of the electrode. The sensitivity of electrode was decline after the life time period as a result of the leaching of the ion pair complex active ingredient outside the membrane upon the immersing of the membrane in the aqueous test solutions.

The potentiometric properties with respect to sensitivity, detection limit, linear range, response time, effect of pH and life span of the elaborated coated wire quetiapine electrode were compared with those reported for quetiapine ion selective bulk electrodes (Table 3). Different types of electrodes and consequently, different methods of analysis were summarized in this comparison study. Such study comprises two different techniques namely; potentiometry (Ref. [25], this work), and voltammetric method of analysis (Ref. [23], [24], [26], [27], [28]) as well as ten different electrodes namely; three ion selective electrodes (Ref. [25]; electrodes I &II, this work) and seven working voltammetric electrodes (Ref. [23], [24], [26], [27]; III & VI, [28]; DC&DDP). As can be seen from the results presented in Table 3, the voltammetric methods of analysis offer superior detection limits values ranging from 2.9×10^{-7} to 3.1×10^{-12} (Ref. [23], [24], [26], [27], [28]) compared to the detection limit of the potentiometric methods which ranging from 3.2×10^{-6} to 2×10^{-7} (Ref. [25], this work). Nevertheless, the voltammetric methods show relatively narrow linear range (~ 2 concentration decades) than the linear range of the elaborated coated wire quetiapine electrode (3 concentration decades) and longer response time. The voltammetric methods require, however expensive and sophisticated instruments as well as tedious methodology. Moreover, the coated wire electrode offers faster response time (< 10 s), longer life span (30 days), wide independent pH range (3.8 – 7.9) and small size with automation and integration feasibility. On the other hand, the elaborated coated wire quetiapine electrode offers higher sensitivity (57±2 mV/decade), wider linear range, faster response

time, longer life span and small size than those reported for the potentiometric quetiapine sensors (Ref. [25]).

Based on this comparison study, the quetiapine coated wire electrode offered potentiometric properties comparable and in some cases (sensitivity, response time, life span) better than those reported in literatures. Moreover, the small size of the coated wire provides automation and integration feasibility of the elaborated electrode. Thus, the merits offered by the coated wire quetiapine potentiometric sensor over quetiapine electrodes previously reported in literature for quetiapine drug include high sensitivity, fast response time, long life span and small size assembly.

Table 3. Comparison between potentiometric characters of different quetiapine electrodes.

Parameter	Ref. [23]	Ref. [24]	Ref. [25]*	Ref. [26]	Ref. [27]**	Ref. [28]***	This work
Slope	--	8.96×10^{5}, µA mole/L	I; 27.5±0.45 II; 39.85±0.3 mV/decade	--	III; 9.45×10^{4}, VI; 6.21×10^{5} µA mole/L	DC; 4.3×10^{-3} DPP; 4.3×10^{-3} µA mole/L	57±2, mV/decade
Linear range, mol/L	17×10^{-9}- 3.1×10^{-12}	7.5×10^{-6}- 8×10^{-8}	I; 1×10^{-2} - 1×10^{-6} II; 1×10^{-2} - 1×10^{-7}	5×10^{-6}- 2×10^{-8}	III; 1×10^{-4}- 1×10^{-6} VI; 1×10^{-5}-1×10^{-7}	DC; 1.1×10^{-7}- 2×10^{-8} DPP; 1.1×10^{-7}- 1×10^{-8}	1×10^{-2}- 2×10^{-5}
The correlation coefficient, R	0.99	--	I; 0.9994 II; 0.9996	0.9956	0.999	0.9999	0.994
Detection limit, mol/L	3.1×10^{-12}	1.9×10^{-8}	I; 1.8×10^{-6} II; 2×10^{-7}	1×10^{-8}	III; 2.9×10^{-7} VI; 2.2×10^{-8}	DC; 1.5×10^{-10} DPP; 1×10^{-10}	3.2×10^{-6}
Response time	60, s	120, s	I; 14, s II; 10, s	< 5, min.	III; 40 s VI; 120 s	--	<10
Life span, day	One measurem-ent per membrane	--	I; 21 II; 28	--	--	--	30
pH range	--	--	2.5-7	2 - 2.7	--	--	3.8 - 7.9
Sensor type	Membrane electrode	Glassy carbon electrode	Bulk electrode	Glassy carbon electrode	Glassy carbon electrode	Hg Drop	Coated wire electrode
Technique	Voltam-metry	Voltam-metry	Potentio-metry	Voltam-metry	Voltam-metry	Voltam-metry	Potentio-metry

**Electrode I; sodium tetraphenyl borate sensitive material, Electrode II; sodium tetraphenyl borate and β-cyclodextrin sensitive material.*

***Method III; without accumulation step, Method VI; with accumulation step.*

****DC; direct current, DPP; differential pulse polarography.*

3.2. Application of the coated wire quetiapine electrode.

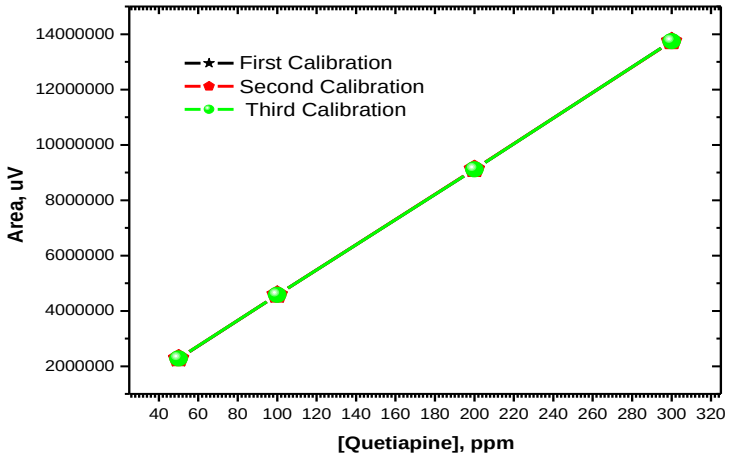

Figure 6. Typical three-calibration plots of HPLC, (mobile phase; phosphate:acetonitrile buffer, 6:4, pH=3, column; RP-C18, flow rate; 1 mL/min, sample size; 20 µL.

Table 4. Quetiapine potentiometric estimation of Seroquel (200mg) in aqueous and urine samples.*

Added, ppm	Aqueous samples		Urine samples	
	Found, ppm	Relative error	Found, ppm	Relative error
500	482.8	0.03	607.8	0.21
1000	1080.9	0.08	1080.9	0.08
2000	2012.7	0.01	1966.9	0.01

* *Average of three times.*

Taple 5. Quetiapine estimation of Seroquel (200mg) in aqueous and urine samples using HPLC.*

Added, ppm	Aqueous samples		Urine samples	
	Found, ppm	Relative error	Found, ppm	Relative error
50	46.75	0.065	63.02	0.26
100	105.87	0.059	111.07	0.11
200	203.66	0.018	201.78	0.01

* *Average of three times.*

The realized coated wire quetiapine electrode was successfully applied in the determination of the drug species in different real samples of the drug formulation (Seroquel, 200mg) by direct potentiometry using the calibration plot of the electrode conducting at the same conditions. Further, these samples were also measured using HPLC as independent standard method, in order to assess the reliability and credibility of the electrode. Under optimized conditions specified in the experimental section, HPLC was calibrated three times and the plots were presented in Fig. 6. The drug species concentrations of Seroquel (200 mg) were determined in some aqueous and biological (urine) samples

using the new electrode and HPLC, as well. For comparison, the data obtained by the electrode and HPLC was summarized in table 4 and 5, respectively. It was clear from the results obtained that, the new quetiapine coated wire electrode offered high credibility and validity of good analysis in the investigated pharmaceutical and biological (urine) samples, with respect to the independent certified standard HPLC method.

In order to assess the reliability and applicability of the new coated wire quetiapine based electrode, the data obtained was compared with those obtained using the independent standard HPLC method of analysis. The accuracy and precision data obtained were summarized in tables 6 and 7, respectively. As can be seen the elaborated new electrode exhibits excellent accuracy and precession with respect to the official method of analysis.

Table 6. Accuracy study of the new quetiapine coated wire electrode.

Added, ppm	Aqueous samples			Urine samples		
	Found, HPLC, ppm	Found, new electrode, ppm	Recovery, %	Found, HPLC, ppm	Found, new electrode, ppm	Recovery, %
50	46.75	48.28	103.27	63.02	60.78	96.45
100	105.87	108.09	102.10	111.07	108.09	97.32
200	203.66	201.27	98.83	201.78	196.69	97.48
Average recovery			101.4	Average recovery		97.1

Table 7. Statistical data of the "t- test" of the drug in aqueous and urine samples.

Sample	(T) value	Degree of freedom (dt)	Standard deviation (SD)	Probability, P.value (sig)
Aqueous	-0.316	2	2.49	0.782
Urine	4.025	2	1.48	0.057

On the other hand, the t - test study (Table 7) showed that, the p values are 78.2 %, and 5.7 %, which are greater than the level of significance of 5% , and therefore the average concentration of drug quetiapine in the pharmaceutical formulation using quetiapine ion selective electrode equals the average concentration of drug quetiapine in pharmaceutical using (HPLC) by 95% , and a common standard deviation was 2.49 and 1.48 between the two methods.

4. CONCLUSIONS

Novel coated wire quetiapine electrode was realized and electrochemically evaluated. The merits of the elaborated electrode include high sensitivity, short life time, good selectivity of the drug and long life span. The new electrode was successfully applied in the determination of the drug in some pharmaceutical and biological (urine) real samples. The results obtained come in good agreement

with those obtained using independent standard HPLC method of analysis with good accuracy and precession.

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