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Full Paper

Direct Potentiometric Evaluation of Trazodone Hydrochloride by Novel Ion Selective Electrodes

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Abstract- This study improved three potentiometric sensors for measuring the drug trazodone hydrochloride. The constructive sensors were designed for the preparation of electro-active plasticized membranes representative of ion-association complexes. Trazodone cation and phosphomolybdate acid anions used a plasticized poly(vinyl chloride) membrane sensor acting as an electro-active material in a plasticized polyvinyl chloride electrode. The sensors showed agreement at near-Nernstian responses for trazodone hydrochloride-phosphotungstic acid-di-butyl phthalate and trazodone hydrochloride-phosphotungstic acid-o-Nitro phenyl octyl ether with lower detection limits of approximately 2.8×10^{-6} mol.L^{-1} and 1.1×10^{-6} mol.L^{-1}, while the slopes were found to be around 55.00 and 51.70 mV/concentration decade. The pH ranges were approximately 2.0-7.5, 2.5-8.0, and 3.0-8.0 for trazodone hydrochloride-phosphotungstic acid-di-butyl phthalate, trazodone hydrochloride-phosphotungstic acid-o-Nitro phenyl octyl ether and trazodone hydrochloride-phosphotungstic acid-di-butyl phthalate, respectively. The sensor hydrochloride-phosphotungstic acid-di-butyl phthalate showed small values of the slope near the 31.20 mV/concentration decade, while the detection limit was around $5.0\times10\text{-}^{6}$ mol.L^{-1}. The three sensors indicated a high selectivity for the TRZ drug over several inorganic cations for different drug formulation samples. The dissolution profiles showed good relationships when plotted for use in the proposed sensor at optimum electrode conditions. The investigated sensors can be applied for the direct determination of TRZ in some pharmaceutical preparations, and can be used for the investigation of many TRZ tablets.

Keywords- Ion elective electrodes; Potentiometric method; Trazodone hydrochloride; PVC membrane; Sensor

1. INTRODUCTION

Trazodone (TRZ) 2-[3-(4-m-chlorophenylpiperazin-1-yl)propyl]-1,2,4-triazolo[4,3-a]pyridin-3(2H) is an active ingredient of pyridine derivative compounds [1]. Recently, trazodone was found to have significant effects for many psychological problems, and it is a medication used for the treatment of depression, anxiety, and to facilitate sleep [2]. TRZ is one of the main oral treatments for humans and is commonly prescribed for its antidepressant activity due to the fact of its vital effects in the blockage of serotonin reuptake by inhibiting serotonin reuptake pump at the presynaptic neuronal membrane. Some orthopedic surgeries use TRZ in a well-tolerated oral dosage of approximately 75-150 mg per day for cases of depression and anxiety [3,4]. The main therapeutic activity of trazodone is according to their 5-HT2A receptors [5]. In terms of its chemical structure, trazodone hydrochloride is generally a white crystal powder that is easily soluble in water and practically soluble in ether solvents. Its general molecular weight is 408.30 g.mole^{-1}, and the common chemical structure of trazodone hydrochloride is shown in Figure 1 [6].

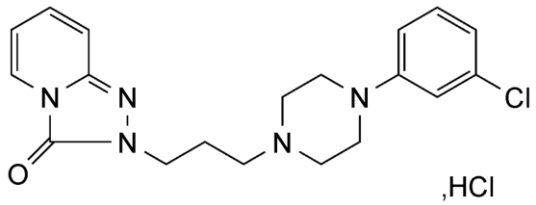


Figure 1. Main chemical structure of trazodone hydrochloride

The importance of trazodone hydrochloride as a drug is not specific only for use in humans. It has been found to be an efficient medication for helping dogs, improving their welfare with few side effects and enhancing the behaviour of dogs suffering from anxiety and other disorders [7]. Many analytical methods have studied the quantification of trazodone hydrochloride, such as in complexes, using 1HNMR [8], high-performance liquid chromatography (HPLC) [9-11], spectrophotometric [12] and voltammetry [13,14]. Although these series of attempts to create a new and simple analytical technique that can be used to detect a variety of trazodone hydrochloride derivative drugs [15-17], the main weakness of most of these studies is their failure to address simple processes to quantify trazodone. It is true that a recent study by Salama et al. showed good results for measuring trazodone in pharmaceutical forms. They designed screen-printed electrodes with gold nanoparticles functionalized in different ranges of trazodone hydrochloride. The study had a long experimental process and complex system with slightly expensive compounds such as using 1.5 mL of gold nanoparticles as a functional past sensor. Another major drawback of this approach is that the equilibrium for the construction sensors necessary for a potential response was found to be 30, 45, 60, 90, 120 and 150 minutes, which is consuming time [18]. As the importance of trazodone hydrochloride is essential in

some medical cases; therefore, it is necessary to improve and develop a new system sensor that has better efficiency properties than previous ones with shorter time responses and higher selectivity. This paper attempted to advance three new ion-selective electrodes for measuring TRZ in bulk and pharmaceutical samples. This was conducted by preparing three ion-selective electrodes in simple and accurate steps with a fabrication electrode with reasonable time responses.

2. METHODS

2.1. Chemicals and preparation reagents

Chemicals and reagents were used from analytical grade. All diluted samples were prepared from distilled water. The pure TRZ was supplied from (IRAQ-SDI, Samara) State Company of Drug Industries and Medical Appliance. Trazodone hydrochloride tablets (50 mg), Oleptro tablets (150 mg), phosphotungstic acid (PTA), tetrahydrofuran (THF), polyvinyl chloride (PVC), di-butyl phthalate (DBP) and *o*-Nitro phenyl octyl ether (NPOE) were provided from BDH and MERCK. The aqueous solutions of 0.01 mol.L^{-1} of PTA were prepared by dissolving the required weights of the competent materials in deionized water for the formulation of ion-association complexes and TRZ.

2.2. Instrumental analysis

The potential for all electrochemical experiments was determined using a pH meter (HANNA-Romania). The homemade reference electrode used a double junction Ag/AgCl electrode (Metrohum); the preparation of the active electrode was applied to the selective electrodes.

2.3. Preparation standard TRZ solution

A standard sample of 0.01 mol.L^{-1} TRZ was prepared by mixing accurate amounts required of the pure drug and aqueous dilution in a 100 ml volumetric flask.

2.4. Methods

2.4.1. Synthesis of ion-associates

The 25 ml of 0.01 mol.cm^3 samples of TRZ and PTA were placed in suitable containers and stirred for approximately 20 min at 25 ^oC. The sample was then filtered using Whatman No. 41 filter paper; after the filtration process, the residual compound TRZ-PTA ion-associate was left to form precipitate overnight at 34 ^oC. The resultant was then utilized for membrane probe preparations.

2.4.2. Fabrication of the TRZ-PTA ion-selective electrodes

Approximately 0.04 g were weighted from the dried residual TRZ-PTA ion-associate, which was put in a Petri dish approximately 6 cm in size. Next, 1.7×10^{-2} mg each of PVC and 0.36 g of (DBPP or NPOE) was added to resolve 10 ml THF. The mixture was left to dry at room temperature for approximately 24 hours. A 0.4-mm thick membrane was removed cautiously and fused at the end side of Pyrex glass tube using THF. The probe was left to dehydrated for 24 hours at 25 ^{o}C. The next step was filled 3 to 5 ml internal sample of 5 mmol/cm^3 TRZ. Then, the sample was immersed for approximately 1.5 hours in the drug sample at the same concentrations as the internal sample.

2.4.3. Calibration curve method

Various TRZ solutions of 0.01 mol. L^{-1} was moved into a series of 100 ml volumetric flasks. The potential measurements were carried out for TRZ-PTA-ISE and Ag/AgCl reference electrodes by immersing them into each preparation solution. The calibration diagrams were separately calculated for the measured potentials versus logarithms (TRZ) in each ISE. The concentration of the unknown sample was measured by using a calibration curve or assumption derivative equation and applying potential and log [TRZ] data.

2.5. pH effects

The influence of pH on the electrode potential at various times for concentrations of distigmine in the range 1×10^{-3} mol.L^{-1} was described. Different amounts of NaOH or HCl were added to alter the pH range of the solutions.

2.6. Interferences

A series of 25 ml beakers were each filled with 4 ml of 0.01 M standard sample drug, and 8 ml of water was then added to each beaker. Next, 2 ml of 1.0 mol.L^{-1} of different interferes were added and mixed well. The measurements of potential for each preparation sample in the beakers were examined using the above method for electrochemical cells with calibration curves.

2.7. Potentiometric determination of TRZ

In terms of potentiometric measurements, the standard solution was added to the sample. Gradually changes were prepared for the additive standard solution into the sample. The analytical method used in this section of work was the standard addition method. This was succeeded by adding identified volume values from standard drug analyte to 50 ml water containing various quantities of the investigated drug in its pure form. The conversion in the

mV evaluation was verified for each increasing value; then, it is applied to determine the amount of the drug in an unknown sample by the chemical expression [19]:

$$Cx = CsVsVx+Vs10n(\Delta E/S)-VxVs+Vx-1 \ldots\ldots\ldots\ldots\ldots\ldots (1)$$

where V_x is the volume of the original sample solution, and Vs and C_s are the concentration and volume, respectively, for the standard additive solution into the sample to be examined. C_x is the concentration that needs to be determined, ΔE is the change in the potential once a certain amount (volume) of standard solution is determined, and *S* refers to the slope for the calibration diagram.

2.8. Pharmaceutical applications

The determination method for optimum measurement of TRZ and pure pharmaceutical preparations are described. The recovery data and the ability of the proposed probes were applied in the direct potentiometric determination of drugs, which are given in Table 5. This represents two cases: one in pharmaceutical forms and the other without any interference from the excipients.

3. RESULTS AND DISCUSSION

To confirm that the prepared membranes are suitable and reliable probes for measuring different concentrations of the samples. It was necessary to apply a Nernstian equation for all prepared membranes. This was successfully described using the three construction membranes: TRZ-PTA-DBP, TRZ-PTA-DBPH, and TRZ-PTA-NPOE, as shown in Figure 2. From the demonstration data, it could clearly be seen that individual measurements for the electrochemical sensors were in different drug forms to adhere to IUPAC recommendation for selective membranes incorporating ion associates under static conditions [20,21].

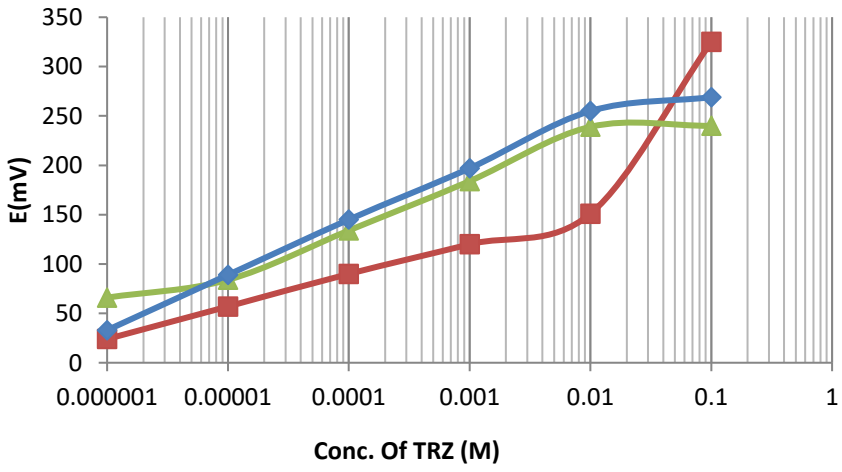


Figure 2. Calibration curves of TRZ electrodes in three electrodes: (▬-TRZ -PTA-DBP), (▲TRZ-PTA-NPOE) and (■ TRZ-PTA-DBPH)

The near-Nernstian slope of the TRZ-PTA-DBPH and TRZ-PTA-NPOE membrane sensors were found to be 55.00 and 51.70 mV decade^{-1}, respectively, with 2.8×10^{-6} mol.L^{-1} and 1.1×10^{-6} mol.L^{-1} as the lowest detection limits.

However, it is interesting that at approximately 31.20 mV decade^{-1} the Nernstian slope value for the TRZ-PTA-DBP membrane showed a detection limit of 5.0×10^{-6} mol.L^{-1}.

In terms of lifetime, the TRZ electrodes were examined by open circuit potential (OCP). From Figure 3, it can be seen that response times of the three preparation probes showed stability times at approximately 34, 30 and 12 days. These data are in good agreement with the literature [22]. The preparation of screen-printed electrodes with gold nanoparticles for the determination of trazodone hydrochloride has previously been demonstrated. The data showed that the maximum response time was approximately 180 minutes; however, in this study, two sensors successfully gave good stability for more than 3 days, as shown in Figure 3.

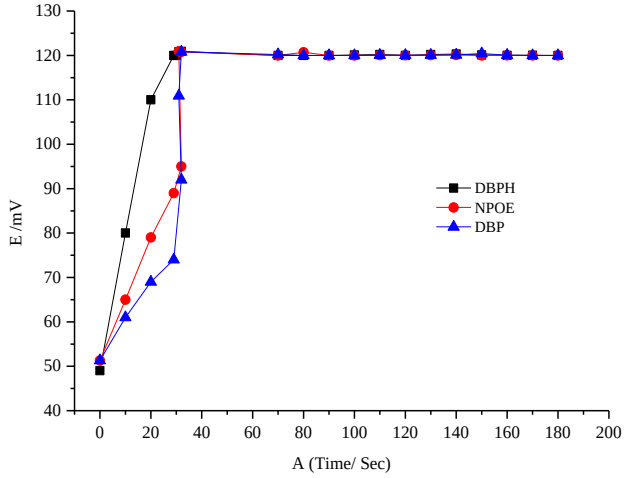


Figure 3. Mechanism of the time response for different concentrations of trazodone hydrochloride

Table 1. The characteristics analytical factors suggested in the TRZ sensors matrix probe

Parameters	**Electrode DBPH**	**Electrode NPOE**	**Electrode DBP**
Slope (mV/decade)	55.00	51.70	31.20
Detection limit (mol.L^{-1})	2.8×10^{-6}	1.1×10^{-6}	5.0×10^{-6}
Correlation coefficient	0.996	0.998	0.996
Range of linearity (mol.L^{-1})	7.7×10^{-6}-1.0×10^{-2}	8.3×10^{-6}-1.0×10^{-2}	8.4×10^{-6}-1.0×10^{-2}
Working pH range	2.0-7.5	2.5-8.0	3.0-8.0
Regression equation Y = mX + b	Y=23.886 ln(x)+364	Y=22.453ln(x)+341.7	Y=13.55ln(x)+213.7
Lifetime (day)	34	30	12

The analytical parameters of the matrix membrane for all preparation TRZ electrode types were characterized. This clearly showed that the performances of the DBPH probe were better than NPOE and DBP probes as illustrated by the data in Table 1.

3.1. Influences of pH

The determination of the transfer of protons in electrochemical electrodes is an important factor that should be considered in potentiometric reactions. In this section, the pH of the potentiometric measurements for TRZ-PTA-DBPH, TRZ-PTA-NPOE and TRZ-PTA-DBP membrane sensors were examined for standard 1×10^{-3} mol. L^{-1} TRZ solutions in different ranges of pH (2.0-8.0). The reason for this was to control the best series of chemical reagent samples that could be tested. Known concentrations of sodium hydroxide or hydrochloric acid solutions were added to the pH samples.

The results in Figure 4 indicated three categories of pH ranges 2.0-7.5, 2.5-8.0 and 3.0-8.0 at 1×10^{-3} mol.L^{-1} TRZ reagents. It was noticed that there was no substantial effect on the probe performances for TRZ-PTA-DBPH, TRZ-PTA-NPOE and TRZ-PTA-DBP, respectively. The potentials measurements for all probes were extremely ignored with negative drift at higher pH due to the progressive precipitation of the free meantime base. At pH less than 2, the sensor performances were significantly impacted by H_3O^+ molecules.

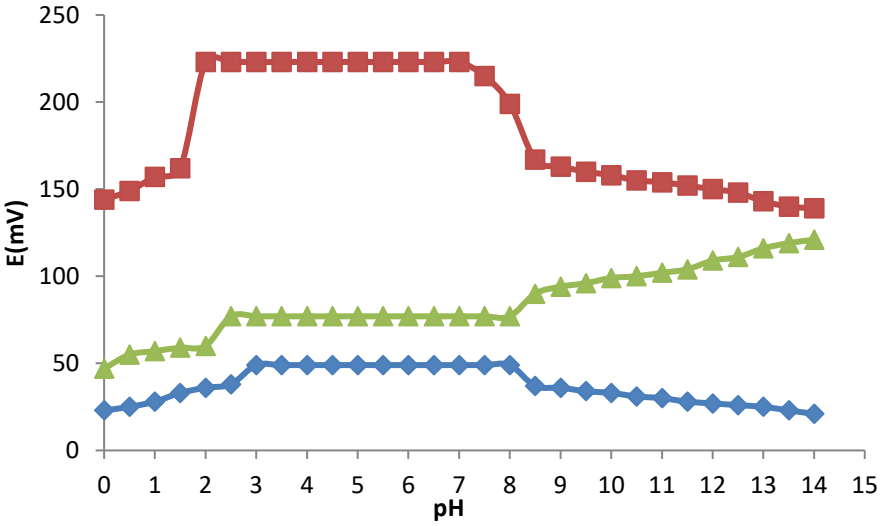


Figure 4. Ranges of pH for (TRZ-PTA-DBPH), (▲TRZ-PTA-NPOE) and (■ TRZ-PTA-DBP) electrodes at 1.0 $\times10^{-3}$ mol.L^{-1}

3.2. Selectivity

The performances of ISEs probes were mostly influenced by the presence of foreign cations. To ensure that the ion-selective electrodes were accurate sensors with reliable measurements, the matched potential method (MPM) for all constructed probes in the presence

of different interfering foreign anions was used. The MPM is mainly useful for avoiding the limitations of the corresponding manners dependent on the Nicolsky–Eisenman equation for measuring potentiometric selectivity coefficients [23]. These limitations consist of non-Nernstian functions of interfering ions and the inequality of charges of any primary interfering ion.

The inorganic cations did not interfere in the differences in mobility, permeability and size of the ions. The conditional factors in FI were controlled by the values of selectivity coefficients dependent on measured potential values produced at the tops of the peaks in the same drug concentrations. In Table 2, it can be seen how most foreign anions showed slight values for the selectivity coefficient and all membranes in the sensors reported good agreement performances with indicated and negligible interferences.

Table 2. Coefficient of the selectivity calculated for the TRZ+DBPH+PTA and TRZ-PTA-NPOE electrodes

Electrode TRZ+DBPH+PTA and TRZ-PTA-NPOE					
Concentration of TRZ					
Ion	**10^{-3}**	**10^{-4}**	**Ion**	**10^{-3}**	**10^{-4}**
Na^{+}	0.0172	3.8178×10^{-3}	**Na^{+}**	0.0139	0.0986
K^{+}	0.02619	2.8480×10^{-3}	**K^{+}**	0.0755	0.0902
Ca^{2+}	1.0427×10^{-3}	4.1512×10^{-4}	**Ca^{2+}**	7.7926×10^{-4}	9.7363×10^{-4}
Mg^{2+}	4.9080×10^{-4}	8.1113×10^{-4}	**Mg^{2+}**	8.5185×10^{-4}	7.7926×10^{-4}
Fe^{3+}	1.3975×10^{-5}	8.8176×10^{-5}	**Fe^{3+}**	1.2521×10^{-5}	4.3574×10^{-5}
Al^{3+}	1.4572×10^{-5}	6.577×10^{-5}	**Al^{3+}**	1.1975×10^{-6}	2.9484×10^{-5}

3.3. Potentiometric Analysis

To ensure that the current method is applicable in different kinds of samples in the same manner and constructed electrodes; therefore, another investigation was conducted using potentiometric measurements of TRZ in pure form and tablets. Direct, standard addition method or potentiometric titrations were carried out for different samples as shown in Table 3. Analyses of trazodone hydrochloride tablets (50 mg) and oleptro tablets (150 mg) in pharmaceutical dosage forms were examined using the proposed method, the results for the two methods obtained are represented in Table 4. The calculation of the recovery and concentration of TRZ (found) indicated no significant changes in accuracy and reproducibility. It was previously shown that the standard addition method for different samples gave relativity the best results with less errors compared with the other analytical methods, which are typically used in current work [24-27].

García et al. constructed a trazodone-selective electrode. The electrode showed a small response to all the species assayed compared with the response to TRZ with pH ranges of 5–7.5, while in a recent study, wider pH ranges of approximately 2-8 were recorded. This could possibly improve the application of trazodone-selective electrodes in some special cases where there is the need to apply trazodone in an acidic medium [28].

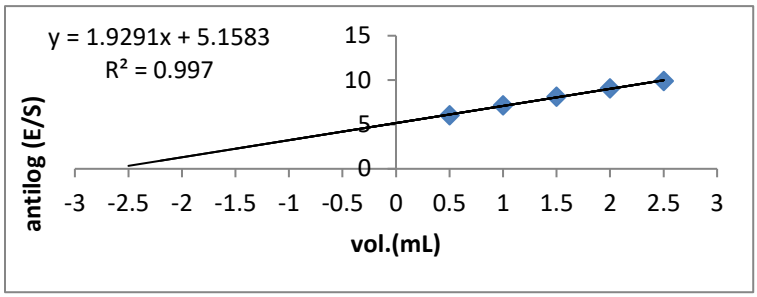
Table 3. TRZ measurements in the pure drug form using the suggested sensors

Type of Electrode	Sample	Responses Using the Potentiometric Method			
		Direct	SAM	MSA	Titration
TRZ+PTA+DBPH	1×10^{-3}	0.9529×10^{-3}	0.9658×10^{-3}	0.9787×10^{-3}	0.9811×10^{-3}
	RSD%	1.16	1.55	-	-
	Recovery%	95.29	96.58	97.87	98.11
	Error%	-4.71	-3.42	-2.13	-1.89
	1×10^{-4}	0.9526×10^{-4}	0.9715×10^{-4}	0.9610×10^{-4}	0.9830×10^{-4}
	RSD%	1.29	1.76	-	-
	Recovery%	95.26	97.15	96.10	98.30
	Error%	-4.74	-2.85	-3.90	1.70
TRZ+PTA+NPOE	1×10^{-3}	0.9517×10^{-3}	0.9816×10^{-3}	0.9720×10^{-4}	0.9807×10^{-4}
	RSD %	1.90	0.27	-	-
	Recovery%	95.17	98.16	97.20	98.07
	Error %	-4.83	-1.84	-2.80	-1.93
	1×10^{-4}	0.9477×10^{-4}	0.9795×10^{-4}	0.9708×10^{-4}	0.9800×10^{-4}
	RSD %	2.31	0.08	-	-
	Recovery%	94.77	97.95	97.08	98.00
	Error%	-5.23	-2.05	-2.92	-2.00

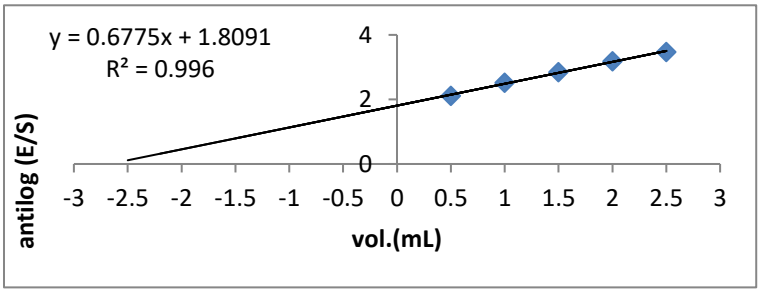
Table 4. Direct potentiometric method using the TRZ-PTA-DBPH electrode

Pharmaceutical Tablets	Trazodone Hydrochloride Tablets (50 mg)	Oleptro Tablets (150mg)
Concentration of TRZ (Prepared)	1.0×10^{-3}	1.0×10^{-3}
Concentration of TRZ (Found)	0.979×10^{-3}	0.981×10^{-3}
% Recovery	97.98	98.15
% Error	-2.02	1.85

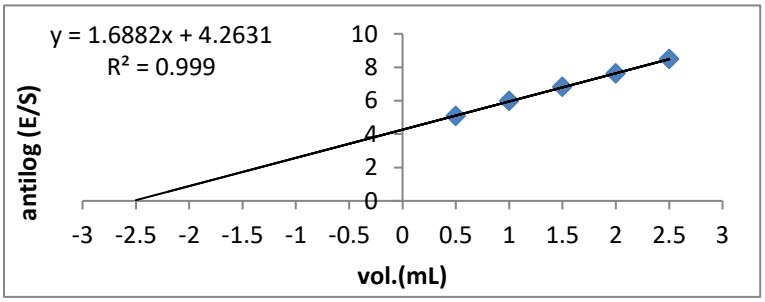
a) TRZ-PTA-DBPH at 10^{-3}



b) TRZ-PTA-DBPH



c) TRZ-PTA-NPOE



d) TRZ-PTA-NPOE

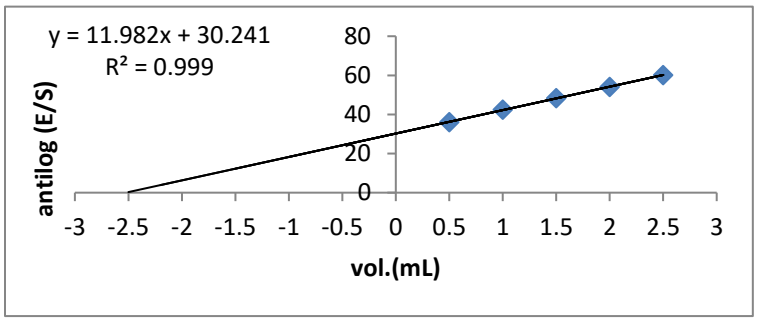


Figure 5. Potentiometric method applied at (a) 10^{-3} mol.L^{-1}; (b) 10^{-4} mol.L^{-1}; (c) 10^{-3} mol.L^{-1}; (d) 10^{-4} mol.L^{-1} of TRZ solution

The data in Figure 5 represent the application of the current method for the two sensors with the pharmaceutical tablets. From the experimental data, it can clearly be confirmed that the standard additions method was the better method for quantifying the drug in the pure (standard preparation of TRZ) form than other potentiometric methods.

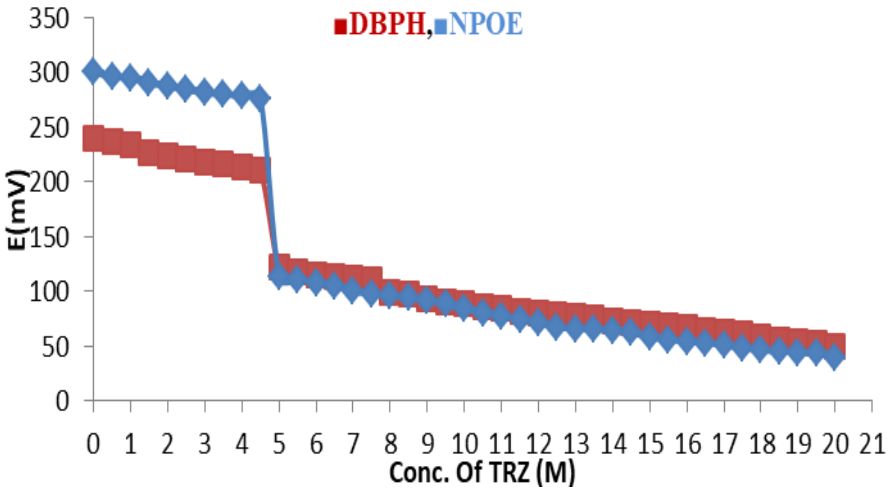


Figure 6. Application of potentiometric method by TRZ-PTA-DBPH and TRZ-PTA-NPOE at 10^{-3} mol.L^{-1} of TRZ solution

4. CONCLUSION

In this study, the development, validation, and application of three novel ion-selective electrodes (ISEs) were described. The method involved using phosphotungstic acid as a selector of trazodone (TRZ) in pharmaceuticals. In the current study, the highly selective and accurate quantification of TRZ in amounts with a wide linear range was successfully obtained. The Nernstian response showed good agreement values and low detection limits. The pH tested using all constructed sensors gave a wide range of approximately 2-8. This could possibly be useful, suggesting the advantages of applying electrodes for verifying pharmaceutical samples in direct measurements such as in TRZ drugs.

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Abbreviation

TRZ-PTA-DBPH: trazodone hydrochloride-phosphotungstic acid-di-butyl phthalate
TRZ-PTA-NPOE: trazodone hydrochloride-phosphotungstic acid-o-Nitro phenyl octyl ether
TRZ-PTA-DBP: trazodone hydrochloride-phosphotungstic acid-di-butyl phthalate
TRZ: trazodone hydrochloride
SAM: standard addition method
MSA: multistandard addition.

REFERENCES

[1] B. Wen, L. Ma, A.D. Rodrigues, and M. Zhu, Drug Metabolism and Disposition 36 (2008) 841.
[2] R.N. Hegde, N.P. Shetti, and S.T. Nandibewoor, Talanta 79 (2009) 36.
[3] S. Rotzinger, J. Fang, and G.B. Baker, Drug Metabolism and Disposition 26 (1998) 572.
[4] Z. Korade, L.B. Allen, A. Anderson, K.A. Tallman, T.C. Genaro-Mattos, N.A. Porter, and K. Mirnics, Translational Psychiatry 11 (2021) 1.
[5] A.V.S.S. Prasad, and C.S.P. Sastry, J. Chem. Sci. 115 (2003) 29.
[6] S. Mennickent, A. Gonzalez, M. Vega, G. Rios, and M.D. Diego, J. Chilean Chem. Soc. 59 (2014) 2408.
[7] A.R. Jay, U. Krotscheck, E. Parsley, L. Benson, A. Kravitz, A. Mulligan, J. Silva, H. Mohammed, and W.S. Schwark, American J. Veterinary Res. 74 (2013) 1450.
[8] W. Misiuk, and M. Zalewska, Carbohydrate Polymers 77 (2009) 482.
[9] S. Carda-Broch, M.T. Gil-Agustí, M. Rambla-Alegre, L. Monferrer-Pons, and J.S. Esteve-Romero, J. Chromat. A 51 (2007) 9295.
[10] L. Mercolini, C. Colliva, M. Amore, S. Fanali, and M.A. Raggi, J. Pharm. Biomed. Anal. 47 (2008) 882.
[11] L.J. Lovett, G.A. Nygard, and S.K. Khalil, J. Liq. Chromat. 10 (1987) 909.
[12] R.S. Kumar, D.H. Manjunatha, S.M.T. Shaikh, J. Seetharamappa, and K. Harikrishna, Chem. Pharm. Bull. 54 (2006) 968.
[13] N. El-Enany, F. Belal, and M.S. Rizk, J. Pharm. Biomed. Anal. 30 (2002) 219.
[14] I. Azeem, S. Mohiuddin, and A. Fatima, J. Basic Applied Sci. 12 (2016) 351.
[15] J.A. Ortuno, M.S. Garcia, M.I. Albero, and M. Cuartero, Sens. Lett. 7 (2009) 615.
[16] R. Ammar, and A. Al-Warthan, J. Inclusion Phenomena and Macrocyclic Chem. 69 (2011) 287.
[17] M.R. Ganjali, F. Aboufazeli, F. Faridbod, S. Riahi, and P. Norouzi, Chimica Oggi. 28 (2010) 4.
[18] F.M. Salama, K.A. Attia, R.A. Said, A. El-Olemy, and A.M. Abdel-raoof, RSC Advances 8 (2018) 11517.
[19] A. Amina, M. Al-Nahrain J. Sci. 2 (2018) 73.
[20] British Pharmacopoeia, Version 17 Copyright by, London (2012).
[21] V.M. Serrano, A.R. Cardoso, M. Diniz, and M.G.F. Sales, Sens. Actuators B 311(2020) 127902.
[22] S. Khalil, Analyst 124 (1999) 139.
[23] E.H. El-Naby, Chemosensors 7 (2019) 46.
[24] R.S. Kumar, D.H. Manjunatha, S.M.T. Shaikh, J. Seetharamappa, and K. Harikrishna, Chem. Pharm. Bull. 54 (2006) 968.

[25] A.Z. Yasser, R.S. Farag, M. Elnawawy, M.A. Ahmed, and S.R. Abd Alsalam, Int. J. Pharm. Sci. Res. 2 (2011) 2798.
[26] A. El-Gindy, B. El-Zeany, T. Awad, and M.M. Shabana, J. Pharm. Bioamed. Anal. 26 (2001) 211.
[27] S. Isabel, P. Rebelo, J. G. Pacheco, and C. Delerue-Matos, Sensors 7 (2022) 2819.
[28] G.M. Soledad, J. Ortuño, M. I. Albero, and M. Cuartero, Anal. Bioanal. Chem. 6 (2009) 1563.