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Potentiometric Determination of Chlordiazepoxide Using PVC and Carbon Paste Electrodes

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ABSTRACT
potentiometric technique is described for determination of chlordiazepoxide .A sensitive rapid ,simple method for evaluation of Chlordiazepoxide in pharmaceutical preparations and pure by using modified PVC and carbon paste electrodes is established. Chlordiazepoxide selective electrodes were produced as of chlordiazepoxide- phosphotungetic acid as an electroactive with n-Di-butyl phthalate(DBPH) in THF as a solvent. Various factors influencing the response of electrodes were improved and plotted the calibration curve . PVC and Carbon paste electrode constructed were gave a Nernstian response about 54.00, 57.51 mVdecade^{-1}, respectively with an extensive range of concentration , from 3.0×10^{-6}-1.0×10^{-2} and 1.8×10^{-6}-1.0×10^{-2} M, for PVC, carbon paste electrode, respectively, with a little detection limit near to 2.2×10^{-5}, 1.4×10^{-5}M. The pH values for quantifiable was detected .Lastly, the projected electrode was used as effectively for the determination of chlordiazepoxide by potentiometric techniques in pure and pharmaceutical samples.
Keyword: carbon paste electrodes, chlordiazepoxide, potentiometric method, ion selective electrode.
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INTRODUCTION

Chemically, chlordiazepoxide is:7-chloro- -methyl-5-phenyl-3H-1,4-benzodiazepin-2-amine 4-oxide.Almost white or light yellow, and crystal clear powder, practically unsolvable in water, sparingly in ethanol solvable .Molecular weight of it equal to 299.8 g /mole and It is used as benzodiazepine [1].

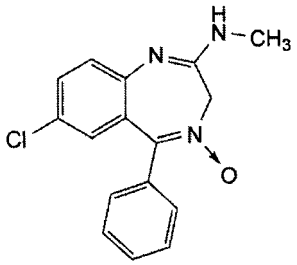

Figure1: Chemical Structure of Chlordiazepoxide.

It is needed to improve a quick and special process for the assessment of chlordiazepoxide .Several methods were already published involving: Spectrophotometric methods [2,3]. Voltammetric method [4]. HPLC Method [5-10]. The technique of analytical more used for observing ,the reason, it's today a numeral of benefits, for instance little time of response, easiness, selectivity, little charge, precision, suitable accuracy plus capability to evaluation the analytes in turbid and coloured samples, it is called potentiometry [11]. Electrochemical sensors depended on paste of carbon templates are easy and economic at ease to fabricate, also steady electrochemical replies and have lesser ohmic resistance and lengthier functional lifetime [12]. Further fascinatingly, a number of electroactive convertors make available an excellent electro catalytic. Electroactive modernizers, oppositely, interrelate with change chemical reactions or alternatively and analyte molecules, they doing as a novel part on the showing part of the electrode [13] .There are many carbon paste electrodes prepared to determination drugs in pure and pharmaceutical formulations such as: Dopamine[14], Flavoxate hydrochloride [15], Antidiabetic drugs [16], Ketotifen Fumarate [17], Clonazepam[18], Asenapine Maleate [19], Pethidine hydrochloride[20], Losartan potassium [21]. In this research, It has been prepared PVC electrode and carbon paste electrode have been made to measurement widen the concentration range and lower detection limit with using ion-association(CDP-PTA) which show a good performance properties and sensitive response. These electrodes were prepared to provide perfect data for the evaluation of chlordiazepoxide in pharmaceuticals formulation.

EXPERIMENTAL PART

Equipment

Every part of potentiometric analysis were made at room temperature with an Micoprocessor pH211, pH/mV/C Meter, HANA, Made in Romania. The potentiometric analysis were showed using the made-up chlordiazepoxide CDP-PTA electrodes with a reference electrode: calomel electrode (SCE). The pH data were verified by using a PH Electrode, H11131, HANA. The procedure were a included assembly of the electrode body with chlordiazepoxide CDP–PT membrane in matrix of PVC which be there made by follow method which applied by Craggs et al. [22]

Chemicals

All chemical used were highest purity with reagent grade. Chlordiazepoxide (CDP) supplied from State Company and Medical Appliance and Drug Industries (Samara, RAQ-SDI),Librium was from(Medical Union Pharmaceuticals (MUP), Ismailia, Egypt),Chloridazachel was from (Hikma Pharma S.A.E, Egypt), Lygen was equipped from(production of veterinary drugs, Al-Mahalla Al-Kubra, Al-Gharbia, Egypt).

Phosphotungestic acid was from BDH, Di-n-butyl phthalate(DBPH) as a plasticizer, was given by Fluka AG, Chemical Poly(vinyl chloride) was provided as of U.K. Ltd., (BDH) was supplied Tetrahydrofuran (THF) and the solutions at concentration 0.1M were provided from as: $MgCl_2$, KCl ,$AlCl_3$, $CaCl_2$,NaCl , $FeCl_3$, at then balancing diluted solutions arranged by consecutive thinning from the primed solutions. and, Each chemicals composites of analytical were equipped from Aldrich, BDH Fluka, .

Construction of Membrane

The PVC membrane was prepared with mix 0.04 g of the ion-pair, 0.17 gm of PVC and plasticizer (DBPH) equal to 0.4 gm .Later homogenization, 5-7 mL of THF as a solvent was used by stir up. The admixture was transported inside glass ring which have a 5 cm in diameter and let to vaporize for one day. The electrode was prepared by used Tygon tube by cut the membrane of PVC and paste at the end of tube with used mixture PVC/THF solution as an paste. A reference electrode was used with silver wire which coated with silver chloride and contain 0.01 M solution of CPD put in the second end of the Tygon tube .The electrodes were immerse in 0.01 M solution previous to use.

Formulation of carbon paste electrode

Improved carbon paste electrode by weighed quantities of high purity graphite and ion pair (CPD-PTA) till gaining an equally moistened paste. Then the mix was packed at the end of syringe made from a polypropylene (1 mL, 3 mmi d,). The carbon paste electrical connection by used a copper wire, with smoothened by paper till it be a polished attendance and used soon. Figure 2 shows the construction of carbon paste electrode.

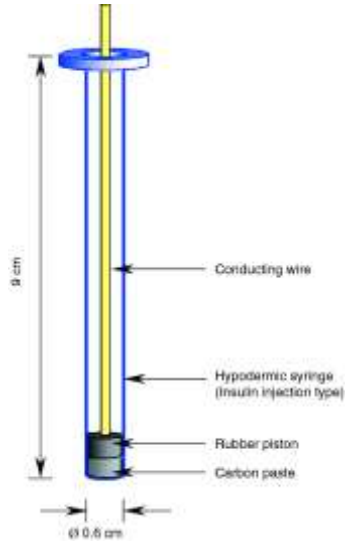

Figure2: Assembly of carbon paste electrode

Consequences and Argument

Electrochemical performances are adaptable and useful analytical methods that proposal high precision sensitivity, and accuracy, in addition to a wide linear dynamic range, with little-price instrumentation [23]. Two ion selective membrane electrodes, PVC, CPE membrane was fabricated for evaluation of CPD. The properties of CPD electrodes shown in diagram 1,2 and recorded in Table 1.

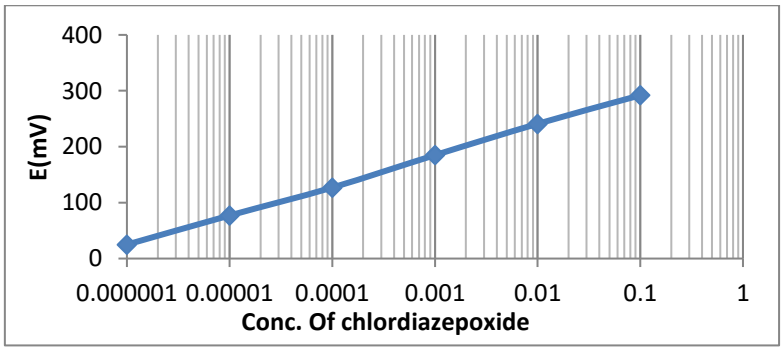

Diagram 1: Correction Curvature of chlordiazepoxide (PVC) electrode

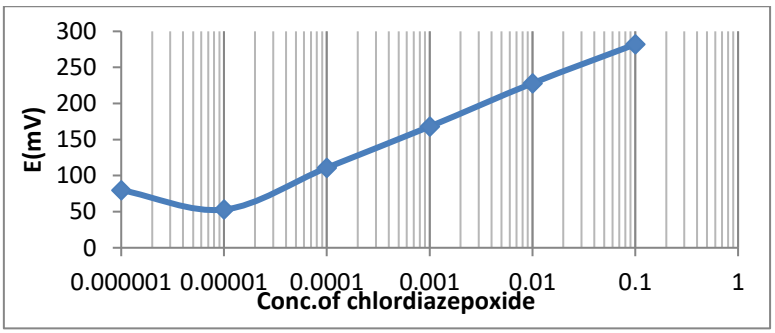

Diagram 2: Correction Curvature of chlordiazepoxide (CPE).

Table 1: Response of chlordiazepoxide electrodes

Parameters	PVC)electrode(	CPE(electrode)
Slope(mV decade^{-1})	54.00	57.51
Concentration Range(mole L^{-1})	3.0×10^{-6}-1.0×10^{-2}	1.8×10^{-6}-1.0×10^{-2}
Detection Limit(mole L^{-1})	2.2×10^{-5}	1.4×10^{-5}
Correlation coefficient	0.9992	0.9998
Regre. Eq.Y=mX+b	Y=23.452ln(x)+347	Y=24.972ln(x)+340.9
Life Time(week)	3	5

PH Influence

The Influence of pH for chlordiazepoxide solutions at concentration equal to 10^{-3} M was examined .It was studied at range(2.0-5.0) as well as (1.0-6.0) of pH aimed at PVC and CPE electrodes ,respectively .The alteration of pH limitation in measurement of solutions by used electrode is imperative. On the other hand, there is not variation in changing the pH at range of (1.0-6.0) when there is no conductivity of the carbon paste electrode .Diagram 3 shows the influence of PH, also the values of changes in PH listed in Table 2.

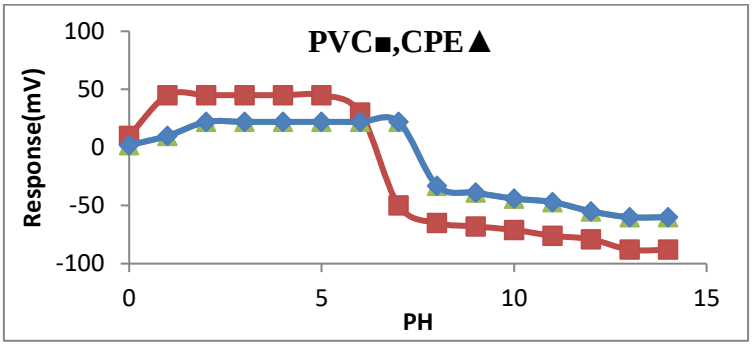

Diagram 3: PH Effect of chlordiazepoxide Electrodes

Table2: PH Influence for chlordiazepoxide Electrodes

Type of Electrode	Range of PH
PVC (electrode)	2.0-5.0
CPE(electrode)	1.0-6.0

The potential of examined electrodes was changed by report of difference in the potential of cell while little volumes of sodium hydroxide or / and hydrochloric acid were added to 1.0×10^{-3} mol/L of chlordiazepoxide (Diagram 3). It is clear that the electrodes do not respond to pH changes in the range from 2.0-5.0and 1.0-6.0 for electrodes PVC, CPE, respectively Table 2). The decrease in the cell potential at pH values higher than 5 is utmost possibly because of the construction of the non-protonated drug or the construction of free chlordiazepoxide base in the trial solution. The suggested electrodes were effectively used for the determination of chlordiazepoxide.

Studies of Interference

Matched potential method (MPM) was applied for calculation the selectivity and determination of interferences, The selectivity coefficient was determined for interferences. By use main ion concentration (activity) to the interfering ion by following equation[24,25]:

Log. Kpot A,B = [(EB– EA) z A F / 2.303 RT] + (1 – z A / z B) log a A.

In addition, the selectivity coefficients of interfering species for the chlordiazepoxide ion-selective electrode to assayed. Magnetic stirrer was used for stirred the solution and with every addition. The selectivity coefficients for the chlordiazepoxide PVC and carbon paste electrode are presented in Table 5.

Table3: Calculated of Selectivity coefficients for 1×10^{-3} M chlordiazepoxide using PVC and CPE electrodes.

Interfering Ions	$K^{POT}_{A,B}$ for PVC Electrode	$K^{POT}_{A,B}$ for CPE Electrode
K^+	1.3180×10^{-4}	5.1744×10^{-4}
Na^+	7.1676×10^{-5}	5.6081×10^{-4}

Ca^{+2}	2.4237×10^{-5}	1.3169×10^{-5}
Mg^{+2}	1.3726×10^{-5}	2.9454×10^{-5}
Fe^{+3}	1.4262×10^{-6}	3.8150×10^{-6}
Al^{+3}	6.0790×10^{-7}	2.8788×10^{-6}

Diagram of the selectivity coefficient vs. log [CPD] for PVC,CPE electrode are illustrated in Diagram 4,5. The values of the selectivity coefficients ranged from1.3180×10^{-4} to 6.0790×10^{-7} and from5.1744×10^{-4} to2.8788×10^{-6} for chlordiazepoxide PVC and CPE electrodes, respectively over chlordiazepoxide concentrations for 10^{-3} M However, values were great for trivalent rather than monovalent and divalent.

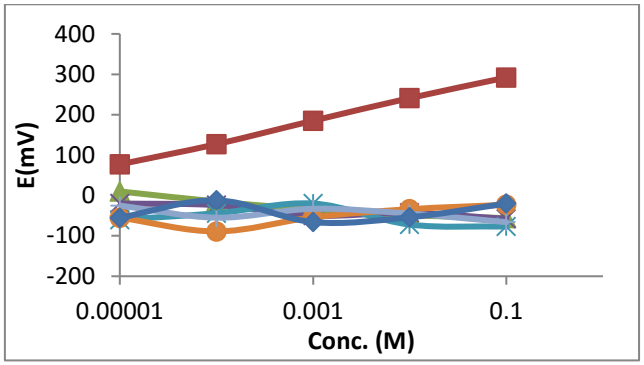

Diagram 4: Selectivity of PVC electrode for cations interferings.

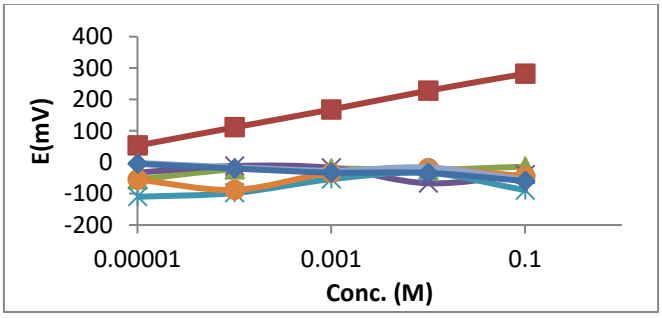

Diagram 5: Selectivity of CPE electrode for cations interferings.

The selectivity of the suggested electrodes to chlordiazepoxide in existence of inorganic linked materials, was evaluated. Table 2 listed the values of selectivity coefficient for two electrodes for some general cations, Because of the very small values of (–), which shows in Diagram 4 and 5, they were as the negative logarithm (–). The lesser values of the coefficient of selectivity for the electrode reflect a very in height selectivity for cations of chlordiazepoxide in the existence of interfering ions.

Quantifiable Exploration of chlordiazepoxide

Standard addition technique [26] was utilized for the evaluation the concentration of CPD tablet supplied from. The results were found by use PVC and carbon paste electrode are recorded in Table 4. The range of recoveries were from 95.70% to 96.18 % and 94.62 to 96.37 for PVC electrode and from 93.90% to 97.11% and 95.41% to 97.48%for CPE electrode were calculated for the four methods .Values of percent recoveries and relative standard deviation of chlordiazepoxide shown in Table 4 with diagram 6,7,8,9.

Table 4: Analysis of chlordiazepoxide samples by Potentiometric techniques

Electrode Type	Concentration(M)				
	Sample	Response by potentiometric method			
		Direct	SAM	MSA	Titration
PVC+ DBPH+PTA	1×10^{-3}	0.9570×10^{-3}	0.9642×10^{-3}	0.9834×10^{-3}	0.9618×10^{-3}
	RSD%	2.3	1.5	-	-
	Re%	95.70	96.42	98.34	96.18
	Er%	- 4.3	-3.58	- 1.6	-3.82

	1×10^{-4}	0.9462×10^{-4}	0.9597×10^{-4}	0.9715×10^{-4}	0.9637×10^{-4}
	RSD%	1.5	0.8	-	-
	Re%	94.62	95.97	97.15	96.37
	Er%	-5.38	-4.03	-2.8	-3.63
CPE+ DBPH+PTA	1×10^{-3}	0.9390×10^{-3}	0.9766×10^{-3}	0.9722×10^{-3}	0.9711×10^{-3}
	RSD%	3.1	2.00	-	-
	Re%	93.90	97.66	97.22	97.11
	Er%	-6.1	- 2.34	-2.7	-2.89
	1×10^{-4}	0.9541×10^{-4}	0.9819×10^{-4}	0.9844×10^{-4}	0.9748×10^{-4}
	RSD%	2.6	1.7	-	-
	Re%	95.41	98.19	98.44	97.48
	Er%	-4.5	-1.8	-1.56	-2.52

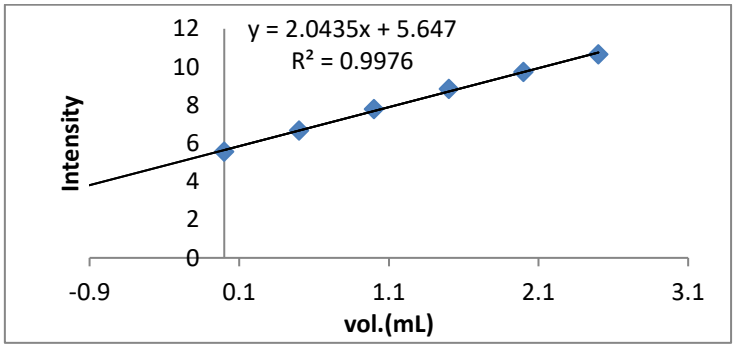

Diagram 6: Intensity vs. volume of chlordiazepoxide at 10^{-3}M with using electrode PVC

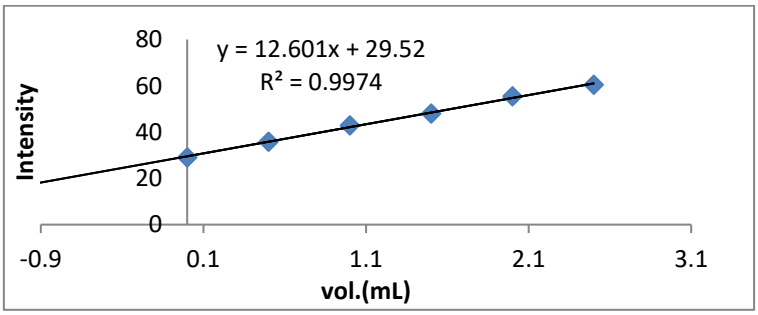

Diagram 7: Intensity vs. volume of chlordiazepoxide at 10^{-4}M with using electrode PVC

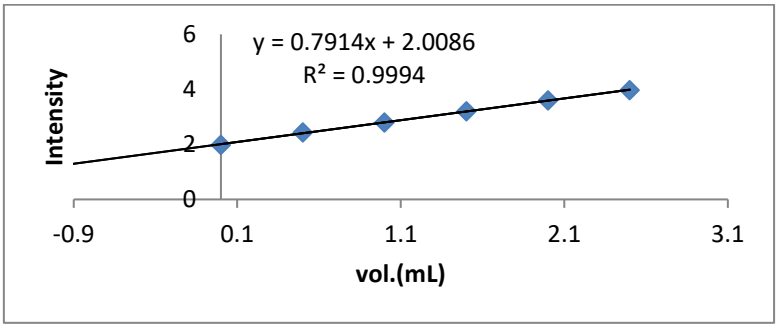

Diagram 8: Intensity vs. volume of chlordiazepoxide at 10^{-3}M with using electrode CPE

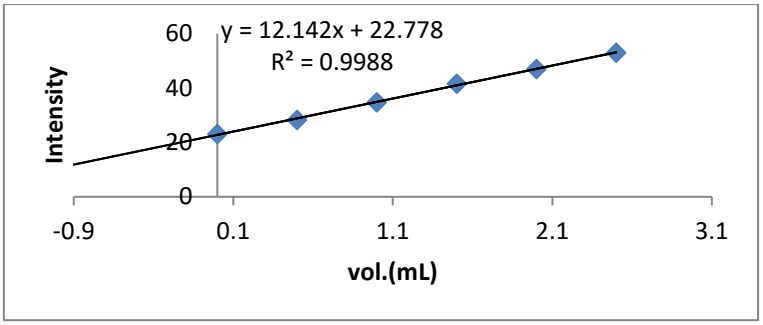

Diagram 9: Intensity vs. volume of chlordiazepoxide at 10^{-4}M with using electrode CPE

Table 5: Direct potentiometric method for analysis Pharmaceutical drugs using the chlordiazepoxide selective electrode based on CPE.

Pharmaceutical drugs	Librium	Chloridazachel	Lygen
Concentration of CDP(prepared)	1.00×10^{-3}	1.00×10^{-3}	1.00×10^{-3}
Concentration of CDP(found)	0.9815×10^{-3}	0.9989×10^{-3}	0.9868×10^{-3}
RE%	98.15	99.89	98.68
Er%	-1.8	-0.1	-1.3

By applied the direct potientiometric method for the determination chlordiazepoxide with using three types of drugs (Librium, Chloridazachel, Lygen), the results were listed in Table 5 shows the values of concentration which equal to 0.9815×10^{-3}, 0.9989×10^{-3} and 0.9868×10^{-3} mole /L with recovery near to 98.15, 99.89 and 98.68 with relative error were about -1.8,-0.1 and -1.3, respectively for CPE electrode. Direct potentiometric method was used to determination chlordiazepoxide due to the two type electrode were given a similar Nernstain response.

CONCLUSION

The carbon paste electrode is a good device for soon chlordiazepoxide hydrochloride determination and can be used for soon uses in actual samples without any pretreatment. Chlordiazepoxide selective electrodes based on PVC and CPE membrane were prepared effectively. The electrodes gave excellent response near to Nernstian slopes were ranging from 54.00 to 57.51 mV decade $^{-1}$ with operating in excess of the concentration range of 3.0×10^{-6} to 1.0×10^{-2} and 1.8×10^{-6}-1.0×10^{-2} M for PVC and CPE electrodes, respectively. The novel electrodes were gave sensitivity and selectivity, short response time, life times of more than three weeks and five weeks, and good stability. The electrodes have a wide-ranging of pH (2.0-5.0) and (1.0-6.0). The suggested potentiometric technique displays a better sensitivity, little limit of detection, and excellent steadiness of carbon paste electrode rather than the PVC membrane. The CPE and PVC membrane have shown relatively long term stability, quick response time, and better Nernstian slope, To finish, the made chlordiazepoxide electrodes can be used for the evaluation of CPD in pharmaceutical product.

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