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Research Article

Novel Sensors for Potentiometric Determination of Diphenhydramine Hydrochloride

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Abstract

The formation and working properties of sensor membranes for a just now found Diphenhydramine (DPH) deal with its ion-pair complexes with Phosphotungestic Acid (PTA) in a poly (vinyl chloride) (PVC) matrix were explained. More suitable sensor for determination of diphenhydramine was based on di-n-butyl phthalate (DBPH) as the plasticizer. This sensor exhibits a Nernstian response (52.50mV decade^{-1}) with range 4.7x10^{-6} to 1.0x10^{-1} M of DPH solutions with PH working about (3.0-5.5). Selectivity of this sensor to DPH in the existence of cations is reported. The second electrode which prepared from di-n-butyl phosphate (DBP) as a plasticizer was gave a small value of slope near to (8.5mV per decade) with concentration range equal to 4.8x10^{-6}-1.0x10^{-3} M, PH range was (1.5-3.5). Also selectivity coefficient was calculated for electrode depended on DBPH as a plasticizer in opposition to some cations. The potentiometric methods are used to determine the DPH quantity in pure and pharmaceutical production.

Keywords: Diphenhydramine; Sensors; Liquid Membrane; Plasticizers; PVC; Selectivity

Introduction

Sensors have long suit vital and trustworthy devices for chemical, biomedical and pharmaceutical laboratory research; they are have a varied range of usage, well to use, also low-cost. More of prevailing values for the formation of membrane, s sensor is the adding up of a lipophilic ion-pair complex into a to a great extent plasticized membrane. Suitable sensor or liquid membrane electrode for drugs have sufficient selectivity to the drugs over pharmaceutical excipients and they can be beneficial in the quantifiable analysis of the drugs in pharmaceutical formulations with no earlier separations. In specific, sensors are actual beneficial in the item in point of drugs which are unsteady through prior separation. Diphenhydramine(2-(diphenyImethoxy)-N, N- dimethyethylamine hydrochloride, see in Figure 1, is a H_1-receptor antagonist used clinically for its antihistaminic, antiemetic, sedative and local anaesthetic influences. It has also been used for the prevention and treatment of vomiting, nausea, and for the control of Parkinsonian symptoms [1,2].

It's crystalline powder, white or almost white and freely soluble in alcohol, very soluble in water, with molecular weight equal to 291.8gm per mole [3]. The measurement of this drug were recorded by using Spectrophotometer with HPLC methods were developed at λ_{max} = 254nm [4]. Spectrophotometric method has been described for determination of diphenhydramine hydrochloride (DPH) [5,6,7]. New Conductometric Titration Methods for Determination of Diphenhydramine Hydrochloride Using Sodium Tetraphenylborate and Cetylpyridinium Bromide [8]. New method was developed and validate a single HPLC method, in order to separate and assay diphenhydramine [9], In this work sensors for determination diphenhydramine based on two type of plasticizers in PVC matrix with study the characterization of sensors with the effect of PH and applied these sensors in its pure form and pharmaceutical samples then compared the results with the another sensors of diphenhydramine hydrochloride.

Materials and Methods

Experimental part

Diphenhydramine pure sample was supplied by (Samara, RAQ-SDI) Drug Industries and State Company and Medical Appliance, Benadryl (diphenhydramine HCl 25mg, ULTRATABS), Equate (diphenhydramine HCl 25mg), Diphenhydramine HCl Capsules, USP, 50mg). All chemicals use up were and solvents of analytical reagent grade. Distilled water was use up. Phosphotungestic acid was from BDH, Plasticizers: Di-n-Butyl Phosphate (DBP), Di-n-Butyl Phthalate (DBPH), were given from Fluka AG, Chemical PVC was supplied from UK. Ltd., Phosphotungestic Acid (PTA) was obtained from (BDH), Tetrahydrofuran (THF) was supplied from (BDH). From stockpile solution which concentration 0.1M were prepared of $AlCl_3$, $FeCl_3$,$CaCl_2$, $MgCl_2$, NaCl, and KCl, complementary thinned solutions prepared by succeeding dilution of the solution. From Fluka, Aldrich and BDH, all chemicals compounds of analytical were supplied.

Instruments

1- pH/mV/C Meter, Micoprocessor pH211, HANA, Made in Romania.

2- Calomel (Gallen Kamp (USA)) as a Reference Electrode.

3- PH Electrode, H11131, HANA.

4-Wire of Ag/AgCl (1mm diameter) was dipped in the inner reference solution as an internal reference electrode.

The measurements for the suggested sensors

Practically, measurements were worked at temperature equal to

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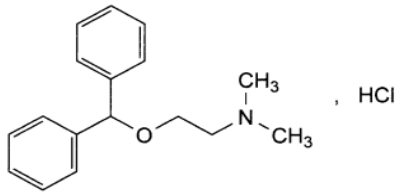


Figure 1: Chemical Structure of diphenhydramine Hydrochloride.

(25±2°C) with stirred solutions. Standard drug solution 1.0×10^{-1}M were thinned for get a successions of solutions and values of the E.M.F were documented by use (DPH) sensor in combination with a SCE as a reference electrode next steadying to ±0.2mV, the measurement curvature was plotted. The measurement curvature was use up to determining the concentrations of solution which were unidentified under the same states [10].

Sensor construction

The electrochemical operation characters of sensors were steadily appraised assenting to (IUPAC) references. The consequences were set in Table 1. Undercurrent work, DPH was institute to be the more suitable plasticizers of sensor1. It plasticized the sensor, and dissolved the ion pair as an active material, and regulated the selectivity of the membranes; therefore, it provided the best results. The components of membrane were liquefied in THF, which was little by little vaporized at room temperature leading to membrane establishment [2].

Effect of pH

The variants of pH were studied by the adding of (HCl) and (NaOH) solutions. Values of pH vs. sensor potential were listed and were plotted [11]. The examinations were achieved in 10^{-3}M of DPH solutions; the potential reached at all pH value was listed in Table 2 [12].

Selectivity of sensors

The influences of the connected interfering composites on the reply of the examined sensors about the drug was examined. The method which applied was separate solution method (SSM), based on determining the potential of 10^{-3}M solution of both interfering ions and drug. By applying the succeeding equation below, the selectivity coefficients were calculated [13-18].

$$E = E_0 + R\,T/Z_A F \ln [aA + \Sigma K_{A,B}(a_B)Za/Zb]$$

Which E = potential was measured; E_0 =the standard potential of the reference electrode, (z_A, z_B, $a_A$and a_B = numbers of activities and charge of the interfering ion B and major ion A), and $K_{A,B}$ = selectivity coefficient for the interfering ion B vs. the major ion A. The interfering composites were chlorides including; (potassium, calcium, magnesium, sodium, magnesium, ferric and aluminum) chlorides. Selectivity coefficients which calculated point to that the suggested sensor was very selective to the studied drug as shown in Table 4.

Result and Discussion

The PVC-membrane sensor based on DBPH as a plasticizer with ion pair: (DPH+PTA) as an active material prepared underneath optimized trial circumstances resulted for the response of a DPH concentration reply by a Nernstian slope of 52.50mV decade^{-1} more

Table 1: Response of diphenhydramine hydrochloride sensors (DFH-PTA).

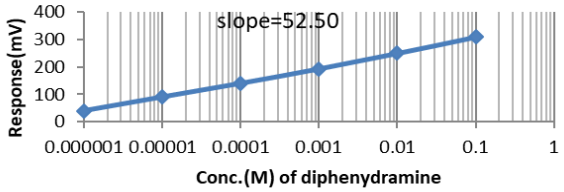
Type of membrane	DPH+ DBPH+PTA	DPH+ DBP +PTA
Range of Concentration(M)	4.7×10^{-6}-1.0×10^{-1}	4.8×10^{-6}-1.0×10^{-3}
Correlation coefficient ®	0.9993	0.999
limit of Detection(M)	1.5×10^{-6}	1.4×10^{-6}
Slope (mV/decade)	52.5	8.5
Regre. Eq. Y= mX+b	Y=22.8ln(x)+352.4	Y=3.691ln(x)+205
Lifetime (day)	41	5

Table 2: Range of the value of PH for diphenhydramine solution.

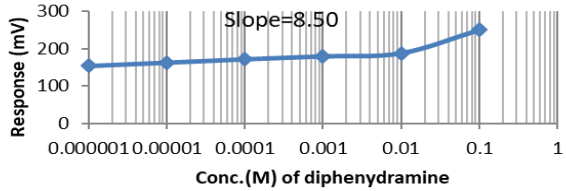
NO. of membrane	Membrane composition	Concentration of solution(10^{-3})M
1	*Dph+DBPH+PTA*	3.0-5.5
2	*Dph+DBP+PTA*	1.5-3.5

Table 3: Selectivity coefficients calculated of 1×10^{-3} M diphenhydramine by (DBPH) sensor.

Interfering Ions	$K^{POT}_{A,B}$
K^+	1.1659×10^{-5}
Na^+	2.7421×10^{-6}
Ca^{+2}	3.0529×10^{-7}
Mg^{+2}	1.6887×10^{-8}
Fe^{+3}	4.5304×10^{-7}
Al^{+3}	3.1897×10^{-7}



Scheme 1: Response of Diphenhydramine sensor, which based on DBPH.



Scheme 2: Response of Diphenhydramine sensor, which based on DBP.

a widespread of concentration range of 4.7×10^{-6} to 0×10^{-1} M. The detection limit, which estimated by the crossing of the two draw conclusions sections of the correction diagram, was 1.5×10^{-6} M. The membrane of sensor was organized can be use up for a minimum 41 days with no a little measurable difference. The slope of the correction curvature reduced afterward 41 days with no a little calculable change in the range of concentration. Another sensor, which prepared from DBP as a plasticizer was, gave non-Nernstian slope equal to 8.5mV decade^{-1} with range of concentration near to 4.8×10^{-6} to 1.0×10^{-3}M. Detection limit was about 1.4×10^{-6}, life time was near to 5 days. This may be due the leakage of the electro active component into the measurement media and swelling of the membrane in water in the

Table 4: Determination of diphenhydramine in pure diphenydramine hydrochloride.

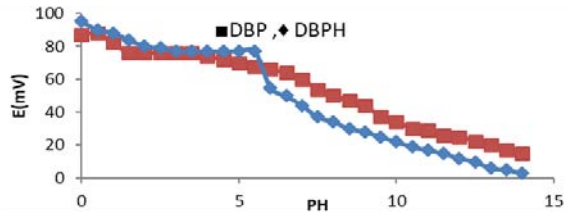
Electrode Type	Concentration(M)v				
	Sample	Potentiometric method Response			
		Direct	SAM	MSA	Titration
	1×10^{-3}M	0.9503×10^{-3}	0.9621×10^{-3}	0.9930×10^{-3}	0.9759×10^{-3}
	RSD%	1.54	3.62	-	-
DPH+DBPH+PTA	Re%	95.03	96.21	99.3	97.59
	Er%	-4.97	-3.79	-0.7	-2.41
	1×10^{-4}M	0.9425×10^{-4}	0.9639×10^{-4}	0.9765×10^{-4}	0.9712×10^{-4}
	RSD%	1.26	0.76	-	-
	Re%	94.25	96.39	97.65	97.12
	Er%	-5.75	-3.61	-2.35	-2.88

Table 5: Determination of diphenhydramine in tablets.

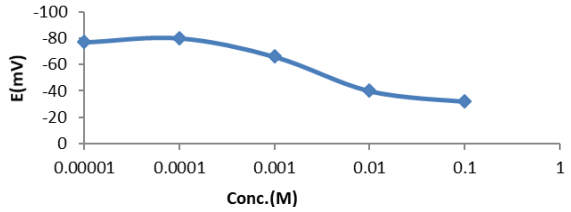
Pharmaceutical tablets	Benadryl (diphenhydramine HCl ,25mg)	Equate (diphenhydramine HCl ,25mg)	Diphenhydramine HCl Capsules, 50mg)
Concentration of TMP(prepared)	1.00×10^{-3}	1.00×10^{-3}	1.00×10^{-3}
Concentration of TMP(found)	0.9745×10^{-3}	0.96854×10^{-3}	0.97123×10^{-3}
RE%	97.45	96.85	97.12
Er%	-2.55	-3.15	-2.88

Table 6: Comparison between potentiometric characters of different diphenhydramine electrodes.

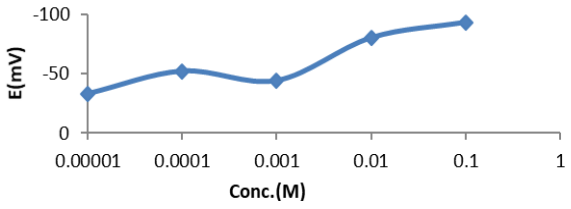
Ref .No.	PH range	Response Time sec	Life Time day	Slope mv/decade	Detection Limit(M)	Range of concentration (M)	Type of electrode
16	10-Jul	<5 s	-	56.86 and 59.8	1×10^{-7}	9.1×10^{-3}-6.3×10^{-7}	DPH-diazacrown ether and tetraflorophenyl borate
17	3.0-8.0 and 3.0-7.0	-	-	55.2±1.0 and 54.7±1.0	9.70×10^{-7} and $9.80.10^{-7}$	1.0×10^{-2}-1.0×10^{-6}	DPH-screen paste electrode
18	2.5-8.0 3.0-9.0, 2.5-7.0 3.0-8.0	5,6,10,11	-	56.20±0.65, 59.14±0.90, 55.86±1.12 and 60.03±1.32	9.76×10^{-7}, 9.78×10^{-7}, 9.68×10^{-7}, 9.65×10^{-7}.	1.0×10^{-6}-1.0×10^{-1}	Sodium tetraphenylborate with Screen printed(SPE) Carbon paste(CPE)
This work	3.0-5.5	-	42	52.5	1.5×10^{-6}	4.7×10^{-6}-1.0×10^{-1}	DPH-PTA



Scheme 3: Effect of PH by diphenhydramine solution.



Scheme 4: Calibration graph for diphenhydramine and interfere ion Na^+ for sensor (DBPH).

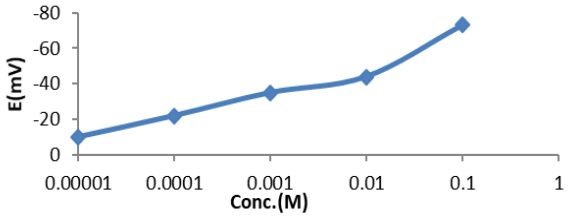


Scheme 5: Calibration graph for diphenhydramine and interfere ion Ca^{2+} for sensor (DBPH).

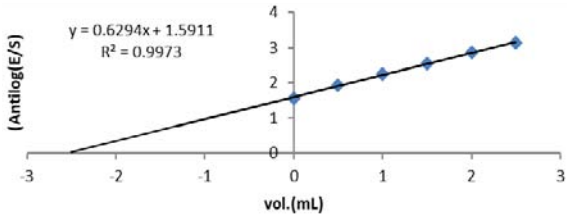
long run causes a loss of performance in potentiometric properties. Scheme 1,2 shows the calibration of DPH sensors and Table 1 shows the values of response for DPH-sensor.

pH of sensors

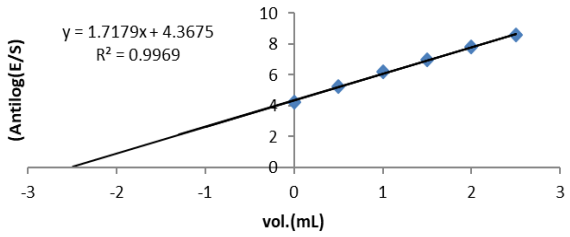
Examines were approved to limit the optimal range of pH. The impact of PH on the reply of the studied sensors was estimated by used the solution of DPH at concentration 10^{-3}M. PH was slowly augmented or reduced by addition drips of HCl or NaOH solutions, respectively. It is seeming from Scheme 3 that the replies were properly perpetual at pH range 3.0-5.5 and 1.5-3.5 for the two sensors, more than and lower these ranges, the potentials showed by the sensors were loud, this may be because the concurrent reply of the sensor to DPH and H^+ at pH upper than 5.5, it possibly will be due of comparatively robust rivalry amid DPH and Na^+ (from NaOH).



Scheme 6: Calibration graph for diphenhydramine and interfere ion Fe^{3+} for sensor (DBPH).



Scheme 7: Antilog (E/S) vs. volume of 10^{-3} M added of diphenhydramine by use electrode (DPH+DBPH+PTA).



Scheme 8: Antilog (E /S) vs. volume of 10^{-4} M added of diphenhydramine by use electrode (DPH+DBPH+PTA).

Scheme 3 show the effect of PH and Table 2 recorded the values of PH range.

Selectivity measurements

Selectivity is a significant quality, which explains the natural surroundings of the device and the range to which it might be well working. The selectivity were examined with esteem to some public cations using SSM. The data listed in Table 3 indicated the selectivity coefficients ($K^{pot}A$, B) values for the verified cations. These values obviously designated that, the suggested sensor was properly selective to diphenhydramine cation above diverse tried cations. However, for entirely of the varied ions was use, the selectivity coefficients were lesser than 1, that the deliberate public cations would not meaningfully interrupt the determination of diphenhydramine. Affording to the SSM, the selectivity coefficients which were determined by use up 1×10^{-3} mole L^{-1} trial solution of diverse cations. The resulting selectivity coefficients are plotted in Scheme 3,4,5.

Analytical chemistry

The constructed and characterized sensor was used to quantify through direct, standard addition, multi standard and titration methods, with direct potentiometry the analytes from some pharmaceutical products such as tablets. The results were recorded in Tables 4,5 plotted in Schemes 6,7,8.

Comparison study

To compare the sensor with the electrodes which prepared from different electro active and plasticizers, the potentiometric properties with respect to detection limit sensitivity, effect of pH, linear range, and life span of the diphenhydramine sensors were recorded in Table 6.

Conclusion

The proposed chemically modified sensor based on diphenhydramine- phusphotungestic acid as an electro active was inexpensive preparation, firm reply, and lesser detection limit, in height sensitivity, better selectivity, and opposition to variation of pH in excess of a wide-ranging. Furthermore, it might be use for measurements of a wide-ranging of concentration above a lengthy lifetime. Then, this sensor may be an exact another analytical implement for the measurement of DPH^{+} in pure forms, samples and in being there of its degradation yields.

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