Analysis of Trimetazidine Hydrochloride Hydrochloride and Diprone Using Ion Selective Electrodes Based on Heterogeneous Ion Exchangers

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1. INTRODUCTION

ION-SELECTIVE ELECTRODES

A chemical sensor is a device that selectively, continuously and reversibly transforms chemical information, ranging from the concentration of a specific sample compopnent to a total composition, into a single of a form that can be processed by an instrument (such as voltage, current or frequency). Ion-selective electrodes (ises) belong to the most widely applied chemical sensors.

TYPE OF ION-SELECTIVE ELECTRODES

A. GLASS ELECTRODES

a. PH ELECTRODES

b. GLASS ELECTRODES FOR OTHER CATIONS

B. LIQUID-MEMBERANCE ELECTRODES

C. ION-EXCHANGER ELECTRODES

D. NEUTRAL CARRIER ELECTRODES

E. ENZYME – BASED ELECTRODES

F. SOLID – STATE ELECTRODES

G. COATED-WIRE ELECTRODES (CWES)

H. ION SELECTIVE FIELD EFFECT TRANSISTORS (ISFET)

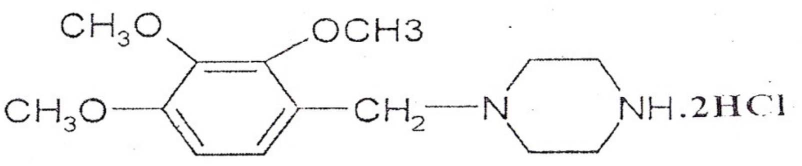
I. GAS – SENSING ELECTRODES

2. METHOD & MATERIAL

There are some compound like :-

TRIMETAZIDINE HYDROCHLORIDE (TMH)

TRIMETAZIDINE HYDROCHLORIDE IS 1-{(2, 3, 4-Trimethoxypheny1)methy1}-piperazine dihydrochloride (TMH). It is used in angina pectoris and in ischaemia of neurosensorial tissues as in menier's diseases. Trimetazidine hydrochloride with proprietary preparations vastarel, which has been given in divided doses of 40 to 60mg daily by mouth as anti -anginal vasodilator drug.



Trimetazidine hydrochloride (TMH)

3. DIPRONE (DP)

DIPRONE (Sodium salt of 1-phenyl1-2, 3-dimethy 1-4-methylaminomethane sulphonate-5-pyrazolane) is marketed in Brazil as such or as the magnesium salt as well as in association with other drugs through 51 and 75 registered trade names, respectively.

4. EXPERIMENTAL

The conventional sensitive electrodes were prepared as described previously. Trials make to attain the optimum membrane composition, result in selecting membranes contained the optimum percentages (in wt %) ion-pairs or ion- associates, PVC and DOP or DBP. The membrane components (totaling 350 mg) were dissolved in THF (10.00) and poured into a 7.5 com Petri dish. Overnight evaporation of the solvent yielded a membrane 0.1 mm thickness, as visually determined by an optical microscope. For each electrode, a disk with 14 mm diameter was punched from the membrane and glued to the polished end of a 2 cm plastic cap attached to one end of a 10 cm glass tube. The electrodes were than filled with 0.1 M Nacl + 10^{-3} M drug solution and Ag/AgCl wire was immersed in this solution. The resulting electrodes were preconditioned by soaking them for appropriate time in 10^{-3} M drug solution.

5. RESULT AND DISCUSSION

The Four electrodes have been prepared and investigated in the present study. The electrodes were based on the incorporation of the ion-exchangers in PVC matrix using DOP or DBP as a platicizer. The optimum composition of membrane were : (5.0% TMH-TPB, 47.5% DOP and 47.5% PVC), (10.0% TMH-PT, 45.0% DBP and 45.0% PVC), (3.0% BETPB, 48.5% DBP and 48.5% PVC) and (4.0% DP-PT, 48.0% DOP and 48.0% PVC), respectively with slopes 56.5, 57.8, 57, 60.2 and 59.1, 57.8, 60.2 and 59.1 mV per concentration decade for TMH-TPB, TMH-PT, DP-TPB, DP-PT, respectively. These compositions have been used to carry out all the subsequent studies.

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The electrodes are characterised by a wide usuable concentration range of 1.01 x 10^{-5}-1.0 x10^{-2} M, respectively for nearly all the studied electrodes at 25°C.

A method for regeneration of the exhausted electrodes was applied successfully in case of all electrodes.

The change of pH does not affect the potential readings of the studied electrodes within the pH ranges, 3.9-9.0, 3.5-10.0, 4.0-11.0 and 3.3-9.6 for TMH-TPB, TMH-PT, DP-TPB, DP-PT, electrodes, respectively.

The study of the effect of temperature change on the potential response of the electrodes showed that they are thermally stable over a wide range of temperature (20-60°C). The thermal coefficient of the electrodes are 0.00052, 0.00113, 0.00207 and 0.00103V/°C for TMH-TPB, TMH-PT, DP-TPB, DP-PT, respectively. This reveals that the electrodes have high thermal stability within the usable temperature range.

The investigated drugs were also determined in aqueous solution, using potentiometric titrations, conductimetric titrations and by applying the standard additions method. The study showed that the electrodes under investigation are highly selective even in the presence of some in organic cations, sugars, amino acids and component of the drug formation.

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TABLE & GRAPH

TABLE 3: PERFORMANCE CHARACTERISTICS OF TMH-ELECTRODES AT DIFFERENT MEMBRANE COMPOSITIONS

Ion-Exchanger	Membrane Composition (%) (w/w)				Slope (mV/decade)	Usable concentration range (mol/L)	RSD* (%)
		DO	DBP	PVC			
H-TPB	1.0		--		50.0	2.01×10^{-5} - 1.00×10^{-3}	0.58
	2.0	49.00	--	49.00	53.0	5.01×10^{-6} - 1.00×10^{-3}	0.71
	3.0	48.50	--	48.50	55.8	1.00×10^{-5} - 4.7×10^{-3}	0.66
	5.0	47.50	--	47.50	56.5	1.00×10^{-5} -1.26×10^{-3}	0.75
	7.0	46.50	--	46.50	55.2	2.00×10^{-5} - 1.00×10^{-3}	0.63
	10.0	45.50		45.50	53.4	4.90×10^{-5} - 5.25×10^{-3}	0.54
	2.0	-	49.00	49.00	51.0	1.00×10^{-5} - 1.00×10^{-3}	0.89
	3.0	-	48.50	48.50	52.0	1.00×10^{-5} - 1.00×10^{-3}	1.12
	5.0	--	47.50	47.50	54.2	2.00×10^{-5} - 1.00×10^{-3}	0.93
	7.0	--	46.50	46.50	53.0	2.0×10^{-5} - 1.58×10^{-3}	0.76
	10.0	--	45.00	45.00	53.0	2.00×10^{-5} - 2.51×10^{-3}	0.62
	13.0	--	43.50	43.50	50.6	3.16×10^{-5} - 2.82×10^{-3}	0.79
MH-PT	3.0	48.50	--	48.50	54.2	1.00×10^{-5} - 2.39×10^{-3}	0.95
	5.0	47.50	--	47.50	54.0	1.00×10^{-5} - 4.57×10^{-3}	1.12
	7.0	46.25	--	46.25	57.3	5.01×10^{-6} - 4.57×10^{-3}	0.83
	10.0	45.00	--	45.00	55.1	2.00×10^{-5} - 4.57×10^{-3}	0.62
	12.0	44.00		44.00	52.0	5.01×10^{-6} - 4.57×10^{-3}	0.81
	15.0	42.50		42.50	49.6	5.01×10^{-6} - 4.57×10^{-3}	0.97
	3.0	--	48.50	48.50	53.5	5.01×10^{-6} - 2.40×10^{-3}	0.86
	5.0	--	47.50	47.50	56.2	5.01×10^{-6} - 2.40×10^{-3}	0.74
	7.0	--	46.25	46.25	57.1	1.00×10^{-5} - 3.16×10^{-3}	0.51
	10.0	--	45.00	45.00	57.8	1.00×10^{-5} - 4.57×10^{-3}	0.46
	13.0	--	43.50	43.50	52.3	2.00×10^{-5} - 2.40×10^{-3}	0.72
	15.0	-	42.50	42.50	50.9	2.00×10^{-5} - 2.40×10^{-3}	0.84

*Relative standard deviation (five determinations)
**Optimum Composition

TABLE 4: PERFORMANCE CHARACTERISTICS OF DP-ELECTRODES AT DIFFERENT MEMBRANE COMPOSITIONS

Ion-Exchanger	Membrane Composition (%) (w/w)				Slope (mV/decade)	Usable concentration range (mol/L)	RSD* (%)
		DO	DBP	PVC			
P-TPB	3.0	48.50	--	48.50	47.4	2.95×10^{-5} - 4.57×10^{-3}	0.91
	5.0	47.50	-	47.50	49.0	4.90×10^{-5} - 6.03×10^{-3}	1.06
	7.0	46.25	-	46.25	52.3	6.92×10^{-5}-6.03×10^{-3}	0.82
	10.0	45.00	-	45.00	54.7	9.77×10^{-5} -7.94×10^{-3}	0.93
	12.0	44.00	--	44.00	51.2	9.77×10^{-5}-7.94×10^{-3}	0.60
	3.0	48.50	48.50	48.50	60.2	6.92×10^{-5} - 7.94×10^{-3}	0.89
	5.0	--	47.50	47.50	61.3	4.90×10^{-5} - 7.94×10^{-3}	0.94
	7.0	-	46.25	46.25	60.8	4.90×10^{-5} - 5.01×10^{-2}	0.47
	10.0	--	45.00	45.00	62.0	6.92×10^{-5} - 5.01×10^{-2}	0.63
	12.0	--	46.00	46.00	61.2	4.90×10^{-5} - 1.00×10^{-1}	0.76
	2.0	49.00	--	49.00	57.0	2.00×10^{-5} - 5.25×10^{-2}	0.98
P-PT	4.0	48.00	--	48.00	59.1	2.95×10^{-5} - 7.94×10^{-3}	0.81
	7.0	46.50	-	46.50	62.4	4.90×10^{-5} - 7.94×10^{-3}	0.90
	10.0	45.00	--	45.00	63.0	4.90×10^{-5} - 7.94×10^{-3}	0.78
	12.0	46.00	-	46.00	61.3	6.92×10^{-5} - 1.58×10^{-3}	1.17
	3.0	--	48.5	48.5	60.0	4.90×10^{-5} - 3.98×10^{-3}	1.21
	5.0	--	47.50	47.50	62.0	4.90×10^{-5} - 3.98×10^{-3}	1.04
	7.0	--	46.25	46.25	64.9	6.92×10^{-5} - 6.03×10^{-3}	0.84
	10.0	-	45.00	45.00	66.2	6.92×10^{-5} - 7.94×10^{-3}	1.00
	12.0	--	46.00	46.00	63.5	9.77×10^{-5}-7.94×10^{-3}	1.11

*Relative standard deviation (five determinations)
**Optimum Composition

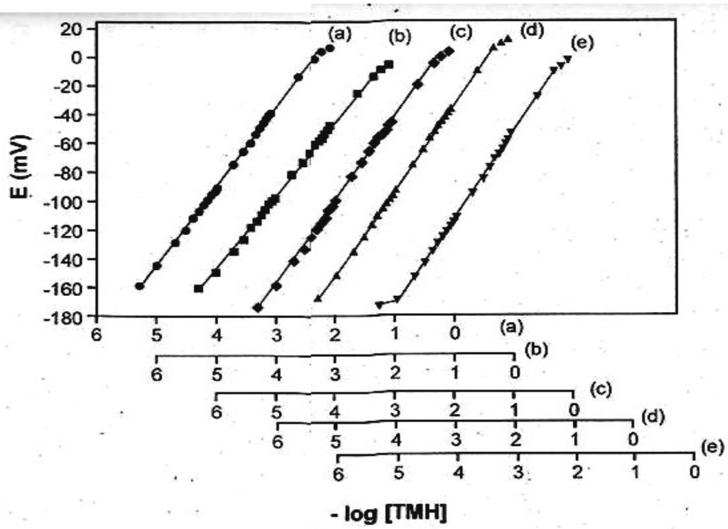

Fig. 3. Calibration graphs of TMH-PT electrodes at different membrane compositions, where (a) 3%, (b) 5%, (c) 7%, (d) 10% and (e) 13% ion-exchanger

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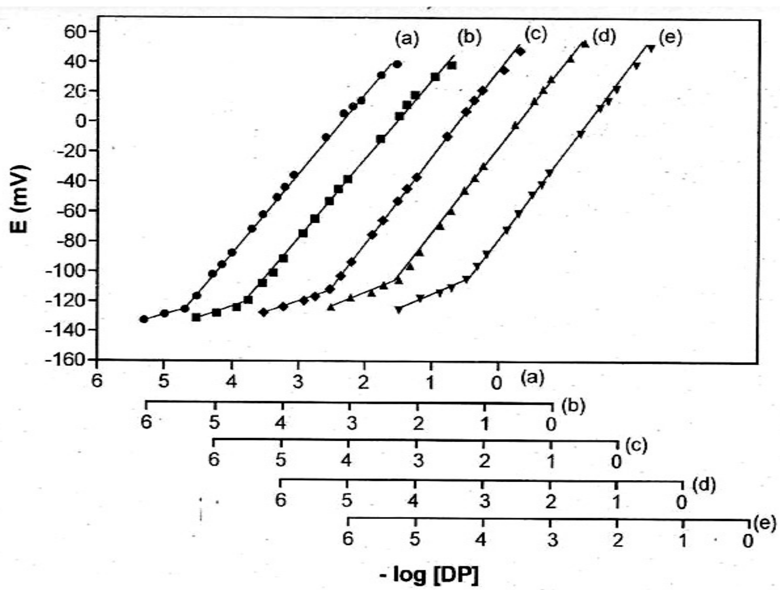

Fig. 4. Calibration graphs of DP-PT electrodes at different membrane compositions, where (a) 2%, (b) 4%, (c) 7%, (d) 10% and (e) 12% ion-exchanger