A NOVEL POLY (VINYL CHLORIDE) MATRIX MEMBRANE ELECTRODE FOR THE SELECTIVE DETERMINATION OF BUFORMIN

Mona A. Ahmed

Department of Chemistry, University College for Women,
Ain Shams University, Heliopolis, Cairo, Egypt.

SUMMARY

A PVC matrix membrane electrode system responsive to buformin cation has been developed, for direct potentiometric determination of buformin in aqueous solutions. It is based on the use of ion association complex of buformin cation with tetraphenyl borate counter anion as ion-exchange site. The electrode shows good selectivity for buformin hydrochloride over the pH range 4.0-9.5 in the presence of some inorganic as well as organic species. It exhibits fast, and stable Nernstian response for the concentration range 10^{-1} - 10^{-3} M buformin hydrochloride. The direct potentiometric determination of of 38.7 ug mL^{-1} - 19.37 mg mL^{-1} of buformin hydrochloride in aqueous solutions shows an average recovery of 99.5% and a mean standard deviation of 0.5%. The electrode is also used for monitoring the titration of buformin with sodium tetraphenyl borate.

INTRODUCTION

Buformin hydrochloride (1-butylbiguanide hydrochloride) (I) is a biguanide hypoglycaemic agent with action and uses similar to those of metformin hydrochloride.

$$CH_3\,CH_2\,CH_2\,CH_2 - NH - \underset{\underset{NH}{\|}}{C} - NH - \underset{\underset{NH}{\|}}{C} - NH_2 \qquad (I)$$
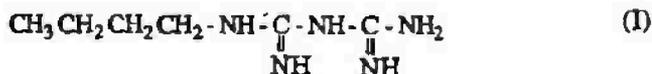
Analytical procedures for the determination of metformin and buformin and / or their derivatives, in pharmaceutical preparations , as well as in biological fluids have been described. Spectrophotometric measurements[1,2] based on the extraction of their ion-pair complexes has been reported. Other spectrophotometric [3,5], colorimetric [6], titrimetric [7], conductometric [8] and fluorimetric [9] methods have been propsed using ion-pair extraction techniques. Metformin was determined by HPLC [10], in plasma and urine. Other HPLC procedures were used for determination of buformin with fluorescence detection [11]. A GC method [12], involving pyrolytic conversion of biguanides into 2,4,6-triamino-1,3,5-triazines proved to be suitable for the assay of buformin in pharmaceutical preparations. A GC - mass fragmentographic method was used for the assay of the drug in biological fluids [13]. Buformin in biological materials, was also determined by GC [14]. Derivative GLC procedure was also used [15]. Thin layer chromatographic methods have been recommended for identification[15-19]. Since no potentiometric methods have been described for the determination of buformin, the present work presents a novel, simple accurate and fast potentiometric method for the determination of this drug.

EXPERIMENTAL

Apparatus

Potentiometric measurements were made at 25 ± 2°C with an Orion digital pH/mV meter (Model 720) using buformin PVC membrane electrode in conjunction with an Orion Ag-AgCl double-junction reference electrode (Model 90-02) containing 10% m/V KNO_3 in the outer com partment. An Orion Ross combination pH electrode (Model 81-02) was used for pH adjustment. A solid - state $Ag-Ag_2S$ membrane electrode (Orion model 94-16) was used for the standardization of sodium tetraphenylborate with silver nitrate. The IR absorption spectra were recorded using a Shimadzu (IR-470) spectrometer
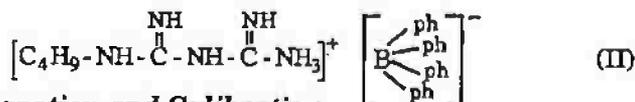
Reagents

De-ionised doubly distilled water was used throughout and all chemicals were of the best laboratory reagents grade, unless stated otherwise. Tetrahydrofuran (THF), dioctyl phthalate and poly (vinyl chloride) powder were purchased from Aldrich Chemical Company, Inc. (Milwaukee, Wiscon-

sin, USA). Sodium tetraphenylborate was obtained from Fluka (Buchs, Swizerland). Standard buformin hydrochloride powder was obtained from El Nasr Pharmaceutical Company.

Buformin Ion-Pair Complex

A 30-ml aliquot of 5×10^{-2}M aqueous buformin hydrochloride solution was mixed and stirred with a 50-ml aliquot of 5×10^{-2}M aqueous solution of sodium tetraphenylborate. The precipitate was filtered, washed thoroughly with distilled water, dried at 80°C for 1h and ground to fine powder (m.p. 139-140°C). Elemental analysis and infrared spectrum of the dry, ground powdered ion-pair confirmed the formula :

$$\left[C_4H_9-NH-\overset{\overset{NH}{\|}}{C}-NH-\overset{\overset{NH}{\|}}{C}-NH_3 \right]^+ \left[B\overset{ph}{\underset{ph}{\overset{ph}{\langle}}} \right]^- \qquad (II)$$

Electrode Preparation and Calibration

Master membranes were casted from (190 mg) PVC, (10mg) buformin - tetraphenyl borate sensor and (360 mg) diocty phthalate (DOP) as the plasticising solvent mediator dissolved in (6 cm^3) tetraphydrofuran (THF). The solution was poured into a petri-dish (3cm diameter), covered with a filter paper and allowed to evaporate slowly over a period of 48h. A disk, approximately 0.2 mm thick, was cut from the membrane with a cork borer and the membrane was mounted in an electrode configuration according to the procedure previously described [20,21].

The internal reference solution was prepared by mixing equal volumes of 10^{-2} M aqueous buformin hydrochloride and 10^{-2} M sodium chloride solutions . A standard 0.1 M buformin hydrochloride solution was prepared for calibration by dissolving 1.937 gm of buformin hydrochloride in 100ml of deionised distilled water, where by solutions (10^{-1} - 10^{-6}M) of buformin hydrochloride were prepared by appropriate dilutions.

E.m.f. measurements were recorded with respect to an Orion double junction electrode for stirred solutions at 25°C and plotted on semilogarithmic paper as a function of buformin concentration. The graph was used for subsequent determination of unknown buformin hydrochloride. Aliquots (10 mL) of aqueous buformin hydrochloride solutions (10^{-1} - 10^{-6}M) were stirred in a 50-ml beakers and the buformin PVC membrane electrode

in conjunction with a double junction Ag/AgCl reference electrode were immersed in each solution. Alternatively, the same procedure was followed, by the standard known addition technique. A 9-mL aliquot of water was transferred to a 50 mL beaker where both electrodes were placed. Aliquots (1.0 mL) of 10^{-5} - 1M standard buformin hydrochloride solution were successively added, the e.m.f. readings recorded after stabilisation to ± 0.1 mV and the e.m.f plotted as a function of logarithmic buformin hydrochloride concentration.

Electrode Selectivity

The potentiometric selectivity coefficients $K_{BufH,B}^{pot}$ for buformin electrode were evaluated by the separate solutions method [22,28]. A 9.0 ml aliquot of distilled water was placed in a 50-mL beaker, where the buformin PVC membrane electrode and the double junction electrode were immersed. The potential response upon addition of 1-mL aliquot of 10^{-2}M solution of the interferent was recorded and compared with that of 10^{-2}M buformin hydrochloride. The selectivity coefficients were calculated using the Eisenman-Nicolsky equation (1)

$$-\log K_{BufH,B}^{pot} = E_1 - E_2 / S \qquad (1)$$

where E_1, and E_2 are the potential readings observed after one min due to the same concentration of buformin hydrochloride and the interferents, respectively and S is the slope of the buformin calibration graph (mV / concentration decade).

Effect of pH

The effect of pH on the potential readings of the electrode system was studied using two pH/mV meters, The Ross combination glass electrode was connected to one instrument, and the buformin PVC electrde with a double junction Ag/AgCl reference electrode were connected to the other - A 30 mL aliquots of 10^{-1}-10^{-3}M buformin hydrochloride solution were consecutively transferred to 100 mL beakers, where the three electrodes were placed. The potential readings were recorded at each pH value. The pH of each solution was gradually increased or decreased by the addition of small aliquots of appropriate concentration of sodium hydroxide or hydrochloric acid, respectively and the mV-pH profil was plotted for the electrode system.

Direct Potentiometric Determination of Buformin

Solutions of unknown concentrations were determined using the PVC buformin electrode in conjunction with an Ag/AgCl double junction electrode. A 10mL aliquot was transferred to a 50 - mL beakers and the potential reading was recorded when become stable. The concentration of each solution was determined from the calibration graph. The electrode system was rinsed with water between measurements.

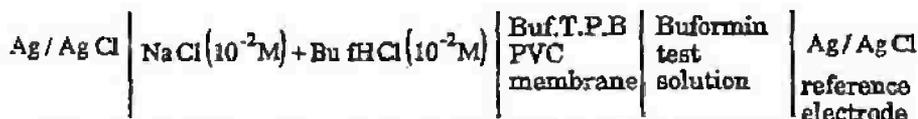### Potentiometric Titration of Buformin Hydrochloride

Aliquots (2-8 mL) of 10^{-2} M buformin solution were transferred to 50-mL beakers and diluted to 10mL with doubly distilled water. In each solution, the PVC buformin electrode and Ag/AgCl double junction electrode were placed and the stirred solutions were titrated with standard 10^{-2} M aqueous sodium totraphenylborate. The e.m.f., (E) was recorded as a function of the added titrant volume (V) and E vs V curves were plotted for each solution. The end point was located from the maximum of the slope of the plotted data of $\Delta E / \Delta V$ vs V.

RESULTS AND DISCUSSION

Electrode Characteristics

Nature and Composition of the Buformin Membrane

Buformin cation forms a water insoluble 1:1 buformin complex of the type II. The structure of this complex was confirmed by infrared spectra. The PVC membrane was prepared by using a casting solution of the composition 28:2: 70 w/w PVC, buformin-tetraphenylborate complex and dioctyl phthalate plasticizer, respectively. The elctrochemical performance characteristics of this electrode system was systematically evaluated according to IUPAC recommendations [23] using the following electrochemical cell.

$$\text{Ag / Ag Cl} \left| \text{NaCl}\left(10^{-2}\text{M}\right) + \text{Bu fHCl}\left(10^{-2}\text{M}\right) \right| \begin{array}{c}\text{Buf.T.P.B}\\\text{PVC}\\\text{membrane}\end{array} \left| \begin{array}{c}\text{Buformin}\\\text{test}\\\text{solution}\end{array} \right| \begin{array}{c}\text{Ag / Ag Cl}\\\text{reference}\\\text{electrode}\end{array}$$

The e.m.f. of this cell was measured using the following equation.

$$E = E_o + S \log\left[a_{Buf}^+ + K_{Buf,B}^{pot}(a_b)^{\frac{1}{z}}\right] \qquad (2)$$

where E_o represents the conditional standard potential of the electrode un- der the conditions used in the cell, S is the slope of the calibration graph, $K_{Buf,B}^{pot}$ is the selectivity coefficient, a_{Buf}^+ and a_B are the activities or con- centrations of buformin ion and the foreign ion, that have a charge Z and present in test solution, respectively.

The calibration curves obtained with the electrode furnish a Nernstian slope for at least two decades for buformin concentrations. The linear re- sponse cover the range $10^{-3}-10^{-1}$M buformin ion with a cationic slope of 60.0 ± 0.2 mV per decade change in concentration (Fig. 1). The lower limit is approximately 2×10^{-4} M. Least squar analysis of these data gives the follow- ing relation.

$$E_1(mV) = \left[+60\pm0.2 \log[Buf]^+\right] + [266\pm0.7] \qquad (3)$$

where E_1 is the e.m.f displayed by the electrode.

Table 1 summarizes the response characteristics of the electrode sys- tem from data collected over a period of 3 months.

Response Time of Buformin Electrode

The dynamic response [24] time of the electrode system was tested for $10^{-1}-10^{-3}$M buformin HCl solutions. The measurement sequence was from law concentration to the higher, and back. The required time for the elec- trode to reach values within ± 0.2 mV from the final equilibrium potential after increasing the buformin concentration level to 10 fold is fairly short, it reaches 95% of its final steady potential after 10 sec for $[Buf]^+ \geq 10^{-3}$ M and 15 sec for $[Buf]^+ \leq 10^{-3}$ M.

Potential Stability of the Buformin PVC Membrane Electrode

The potential displayed by the buformin PVC membrane electrode for consecutive measurements of 10^{-1}- 2×10^{-4} M of standard Buf$^+$ solution did not vary by more than $\pm$ 1mV (n=10) in the same day. The calibration slope did not exceed $\pm$ 0.3 mV per decade change of concentration. The reproducibility and stability of the potential were evaluated over a period of 10 days by determining replicate calibration graphs (n=10). During this period, the electrode was stored in air and washed thoroughly with distilled water between measurements. Although positive shift of the absolute potentials (5-50 mV) was noticed, the slope of the calibration graph remained practically constant within $\pm$ 1mV per concentration decade over this period . The detection limit, linear range, response time, and selectivity coefficient values were almost constant for the electrode during this period.

Effect of pH

The effect of pH of buformin test solutions (10^{-1}-10^{-3} M) on the electrode potential was investigated. Variations of potential caused by pH change over a pH range (1.5-10) was performed (Fig. 2). The potential - pH plots of this electrode revealed that within the working pH range 4.0-9.5 for 10^{-3}M, the potential remains almost constant. With higher concentrations of the test solution $\geq 10^{-2}$ M, the pH working range was extended to higher pH values. The decrease in the potential below pH 4.5 is probably due to the formation of $BufH_2^{2+}$ species.

Effect of Interfering Compounds

The interference effects of 14 diffferent inorganic cations, aromatic, aliphatic amines and amino acids as well as glucose and maltose on the electrode response were evaluated. The interference of these compounds were assessed by measuring the selectivity coefficients $K_{Buf,B}^{pot}$ using the separate solutions method [22,23] with a 10^{-3} M concentration of both the standard buformin and the interferent. The results obtained (Table 2) show a high selectivity for [Buf]$^+$ ion in the presence of many interferents. Up to 100-fold excess of the interferent did not cause significant influence on the electrode performance.

Direct Potentiometric Determination of Buformin

Direct potentiometric determination of buformin hydrochloride using the buformin PVC membrane electrode was performed and calculated from the calibration curve. The results show an average recovery of 99.5% with a mean standard deviation of ± 0.5%. Determination of buformin hydrochloride using the standard addition technique shows an average of 99.2% and a mean standard deviation of ± 0.4%.

In conclusion, the proposed electrode system offers a convenient assay method for buformin drug. It has the advantages of simplicity, selectivity, fast response as well as a wide working pH range.

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Table (1)

Response characteristics of the PVC buformin membrane electrode
with DOP plasticiser

Parameter	DOP
Slope, (m V decade $^{-1}$)	60.0
Standard deviation	0.5%
Correlation coefficient, (r)	0.998
Intercep, (mV)	266 ± 0.7
Lower limit of linear range, (M)	10^{-3}
Lower limit of detection, (M)	2×10^{-4}
Working pH range for 10^{-3}M, (pH)	4.0 - 9.5
Response time for 10^{-3}M buformin,(S)	10
Recovery time, (min)	0.5

Table (2)

Selectivity coeficients for some common organic and inorganic cations
using buformin PVC membrane electrode

Interferente, C	$K_{Buf,C}^{pot}$
Mg^{2+}	2.0×10^{-2}
Ca^{2+}	2.8×10^{-2}
K^+	2.2×10^{-2}
Na^+	1.2×10^{-2}
NH_4^+	2.4×10^{-2}
Glucose	1.2×10^{-2}
Maltose	1.4×10^{-2}
Urea	1.3×10^{-2}
Ethylamine	2.5×10^{-2}
p-Aminophenol	1.2×10^{-2}
o-Amino benzoic Acid	2.0×10^{-2}
Glutamic Acid	8.9×10^{-3}
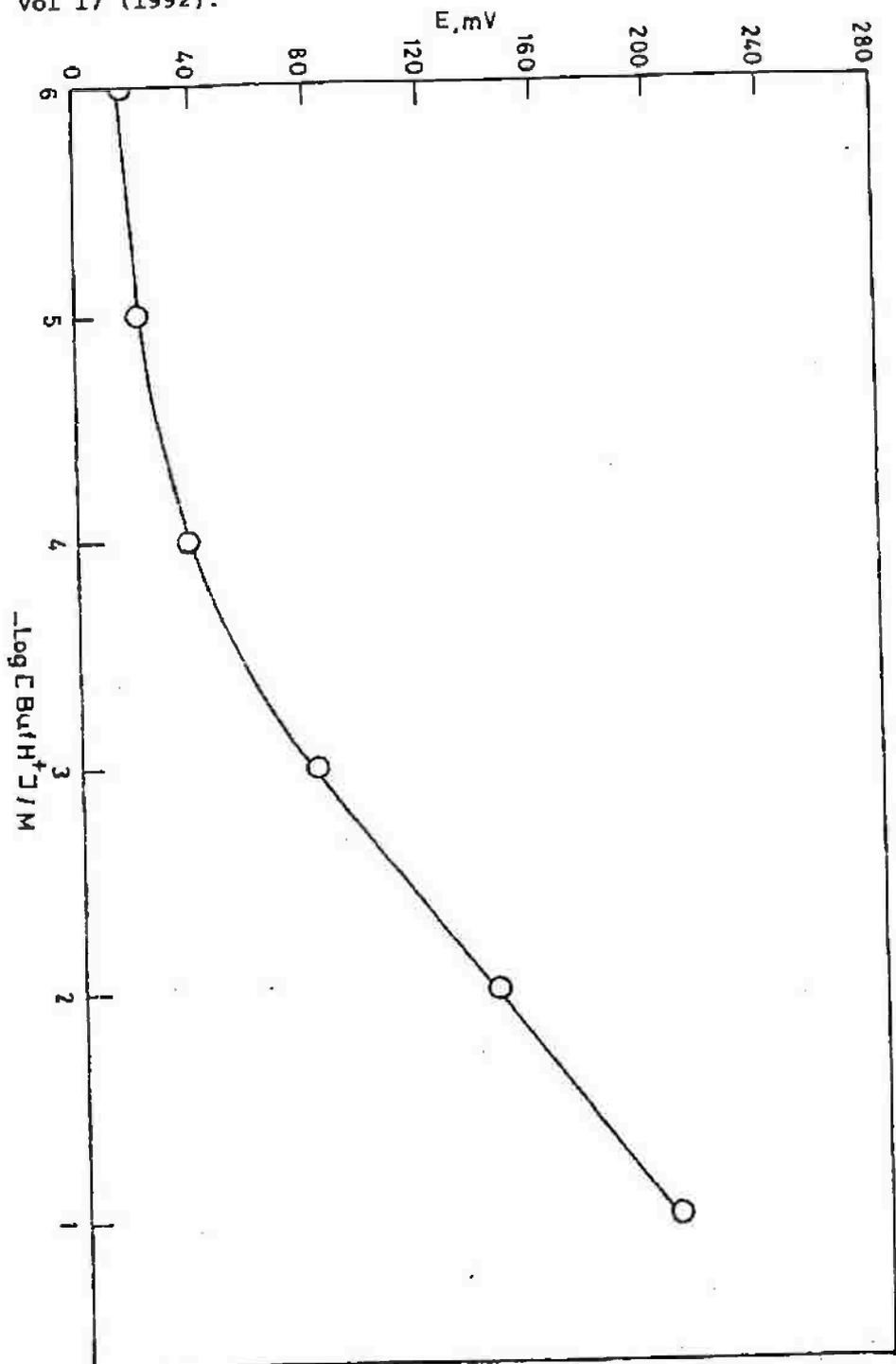
Fig. 1
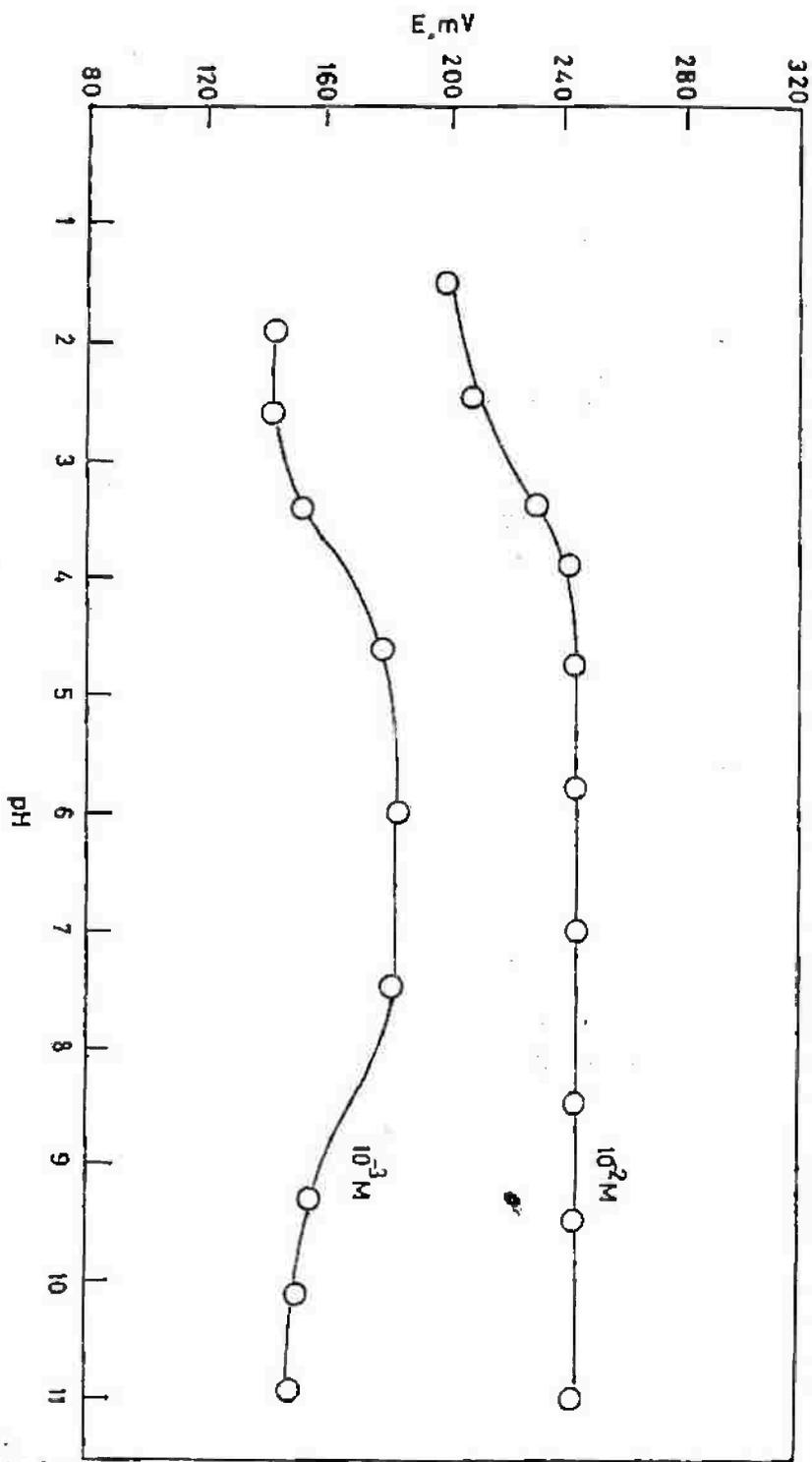
Fig. 2

ابتكار قطب جديد ذو غشاء سائل من مادة

البيوفورمن المحملة على مادة كلوريد البولى ثينيل للقياس

المنتخب لعقار البيوفورمن

منى عبد العزيز أحمد

قسم الكيمياء - كلية البنات - جامعة عين شمس

القاهرة - مصر

يتناول هذا البحث طريقة لتحضير قطب منتخب لمادة البيوفورمن ذو غشاء سائل محمل على مادة كلوريد البولى ثينيل واستخدامه للقياس الجهدى المباشر للبيوفورمن ، وقد أظهر دقة عالية تصل إلى ٥ , ٩٩٪ ومتوسط حيود قياسى قدره ٥ , ٠٪ عند قياس تركيزات مختلفة تتراوح بين ٢٨,٧ ميكروجرام إلى ١٩,٢٧ مللى جرام لكل مللى لتر .

ولقد دلت الدراسة على أن هذا القطب يستجيب استجابة تتطابق تماما مع معادلة نرنست فى مدى تركيز من ٦×١٠⁻³ إلى ١٠⁻¹ مولارى من البيوفورمن مع ميل قدره ٦٠ مللى فولت لكل وحدة تركيز .

ولقد استخدم هذا القطب ايضا للمعايرة المباشرة لمحلول البيوفورمن بواسطة محلول قياسى من الملح الصوديومى لرباعى فينيل البورات .

ولقد أظهر هذا القطب صلاحية للاستخدام فى مدى واسع للاس الايدروجينى يتراوح بين ٤ و ٩,٥ فى محاليل تركيزاتها ١٠⁻² ، ١٠⁻³ مولارى من البيوفورمن ، كما أظهر القطب اختيارية عالية فى وجود بعض المركبات العضوية وغير العضوية .