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# PVC Membrane Sensors for Potentiometric Determination of Bambuterol in Pharmaceutical Formulation

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The construction and electrochemical response characteristics of Poly (vinyl chloride) membrane sensors for bambuterol HCl (Bb) are described. The sensing membranes incorporate ion association complexes of bambuterol cation and phosphomolybdic acid (PMA) (sensor 1) and phosphotungstic acid (PTA) (sensor 2) as electroactive materials. The sensors display a fast, stable and near-Nernstian response over a relative wide bambuterol concentration range ($1 \times 10^{-2}$ to $7\times10^{-6}$, and $1 \times 10^{-2}$ to $6.0\times10^{-6}$M), with detection limits of $5\times10^{-6}$, and $3\times10^{-6}$ for sensor 1, and 2, respectively over a pH range of 3.0 - 8.0. The sensors show good discrimination of bambuterol from several inorganic and organic compounds. The direct determinations of 200 µg/ml of Bb show an average recovery 98.5 and 99.0% and a mean relative standard deviation of 1.5 and 1.7% at 200.0 µg/ml for sensor 1 and 2 respectively. The proposed sensors have been applied for direct determination of Bb in some pharmaceutical preparations. The results obtained by determination of Bb in tablets using the proposed sensors are comparable favorably with those obtained using the British Pharmacopeia method. The sensors have been used as indicator electrodes for potentiometric titration of bambuterol.

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**Keywords:** Bambuterol HCl, Phosphomolybdic acid, Phosphotungstic acid, PVC, Potentiometry.

## 1. INTRODUCTION

Bambuterol hydrochloride (Bb; Figure 1), (*RS*)-5-[2-(*tert*-butylamino)-1-hydroxyethyl] benzene-1,3-diyl bis(dimethylcarbamate) hydrochloride is a direct acting sympathomimetic with predominantly-adrenergic activity β$_2$-agonist) [1]. It is an ester prodrug of β$_2$ adrenergic agonist terbutaline [2]. It is used for the prophylaxis and treatment of chronic asthma and chronic bronchitis in pediatrics. The monitoring of such drug is important for quality assurance in preparations and for optimum therapeutic concentrations.

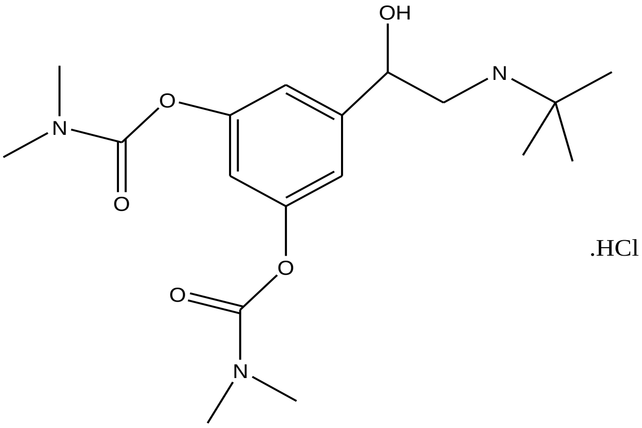

**Figure 1.** Chemical structure of bambuterol hydrochloride.

For determination of bambuterol several methods such as, high performance liquid chromatography (HPLC) [3-5], HPLC-MS [6, 7], gas chromatography-mass detection (GC-MS)[8], capillary zone electrophoresis (CZE)[9], and nuclear magnetic resonance(NMR) [10] and spectrophotometry [11-14] has been used.

However, most of these methods involve time-consuming procedures, derivatization and/ or sophisticated instruments.

In recent years, the potentiometric membrane sensors have been widely used in pharmaceutical analysis [15-17]. This is mainly due to simple design, low cost, adequate selectivity, low detection limit, high accuracy, wide concentration range, and applicability of the selective electrodes to colored and turbid solutions. Potentiometric titrations were suitable for the determination of a relatively large amount of the drugs. The apparatus required for making potential measurements and performing titrations is generally inexpensive and basically simple in details. For this reason, the potential measurements find wide acceptance in industry as an analytical tool, both in the laboratory and in the process and quality control for routine analyses [18, 19].

To the best of our knowledge, only one PVC membrane sensor was developed [20]. The developed method was based on use of bambuterol-tetaphenylborate and bambuterol-renikate as ion-associate complex. The detection limit of bambuterol was ~ $10^{-5}$M using bambuterol-tetraphnyl borate and bambutero-reinkate respectively.

The proposed sensors are based on the use of PVC membrane sensor of bambuterol - phosphotungstate or bamnuterol- phosphomolybdate as electroactive materials. The present work describes the construction and evaluation of novel PVC electrochemical sensors for the sensitive and selective determination of bambuetrol in bulk and its pharmaceutical preparation. The proposed methods are successfully applied for the determination of Bb in some pharmaceutical formulation.

## 2. EXPERIMENTAL

### *2.1. Apparatus*

All potentiometric measurements were made at 25 ± 1 $^oC$ unless otherwise stated using an Orion pH/mV meter (model 330) using bambuterol membrane sensors in conjunction with an Orion double junction Ag/AgCl reference electrode (model 90-02) containing 10% (w/v) potassium nitrate in the outer compartment. Adjustment of pH was made with a combined Ross glass pH electrode (Orion 81-02) for all pH measurements.

### *2.2. Reagents and Materials*

All chemicals used were of analytical reagent grade unless otherwise stated and doubly distilled water was used throughout. Polyvinyl chloride powder (PVC) high molecular weight, dibutyl sebacate (DBS), dioctyl phthalate (DOP), o-nitrophenyl octylether (NPOE), tetrahydrofurane (THF) of purity > 99 % were obtained from Aldrich Chemical Company and bambuterol HCl was obtained from Sigma Chemical Company, Switzerland. Phosphomolybdic acid, and PTA were obtained from BDH, chemical Ltd. Bambec 10 mg was the product of AstraZeneca and was obtained from local pharmacy. The stock solution of $1\times10^{-2}$ M bambuerol-HCl was prepared by dissolving the appropriate amount of Bb in 100ml of water. The standard Bb solution were prepared $1\times10^{-2}$ - $1\times10^{-6}$M by diluting the appreciate amount in double distilled water. Phosphate buffer solution of pH 7.0 was prepared by mixing appropriate amount of 0.05M of $KH_2PO_4$ and $K_2HPO_4$.

### *2.3. Preparation of the Bb -PVC Membrane Sensors*

Upon the addition of 75 ml of $1\times10^{-2}$ M of bambuterol HCl solution to 25 ml each of phosphomolybdic and phosphotungstic acid a greenish precipitate was formed for Bb-PM and whitish precipitate for BB-PT were formed, respectively. The precipitate was filtered off through a Whatman filter paper No.42, washed with cold deionized water until no chloride ion was detected into the washing solution. The precipitate was dried under vacuum for 48h, then grinded to a fine powder in mortar, forming ion-pairs complex. Ten mg portions of the prepared ion associate complexes were thoroughly mixed with 190 mg PVC powder, 350 mg of DBS or DOP or NPOE and 5 ml THF in glass Petri dishes (5 cm diameter). After the constituents being well mixed, the solvent has been allowed to evaporate overnight while the sensing membranes have been formed. The PVC master membranes were sectioned with a cork borer (10 mm diameter) and glued to a polyethylene tube (3 cm length, 8 mm I.D.) using THF [21, 22]. Laboratory made electrode bodies were used, which consisted of a glass tube, to which the polyethylene tube is attached at one end and filled with internal reference solution (equal volumes of $1\times10^{-2}$ M aqueous solution of Bb and KCl). Ag/AgCl internal reference electrode (1.0 mm diameters) was used. The indicator electrode was conditioned by soaking in a $1\times10^{-2}$ M aqueous Bb solution for 1 h and stored in the same solution when not in use.

### *2.4. Procedure*

The bambuterol PVC membrane sensors were calibrated by immersion in conjunction with the reference electrode in a 50 ml beaker containing 9.0 ml of phosphate buffer of pH 7.0. Then 1.0 ml aliquot of Bb solution was added with continuous stirring, to give final Bb concentration ranging from $1\times10^{-2}$ to $1\times10^{-6}$M and the potential was recorded after stabilization to ± 0.5 mV. A calibration graphs were then constructed by plotting the recorded potentials as a function of -log [Bb]. The resulting graphs were used for subsequent determination of unknown bambuterol concentration.

### *2.5. Determination of Bambuterol in the Pharmaceutical Dosage Form.*

Ten tablets of Bambec 10 mg were accurately weighed and crushed and mixed in a mortar. An appropriate amount (10 mg of bambuterol powder, from each) was weighed, transferred to a 100 ml beaker and dissolved in distilled water, sonication for about 15 min and completed to the mark with the water or an equal volume equivalent to 10 mg of Bb was completed dissolve in 50 ml water. A 5.0 ml aliquots of these solutions were transferred to 50 ml standard flask, the pH was adjusted to 7.0 using phosphate buffer and completed to the mark with water. The potential of the solution was measured using Bb-sensors in conjunction with an Orion Ag/AgCl double junction reference electrode. The potential of the stirred solution was recorded after the signal stabilization (± 1 mV/min) and the concentration was calculated from the previous calibration graph under identical experimental conditions from standard solutions of Bb.

Alternatively, the potentials displayed by bambuterol test solution before and after the addition of a 1.0 ml aliquot of $1\times10^{-3}$ M bambuterol were measured. The change in the potential readings was recorded and used to calculate the unknown bambuterol concentration in the test solution using the standard addition technique [23].

Reconstituted powder: one mixture was prepared with a known amount of bambuterol powdered (5 mg) and other components such as starch, lactose and magnesium stearate. The accuracy of the potentiometric determination of Bb in this powdered was checked by evaluation the recovery.

## **3. RESULTS AND DISCUSSION**

Phosphomolybdic acid, and phosphotungstic acid were tested as ion-pairing agent for the preparation of an electroactive ion association complexes for Bb. Sparingly soluble complexes of Bb - PM or Bb - PT have been instantaneously formed upon the addition of Bb solution to solutions of PMA or PTA respectively. The dry powder of the formed ion pairs are used for the construction of a new bambuterol ion selective electrodes. The elemental analysis showed that the composition of the complex is 3:1 for Bb: PM or Bb-PT respectively. Plastic membranes were prepared by using a casting solution of (1.82: 34.45: 63.64) ion pair, PVC and DBS or DOP or NPOE as plasticizer, respectively.

### *3.1. Sensors Characteristics*

The potentiometric response characteristics of the bambuetrol sensors based on the use of Bb-PM or Bb-PT as ion pair complexes as an electroactive materials and DBS or DOP or NPOE as a plasticizer in a PVC matrixes were evaluated according to IUPAC recommendations [24]. Results in Table 1 show the characteristics performance of the PVC membrane sensors. The least squares equations obtained from the calibration data as follows:

$E$ (mV) = $S$ log [Bb] + Intercept ………………...……………………………..(1),

where $E$, is the potential of the electrode, $S$ equal slope of the electrodes (54.0 ± 0.5 and 56.0 ± 0.5 mV for Bb -PM, and Bb-PT, respectively) and intercept (189.0 ± 0.5, and 234.0 ± 0.5 for Bb -PM, and Bb -PT, respectively).

**Table 1**. Response characteristics of bambuterol-PVC matrix membrane sensors.

| **Parameter** | **Bb-PM** | **Bb-PT** |
|---|---|---|
| Slope, (mV/ decade) | 56.0 ± 0.5 | 54.0 ± 0.5 |
| Intercept, mV | 189.0± 0.5 | 234.0 ± 0.5 |
| Correlation Coefficient, (r) | 0.998 | 0.998 |
| Lower limit of quantification, (LOQ), M | $7.0 \times 10^{-6}$ | $5 \times 10^{-6}$ |
| Lower limit of detection limit,(LOD), M | $6.0 \times 10^{-6}$ | $3 \times 10^{-6}$ |
| Response time for$1\times10^{-3}$ M solution, s | 30 ± 0.5 | 25 ± 0.5 |
| Working pH range | 3 – 8.0 | 3 – 8.0 |

### *3.2. Effect of Plasticizer Type on the Characteristic Performance of the Sensors*

Bambuterol ion-selective membrane sensors with different electroactive materials were investigated in order to compare their performance. Two used reagents were investigated as possible counter ion for the preparation of the electroactive complex of BB, namely PMA or PTA. The obtained ion-pairs combined with three plasticizer, DOP, DBS and NPOE to give different combinations. It is well known that the construction of PVC based ISEs required the use of a plasticizer which acts as a fluidizer allowing homogenous dissolution and diffusion mobility of the ion-pair inside the membrane. PVC membrane sensor of Bb-PM or Bb-PT with different plasticizer of different (DBS or DOP or NPOE) was found to be all suitable and optimum available mediators for Bb membrane sensors. In fact, o-NPOE was found to be the optimum available mediator for Bb-PM or Bb-PT membrane sensors (ion-associates). The use of non polar mediators such as DBS, DOP gave less response with little discrimination for concentration change (slope about 40.0 mV per concentration decade for both DBS and DOP respectively). It seems that o-NPOE improves the membrane selectivity due to its high dialectical constant (ε=24), affects considerable dissolution of ion-association within the membrane; consequently enhances its partition coefficient in the membrane and also provided suitable mechanical property of the membrane compared with less permittivity plasticizers DBS (ε= 4) or DOP (ε= 7) and the solubility of electroactive materials are relatively small compared with o-NPOE. NPOE was used in case of Bb-PM or Bb-PT for carrying out other experiments in this investigation.

### *3.3. Effect of pH and the Response Time*

The electrode response for different Bambuterol concentrations was tested at different pH values, the pH being adjusted using hydrochloric acid or sodium hydroxide. The Bb-PVC electrode dipped into bambuterol solution of $1\times10^{-3}$ and $1\times10^{-4}$M the potential of the electrode was plotted against the pH of solution (Fig.2). The potentials show that the slope per concentration decade is constant ~ 54.0 ± 0.5 or 56.0 ± 0.5 for Bb-PM or Bb -PT respectively in the pH range of 3 - 8.0. At higher pH values (> 9.0), the potential decreased due to the gradual increase in the concentration of the unprotonated Bb resulting in the precipitation of Bb base.

The average response time is defined [24] as the time required for the electrode to reach a stable potential within ±1 mV of the final equilibrium value, after successive immersion of the electrode in different bambuterol solutions each having a 10-fold difference in concentration or after rapid 10-fold increase in concentration by addition of Bb. This time was found to be 25s for concentration of $\geq1\times10^{-3}$M and ≤ 30 s for concentration $1\times10^{-4}$M. Day-to-day reproducibility of the sensor is about ± 0.5 mV for the same solution and the useful lifetime of the sensor is 4 weeks, during which the potential slope is reproducible to within ±1 mV/ decade. Also after more than one month a new section from the master membrane was found to function very properly

### *3.4. Effect of Diverse Ions*

The influences of different organic and inorganic ions on the response of bambuterol sensors were investigated. The selectivity coefficients $K_{A,B}^{pot}$ were evaluated according to IUPAC guidelines using the separate solution method (SSM) and mixed solution method [24, 25] in phosphate buffer solution of pH 7.0. The selectivity coefficient $K_{A,B}^{pot}$ measured by separate solution method was calculated from the following equation:

$$\log K_{A,B}^{pot} = E_B\text{-}E_A/S \quad + [\,1\text{-}\ Z_A/Z_B]\log a_A \text{ ------------------------------}(2)$$

where $E_A$ and $E_B$ are the potential reading observed after 1 min of exposing the sensor to the same concentration of Bb and interfering species ($1\times10^{-3}$ each) alternatively. $a_A$ , and $a_B$ are the activity of Bb and interfering species and $Z_A$ and $Z_B$ are the charge of bambuetrol and interfering species and *S* is slope of calibration graph (mV/ concentration). The selectivity coefficient by mixed solution method was defined as the activity ratio of primary and interfering ions that give the same potential change under identical conditions as given in equation 3.

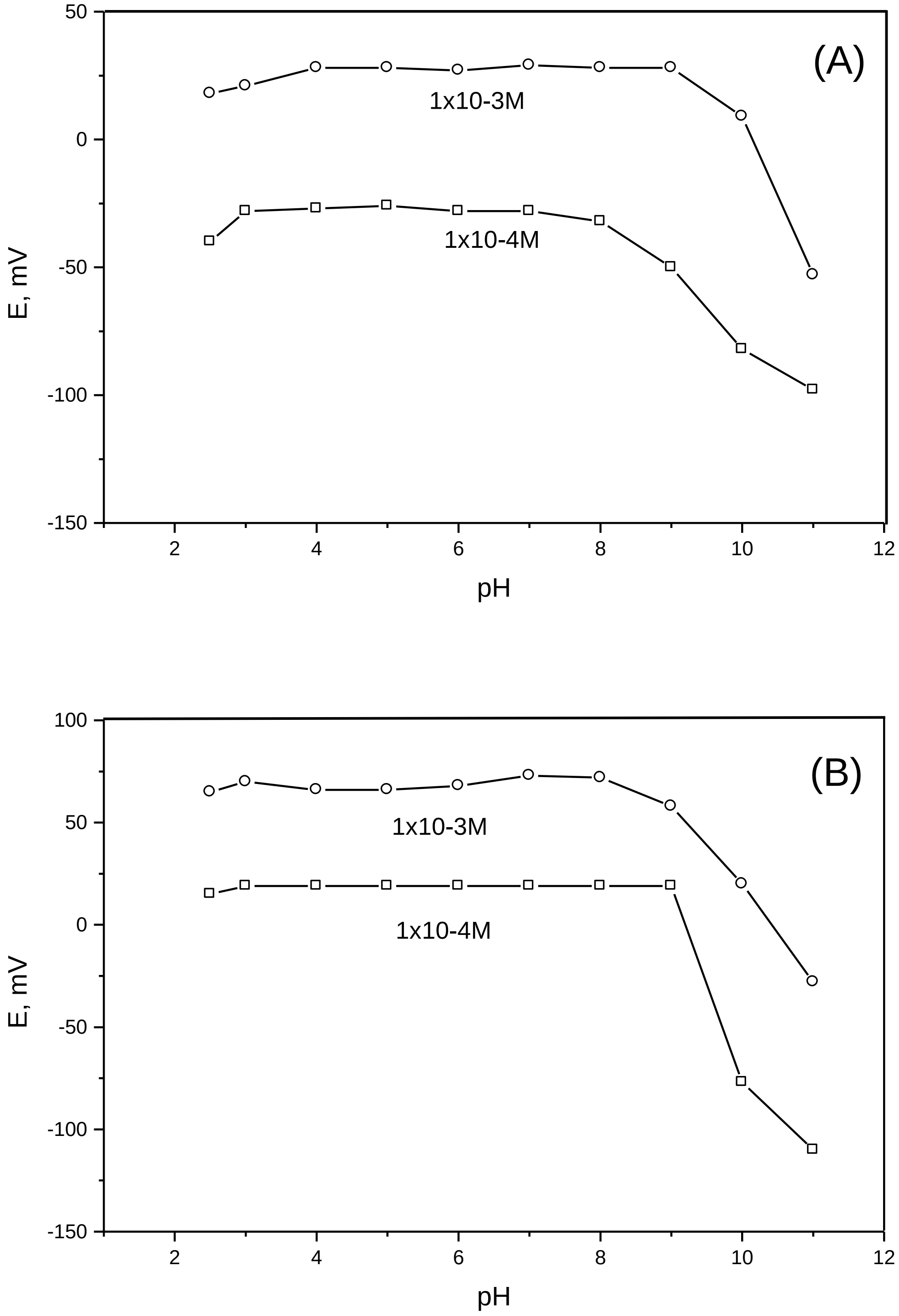

**Figure 2.** Effect of pH on the response of bambuterol sensors a) Bb-PM, and b) Bb-PT using tow series of bambuetrol solutions: 1 ×$10^{-3}$M, and 1 ×$10^{-4}$ M.

$$K^{pot}_{A,B} = (a`_A - a_A)/a_B \text{ ------------------------------------------------------------(3)}$$

Where $a`_A$ known activity of primary ion is added into a reference solution that contains a fixed activity ($a_A$) of primary ions, and the corresponding potential change (ΔE) is recorded. Next, a solution of an interfering ion ($a_B$) is added to the reference solution until the same potential change (ΔE) is recorded. The change in potential produced at the constant back ground of the primary ion must be the same in both cases. The results are given in Table 2 The results reveal reasonable selectivity for Bb in presence of many related substances.

**Table2**. Potentiometric selectivity coefficients of some interfering ions, using bambuterol sensors.

| **Interferent, J** | $K^{Pot}_{Bb,B}$ **B b –PM** | $K^{Pot}_{Bb,B}$ **Bb -PT** |
|---|---|---|
| $Na^+$ | $2.3 \times 10^{-3}$ | $1.8 \times 10^{-3}$ |
| $K^+$ | $2.3 \times 10^{-3}$ | $2.0 \times 10^{-3}$ |
| $Ca^{2+}$ | $2.3 \times 10^{-3}$ | $2.3 \times 10^{-3}$ |
| $Fe^{2+}$ | $2.0 \times 10^{-3}$ | $2.0 \times 10^{-3}$ |
| $Fe^{3+}$ | $2.1 \times 10^{-3}$ | $1.3 \times 10^{-3}$ |
| $PO_4^{3-}$ | $1.2 \times 10^{-3}$ | $2.0 \times 10^{-3}$ |
| Magnesium stearate | $2.3 \times 10^{-3}$ | $2.3\times 10^{-3}$ |
| Acetate | $1.9 \times 10^{-3}$ | $1.0 \times 10^{-3}$ |
| Citrate | $2.1 \times10^{-3}$ | $2.3\times 10^{-3}$ |
| Glucose | $2.3 \times 10^{-3}$ | $2.1\times 10^{-3}$ |
| Lactose monohydrate | $2.3 \times 10^{-3}$ | $2.2\times 10^{-3}$ |
| Starch | $2.0 \times 10^{-3}$ | $2.2\times 10^{-3}$ |
| Microcrystalline cellulose | $2.0 \times 10^{-3}$ | $2.2\times 10^{-3}$ |

### *3.5. Validity of the Proposed Method*

#### *3.5.1. Limit of quantification and limit of detection*

Each of different concentration of standard solution was tested five times. The potentials obtained for the five analyses were averaged at each concentration. The average potential was plotted versus concentration. The relation between potential and concentration is logarithmic (equation 1) $X = S \log [Bb] + Y$, where $X$ is equal the potential, $S$ is the slope, and $Y$ is the intercept and ( $r$ ) is the correlation coefficient. The sensors display a linear response over the concentration range $1 \times 10^{-2}$ to $7.5\times10^{-6}$ , and $1 \times 10^{-2}$ to $6.0\times10^{-6}$, respectively over a pH range of 3.0 - 8.0. The limits of detection (LOD) and limits of quantification (LOQ) were determined using the formula: LOD or LOQ = $k$ S.D.a/b, where k = 3 for LOD and 10 for LOQ, S.D.a is the standard deviation of the intercept, and b is the slope. Also lower limit of detection (LOD) defined as the concentration of Bb corresponding to the intersection of the extrapolated linear segment of the calibration graph which are of $6\times10^{-6}$ and $3.0\times10^{-6}$M for sensor 1 and 2 respectively. The results of the proposed sensors are more sensitive compared with published one ( $6\times10^{-6}$ and $3.0\times10^{-6}$M for sensor 1 and 2 respectively compared with ~10-5M [ 20]).

### *3.5.2. Precision and Accuracy of the method*

The precision and the accuracy of the method were investigated by inter-day (repeatability) by the analysis of bambuterol, five replicate at the limit of qualification range. The precision and the accuracy of the method are expressed as RSD and % of deviation of the measured concentration. Also reproducibility (Day to Day or intraday) was investigated. The results obtained (Table 3) are within the acceptance range of less than 1.8 % (precision) and 2.3 (accuracy).

**Table 3.** Day to day reproducibility of the proposed membrane sensors.

| **Parameter** | **bambuetrol (200µg/ml)*<br>Within-day** | | **bambuterol (200µg/ml)*<br>Within-days** | |
|---|---|---|---|---|
| | **Bb-PM** | **Bb-PT** | **Bb-PM** | **Bb-PT** |
| R, % | 98.5 | 99.0 | 97.7 | 98.0 |
| R.S.D, % | 1.7 | 1.5 | 1.8 | 1.6 |
| Slope | 54.0 ± 1.9 | 56.0 ± 1.7 | 54.5 ± 2.0 | 56.0 ± 1.6 |
| Correlation coefficient | 0.998 | 0.999 | 0.997 | 0.998 |

* Average of 5 measurements ± RSD.

*R%, recovery percentage; RSD relative standard deviation

### *3.5.3. Ruggedness*

The ruggedness of the potentiometric method was evaluated by carrying out the analysis using two different analyst (operator) and different instruments on different days. The RSD of less than 2.0% were observed for repetitive measurements in three different day time periods using two different instruments and operators. The results indicate that the method is capable of producing results with high precision.

### *3.5.4. Robustness*

The robustness of the method is demonstrated by the versatility of the experimental factors that affecting the potential response. Preliminary inspection of the results under these various conditions suggested that the method is fairly robust, but the pH of the measuring solution should be in the range of 3.0 - 8.0.

### *3.6. Determination of bambuterol*

The applicability of the Bb membrane sensors for determination of the drug in the dosage forms was firstly cheeked by the studying the recovery of an accurate amount of pure Bb in solutions.

The direct determinations of bambuterol were carried out using the developed membrane sensors (Bb-PM or Bb-PT). The analysis of 3.0 - 4000.0 µg/ml bambuterol solutions (in five replicate) by direct potentiometry gave a good recovery of values for the proposed sensors, results are shown in Table 4.

**Table 4.** Direct determinations of bambuterol using PVC membrane sensors.

| **Added (□µg/ml)** | **Recovery, % ± RSD** | |
|---|---|---|
| | **Bb -PM** | **Bb -PT** |
| 3.0 | 98.0 ± 2.1 | 98.0 ± 2.1 |
| 5.0 | 98.2 ± 2.1 | 98.4 ± 1.9 |
| 10.0 | 98.5 ± 2.0 | 98.5 ± 1.9 |
| 50.0 | 98.5 ± 1.9 | 98.6 ± 1.7 |
| 100.0 | 98.5 ± 1.8 | 99.0 ± 1.8 |
| 200.0 | 98.5 ± 1.7 | 99.0 ± 1.5 |
| 500.0 | 99.5 ± 1.6 | 99.5 ± 1.5 |
| 1000.0 | 100.0 ±1.5 | 100.0 ± 1.4 |
| 4000.0 | 100.0 ±1.4 | 100.0 ± 1.3 |

* Average of 5 measurements ± RSD.

The applicability of the Bb-membrane sensors to the determination of the drug in the dosage forms was firstly checked by studying the recovery of an accurate amount of pure bambueterol in a reconstituted powder samples. The recovery obtained from five measurements was found to be 98.5 and 98.5 with a relative standard deviation of 1.5 and 1.6 % for Bb-PM, and Bb-PT respectively, results are shown in Table 5.

Results obtained for the analysis of bambuterol in its formulation by direct measurements using the proposed sensors and the British pharmacopeia methods[26] are given in Table 5. The data suggests the proposed method can be carried out on real products with equal confidence and accuracy.

**Table 5**. Determination of bambuerol in some pharmaceutical preparations using the proposed membrane sensors.

| **Preparation** | **bambuetrol (nominal, value)** | **Proposed method* R,% (RSD, %)** | | **British Pharmacopeia** | |
|---|---|---|---|---|---|
| | | **Bb-PM** | **Bb-PT** | **R, %** | **(RSD, %)** |
| Reconstituted powder | 5mg | 98.0 (2.0) | 99.0(1.8) | 98.0 | (1.8) |
| Bambec | 10mg | 98.5 (1.9) | 99.0(1.8) | 99.0 | (1.8) |

*Average of five determinations.

### *3.7. Application of Bb –PVC electrodes as indictor electrode.*

The developed electrodes in conjunction with an Ag/AgCl reference electrode have been examined as an end point indicator electrode for potentiometric titrations of the drug. Titration Bb with sodium tetraphenylborate using Bb-PM or Bb-PT sensors has been performed (Fig. 3). From the results it is clear that Bb reacts with NaTPB in the molar ratio of 1:1. The titration curves were symmetrical with a very well defined potential jump of about 200.0 mV for Bb-PM and Bb-PT respectively, indicating the high sensitivity of the electrodes.

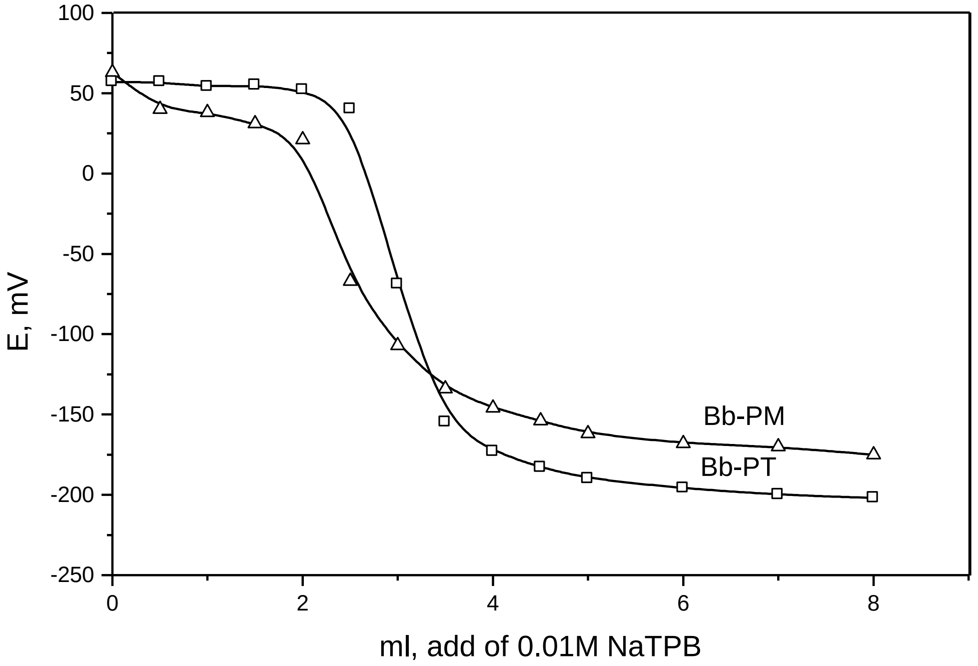

**Figure 3.** Typical potentiometric titration curves of 3.0 ml of 0.01M of bambuterol with 0.01M sodium tetraphenyl borate using sensor 1(Bb-PM) and sensor 2 ( Bb-PT).

## 4. CONCLUSION

Experimental comparison of two ion-pair complexes of Bb for use as electroactive material and different plasticizer in potentiometric membrane sensors revealed that in most cases, the Bb membrane sensor displayed good analytical performance characteristics. The sensitivity, linear range and slope are independent over the pH rang 3.0 - 8.0. The application of the proposed sensors to the determination of bambuterol in its pure solutions and pharmaceutical preparations is characterized by a high degree of precision and accuracy compared with the British pharmacopeia method. The developed sensors are used as indicator electrodes for potentiometric titration of Bb.

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## References

1. S.C. Sweetman, editor. Martindale: The Complete Drug Reference. 33rd ed. London: *Pharmaceutical Press*, 761 (2002).
2. M.J. O'Neil, A. Smith, P.E. Heckelman, S. Budavari Merck index. 13th ed. John Wiley and Sons, 166-167 (2001).
3. Y.L. Zhou, S.J. Zhao, G.L. Zhang, X.D. Li, Zh.Yiy Gon. Zaz., 33 (2002) 245.
4. O. Wannerberg, and B. Persson, *J.Chromatogr*., 435 (1988) 199.
5. A. Bartolinčić, V. Drušković, A. Spores, and V. Vinković, *J. Pharm. Biomed. Analysis*, 36 (2005)1003.
6. W. Luo, L. Zhu, J. Deng, A. Liu, B. Guo, W. Tan, R. Dai, *J. Pharm. and Biomed. Analysis,* 52(2010)227.
7. L. Liu, K.X. Li, A.X. Shi, Q.Ying, G.W. He, C.H. Sun, and Y.H. Song , *Yaowu Fenxi Zazh*i, 21 (2001) 316.
8. C. Lindberg, S. Jönsson, J. Paulson, and A. Tunek , *Biological Mass Spectrometry*, 19(1990)211.
9. A.X. Shi, K.X Li, G.Y. Cao, C.H. Sun, and Y.H. Song, *Yaowu Fenxi. Zazhi*, 21 (2001) 290.
10. R. Harris, P. Hodgkinson, T. Larsson, and A. Muruganatham , *J. Pharm . Biomed Anal*., 38 (2005)58.
11. D.J.Patel, S.A.Patel, and S.JK.Pate, *Intern. J. Pharm. and Biological Research*, 1(2010)71.
12. S.A. Patel, D.J. Patel, and N.J..Patel, *Internat. Research J. pharmacy*, 2 (2011) 145.
13. V. Pawar, S. Pai, and G.K. Roa, *Jordan J.Pharma.Sciences*, 1(2008) 152.
14. A. M. Badawy, N. M. Mostafa, A. E-A. B. Abd El-Aleem and N. T Lamie, *Intern. J. Comprehensive Pharmacy*, 2 (2011) 1.
15. Mostafa GA, Hefnawy M, Al-Majed A., *JAOAC Int*., 93 ( 2010) 549.
16. G.-B. Fatemeh, S. Saeed, and M. Ali, *J. Food and drug analysis*, 19 (2011)445.
17. A.A. Ensafi and A.R. Allafchian, , Sensors Journal, 11(2011)2576.
18. K. Vytras, "Potentiometry," in Encyclopedia of Pharmaceutical Technology, J. Swarbric and J. C. Boylan, Eds., vol. 12, Marcel Dekker, New York, NY, USA, 1995.
19. H. H. Bauer and G. D. Christian, *Instrumental Analysis*, J. E. O'Reilly, Ed.,, Allyn and Bacon Inc., Boston, Mass, USA, 1978.
20. A. M. Badawy, N. M. Mostafa, A. E.- B. Abd El-Aleem and N. T Lamie, *International J. Comperhensive pharmacy*, 6 (2006) 1.
21. S.S.M. Hassan, S.A.M. Marzouk, *Talanta*, 41 (1994)891.
22. A. Carggs, G.J. Moody, J.D.R. Tomas, PVC matrix membrane ion-selective electrodes. *J.Chem. Educ.*, 51(1974)541.
23. T.S. Ma and S.S. Hassan Organic analysis using ion selective electrode, Academic Press, London , UK, ( 1982), vol1 & 2.
24. IUPAC Analytical Chemistry Division, Recommendation for Nomenclature of Ion Selective Electrode. *Pure Appl. Chem.*, 66 (1994) 2527.
25. IUPAC Analytical Chemistry Division, Potentiometric selectivity coefficients of ion selective electrodes. *Pure Appl. Chem*., 72 (2000)1851.
26. The British Pharmacopoeia. 3rd ed. Vol.1. London: Stationary Office Books. 2001, 211-212.