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DETERMINATION OF BROMPHENIRAMINE(DIMETANE) IN DIFFERENT SAMPLES BY POLY (VINYL CHLORIDE) BASED MEMBRANE ELECTRODE

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ABSTRACT
The selective determination of bio-active material is very important for medical point of view. Ion – selective electrode are the device used for the selective determination of target species in solutions because these device measured activity instead of molar concentration. In this work we have tested NaTFPB as potential carrier for the selective determination of Brompheniramine(Dimetane) in solutions. The membrane with composition of Brompheniramine(Dimetane) -tetrafluorophenyl borate (BP – TFPB): DOP: PVC of 4%: 64%: 32% (w/w) works satisfactorily in the concentration range of 1.8×10^{-5} – 1.0×10^{-1} M, has a detection limit of 1.0×10^{-5} M and fast response time of 8 seconds. The proposed electrode can be used for a period of 3 weeks in a pH range of 2.5 – 6.0. The selectivity of membrane sensor towards target ions over some common interfering ions was calculated by MPM method.

KEYWORDS: Brompheniramine, ISE, PVC, ion-pair, Sodium tetrafluorophenylborate.

1 INTRODUCTION
Brompheniramine(Dimetane) is a second generation H_1-receptor antagonist, anti-histamine and anti-inflammatory medication. It also has mast-cell stabilizing effects. Brompheniramine(Dimetane) has been used both as a nasal spray and as eye drops,[1-5] Chemically Brompheniramine(Dimetane is (±)-3-[(4-bromophenyl)-N,N-dimethyl-3- pyridine-2-ylpropan-1-amine.[6- 9]

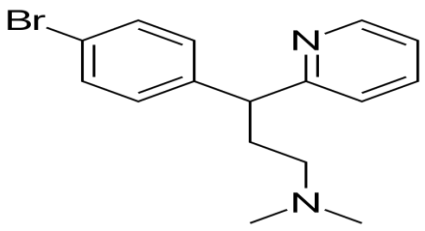

Figure 1: Structure of Brompheniramine(Dimetane).

Brompheniramine(Dimetane) nasal spray offers both flexibility of dose and dosage. Several clinical reports indicate that azelastine with amount of 0.28 – 1.12 mg/day is sufficient for the treatment of seasonal allergic rhinitis. Brompheniramine(Dimetane) is safe and well tolerated in both adults and children. However several side effects like bronchospasm, fast or uneven heartbeats, a bitter taste in mouth, headache, dizziness, dry mouth and sore throat. Thus the determination of Brompheniramine(Dimetane) in different pharmacological samples is a subject of importance.[10] Several methods such as high performance liquid chromatography (HPLC), the UV spectrophotometry, capillary electrophoresis, voltammetric method have been reported for the determination of Brompheniramine(Dimetane) in products and biological samples. But all these methods are relatively expensive, time consuming and require high infrastructure back up. Thus a quick, convenient, and extremely selective method is needed for the selective determination. Ion selective electrode for their low cost, simple infrastructure, high selectivity and high sensitivity are the good candidate for the selective determination of target species. In this work we have fist time tested sodium tetra fluro phenyl borate (NaTFPB) as electro active material for the fabrication of Brompheniramine(Dimetane) selective electrode for the determination of Brompheniramine (Dimetane) hydrochloride in different pharmacological and medicinal samples. The electrode work satisfactorily within the concentration range of 1.0×10^{-5} to 1.0×10^{-1} M for Brompheniramine(Dimetane) hydrochloride solution.

2 EXPERIMENTAL

2.1. Reagents and Instruments used

All the reagents of analytical grade and were used as received. High molecular weight polyvinyl chloride (PVC), sodium tetra fuloro phenyl borate (NaTFPB), dioctyl phthalate (DOP), bis-(2-ethylhexylsebacate (BEHS), dioctylsebacate (DOS) and tetrahydrofuran (THF) were purchased from Merck. All metal salts were brought from Siscolab (Mumbai India). Brompheniramine(Dimetane) hydrochloride and its syrup were obtained from different local pharmaceutical factories. All solutions were prepared using triply distilled water. All potentiometric measurements were made at 25 ±1ºC with a digital potentiometer (ECIL India)) using Brompheniramine(Dimetane)-selective membrane electrode in conjunction with an ECIL, India double junction Ag/AgCl reference electrode. A Stock solution of Brompheniramine(Dimetane) hydrochloride (0.1 M) solution was prepared by dissolving the calculated amount of drug in 20 mL water. The working solutions (1.0×10^{-6} to 1.0×10^{-1} M) were prepared by dilution of stock solution.

2.2. Preparation of ion – pair compound

Ion-pair compound of Brompheniramine(Dimetane) - tetrafluorophenylborate (BP-TFPB): About 20 mL of 0.01 mol L^{-1} solution of Brompheniramine(Dimetane) hydrochloride was mixed with 20 mL of NaTFPB solution (0.01 mol L^{-1}) under stirring. The resulting precipitate was filtered off, washed with water and dried .

2.3. Fabrication of electrode

To prepare membrane electrode the membrane components i.e. Brompheniramine(Dimetane) - tetrafluorophenylborate (BP-TFPB), plasticizers (DOP, BEHS, DOS) and PVC were added in THF (25 mL) and the solution was carefully dissolved to get a homogenous mixture. The resulting mixture was transferred into a glass dish of diameter 2 cm. The solvent was evaporated slowly until an oily concentrated mixture was obtained. A Pyrex tube of diameter of 5 mm was dipped into the mixture for about 10 s so that a transparent membrane of about 0.3 mm thickness was formed. The tube was then pulled out from the mixture and kept at room temperature for about 10 h. The tube was then filled with 0.01M Brompheniramine (Dimetane) hydrochloride as an internal filling solution. The electrode was finally conditioned for 24 h by soaking in a 0.01 M Brompheniramine(Dimetane) hydrochloride solution.[11] The following cell was assembled for the conduction of the emf (electromotive force) measurements; Ag–AgCl |internal solution, Brompheniramine(Dimetane) hydrochloride (0.01M)| PVC membrane | sample solution | Ag - AgCl, KC1 (std.) These measurements were preceded by the calibration of the electrode with several Brompheniramine (Dimetane) hydrochloride solutions.

3 RESULTS AND DISCUSSION

The determination of bio-active components is a subject of great importance especially for pharmacy and medicinal point of view. The use of ion – selective electrode for the determination of target ion in solution provides high selectivity, high sensitivity, fast response time and wide concentration range. Thus ion – selective electrode is one of the best method used for the detection of bio-active material in solution. In present study NaTFPB is tested as electroactive material for the selective determination of anti-histamine drug Brompheniramine(Dimetane) hydrochloride. The experiment is based on ion – dipole interaction between Brompheniramine(Dimetane) hydrochloride and tetrafluoroborate ion.

3.1. Optimization of membrane ingredients

The response of membrane electrode in significantly depends on the membrane components. In present study membranes of various compositions were fabricated and their potential responses were studded. After several experiments it was observed that the membrane with the composition of AZ - TFPB: DOP: PVC of 4%: 64%: 32% (w/w) gives the best possible results. The membrane without ion – pair does not show significant response towards Brompheniramine(Dimetane) hydrochloride. The use of plasticizers (DOP, BEHS and DOP) significantly improves the linear concentration range, and slope of calibration curve. The electrodes (table 1) with DOS and BEHS as plasticizer has a detection limit of 1.0 x10-^{4} M, within the liner concentration range of 3.8×10^{-4} –1.0×10^{-1} M respectively for Brompheniramine(Dimetane) hydrochloride solution. The electrode no. 3 with DOP as plasticizer was found superior in terms of linear concentration range, detection limit, and slope of calibration curve. The electrode no. 3 works satisfactorily in the concentration range of 1.8×10^{-5}-1.0×10^{-1} M, with detection limit of 1.0×10^{-5} and slope 35.5 ± 0.5 mV/decay of activity. Further increasing the amount of ion-pair does not improve the response characters of the electrode, thus membrane with the composition of ion-pair: PVC: plasticizer of 4%: 64%: 32% (w/w) was taken as the most optimized membrane. The best response character of electrode in presence of DOP as plasticizers is due to its high polarity which provides the best possible complexation environment within the solution.

3.2. Response time and life time

The response time of an electrode is evaluated by measuring the average time required to get a static potential within ±0.1 mV of the final steady-state potential, upon successive immersion of a series of test solutions, each having a ten-fold difference in concentration. The proposed electrode no. 3 gets the stable potential in a very short time of about 8 s However the response time for higher concentration is slightly more than for lower concentration. The experiments were performed from lower to higher

concentration (1.0 x 10^{-5} to 1.0 x 10^{-1} M). To evaluate the reversibility of membrane sensor the experiments were also carried in reverse direction by changing the concentration from higher to lower concentration (1.0 x 10^{-1} – 1.0 x 10^{-5} M). The response time to achieve the static potential is about 20 s. The life time of proposed sensor no. 3 is 3 weeks. After this time the slope and concentration range of the electrode will decrease, and the detection limit will increase. The electrode was tested for 5 weeks, during this time the electrode was used at least one hour per day. The change in response character with time is due to leaching of membrane components into the sample.

3.3. pH range

Presence of hydrogen ion in the solution significantly affects the potential response of membrane electrode. Thus the effect of pH on response characters was investigated in the range of 1.0 – 8.0. The pH of solution was adjusted by drop wise addition of HNO_3 and NaOH solution. The actual potential response curve for 0.01 and 0.001 M Brompheniramine (Dimetane) hydrochloride is shown in figure 4. This figure clearly indicates that the potential response of membrane electrode remains same in the pH range from 2.5 – 6.0. Thus the proposed electrode no. 3 can by successfully used in the pH range of 2.5 – 6.0. The fluctuation in potential at higher pH (> 6.0) is due to deprotonation of Brompheniraminenium ion, while at lower pH (< 2.5) hydrogen ion can remove the ion – pair from membrane.

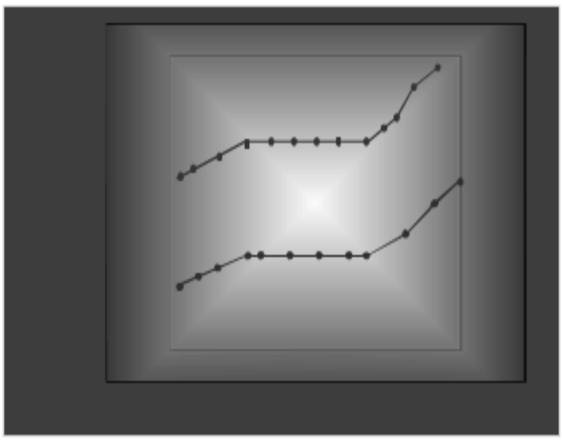

Figure 3: Effect of pH on response potential of electrode no. 3.

4. CONCLUSION

In this work we have tested NaTFPB as potential carrier forthe determination of anti-histamine drug Brompheniramine (Dimetane) in different pharmacological solutions. The proposed membrane electrode work satisfactorily in the concentration range of 1.8 x 10^{-5} – 1.0 x 10^{-1} M, has a detection limit of 1.0 x 10^{-5} M and fast response time of 8 seconds. The proposed electrode can be used for a period of 3 weeks in a pH range of 2.5 – 6.0. The selectivity of membrane sensor towards target ions over some common interfering ions was calculated by MPM method.

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