

NOVEL PVC MEMBRANE SELECTIVE ELECTRODES FOR DETERMINATION OF SALICYLIC ACID IN PHARMACEUTICAL PREPARATIONS

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ABSTRACT

Newly developed coated wire electrodes have been used for the determination of salicylic acid in pure form, pharmaceutical preparations. The proposed sensor incorporated salicylic acid phosphotungstate ion pair complex as electrical material in PVC matrix membrane and dioctylsebacate as solvent mediator. The selective electrodes were fabricated based on the incorporation of salicylic acid with the ion exchangers, phosphomolybdic acid (CTP-PMA), phosphotungstic acid (CTP-PTA) and a mixture of both acid (CTP-PMA/PTA). The potential responses of the electrodes were influenced by the pH of tested solution. The resulting electrode

demonstrates near -Nernstain response over wide linear range (10^{-4} - 10^{-2} M) salicylic acid with lower limit of detection of 3.7×10^{-5} M and slope of 57.46 ± 0.1 mV/decade. The electrode has fast and stable response, good reproducibility, long term stability (4 Months) and applicability over a wide pH range (4.5-8). The sensor displayed a good selectivity for salicylic acid with respective the number of common foreign inorganic, organic species, excipients and the filler added to the pharmaceutical preparation. Fortunately these materials do not interfere with the salicylic acid. The sensor was successfully applied for the determination of salicylic acid. Under the condition of pH 5-10, the electrodes exhibit linear response over concentration range 1.0×10^{-7} - 1.0×10^{-2} mol/L with Nernstian slopes (56.29 ± 0.09 , 54.60 ± 0.09 and 58.17 ± 0.28 mV/ decade at 25°C). The influence of possible interfering species such as common inorganic cations, amino acids and different pharmacological related compounds was studied. The electrodes were successfully applied in determination of the drug in tablets by direct and standard addition potentiometry.

KEYWORDS: Salicylic acid, Ion-selective electrodes, Potentiometry determination, pharmaceutical formulations.

1. INTRODUCTION

The quick determination of minute quantities of ionic species by simple methods has a great importance in analytical chemistry. Potentiometry detection based on ion selective electrodes (ISEs) is the simplest of all and offers unique advantage. Such as simple design and operation, reasonable selectivity, fast response applicability to colored and turbid solution and low cost. These electrodes can be prepared by incorporating any of the many ion exchanger or neutral-sequestering agents within a plasticized PVC matrix and very useful tools for clinical, chemical and environmental agents within a analysis.^[1] Salicylic acid (SA) (Figure 1) (i.e 2-Hydroxybenzoic acid). Salicylic acid is used as a food preservative ^[2], a bactericidal and an antiseptic.^[2] Potentiometry with ion-selective electrodes (ISEs) is still one of the most promising analytical tools capable of determining both inorganic and organic substances in medico-biological practice. These medicinal properties particularly for fever relief were discovered in ancient times. It is used as an anti-inflammatory drug.^[3] Salicylic acid is known for its ability to ease aches, pains and reduce fevers in modern medicine.^[4] Salicylic acid and its derivatives are used as constituents of some aspirin products. For example methyl salicylate is used as a liniment to soothe joint and muscle pain, and choline salicylate is used topically to relieve the pain of mouth ulcers. Salicylic acid is a key ingredient in many skin-care products for the treatment of seborrhoeic dermatitis, acne, psoriasis, calluses, corns.^[4, 5] Particularly without prior separation ISEs are useful in the case of drugs which are unstable.

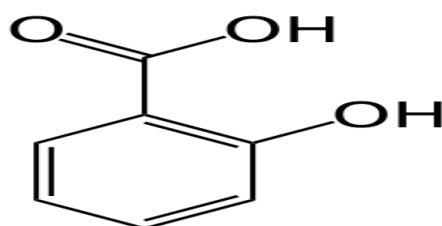


Figure. 1. Structure of Salicylic acid

2. EXPERIMENTAL PART

2.1. Equipment: All potentiometer measurement was made at $25^{\circ}\text{C} \pm 1$ with an Orion (Model 811) pH/mv meter. an Orion double junction Ag/AgCl reference electrode (Model 90-92) containing 10% (w/v) KNO_3 in the outer compartment was used in conjunction with PVC-

Salicylic acid based on sensor combined glass electrode (Orion HI 1332) was used for all pH adjustment.

2.2. CHEMICALS AND SOLUTIONS

AR grade Chemicals were used. Doubly distilled water was used for all experiment. Salicylic acid by sigma Aldrich laboratory. Polyvinyl chloride (PVC), phosphotungstic acid (PTA), Tetrahydrofuran (THF), Dioctyl sebacate (DOC) were obtained from Fluka, 10^{-3} M of solution was prepared with doubly distilled water. Dilute solution (10^{-2} - 10^{-6} M) were prepared by successive dilution of the respective stock solution using acetate buffer of pH 5.

2.3 POTENTIOMETRIC DETERMINATION OF SALICYLIC ACID

2.3.1. Construction of the sensors: Salicylic acid ion pair complexes were prepared by slow addition of 20 ml of 10^{-2} M aqueous solution of phosphotungstate and 10 ml of 10^{-2} M salicylic acid were mixed and stirred for 15 min. The off white precipitate was filtered off with porosity sintered glass crucible, washed with deionized distilled water, dried at room temperature and ground to fine powder. The elemental analysis agreed with the composition.

10 mg portion of salicylic acid ion pair complexes was thoroughly mixed with 0.19 g PVC, 0.35g Dioctyl Seagate and 5 ml of THF in glass petri dish (5-cm diameter) covered with a filter paper and left to stand overnight to allow slow evaporation of the solvent at room temperature. A master PVC membrane approximately 0.1 mm thick were cut with a cork borer and glued on to 7 mm PVC body using THF. The tube was then filled with internal filling solution consistent of equal volume of 1×10^{-2} M of both salicylic acid and potassium chloride. An Ag/AgCl coated wire was employed as an internal reference electrode.

2.3.2. Sensor calibration: The sensor was pre-conditioned after preparation by soaking for at least 24 h in 10^{-2} M Salicylic acid solution and was stored in the same solution when not in use. A solutions (25 ml) of 10^{-6} - 10^{-2} M standard (SA) were transferred in to 50 ml beaker and PCV-SA-PT membrane sensor in conjunction with the Ag/AgCl reference electrode was immersed in the solution. The solution was stirred and the potential was recorded after stabilization and plotted as a function of (SA) concentration, the graph was used for the subsequent determination of unknown concentration of SA.

The potential readings were recorded after stabilization and the emf were plotted as a function of logarithm salicylic acid concentration. The lower detection limit was taken at the point of intersection of the extrapolated linear segments of the salicylic acid calibration curve.

2.3.3. Effect of dynamic response time: The response time of the sensor was measured in constantly stirred solution of varying salicylic acid ions concentration. The stability of the potential was measured for different concentration.

2.3.4. Effect of pH: A standard 10^{-2} M and 10^{-3} M of aqueous Salicylic acid solution were prepared and adjusted to various pH values in the range 2-12 with dilute hydrochloride acid and /or sodium hydroxide solutions. The change was examined by plotting the change of potential against pH values.

2.3.5. Determination of selective coefficients

Selective coefficients of the sensor were determined using the separate solution method (SSM)^{[6][7]} and calculated from the rearranged Nicolsky equation.

$$\text{Log } K^{\text{pot}} = [\text{Ex} - E_{\text{salicy}}/S] - \log a_x (Z_{\text{salicy}} \cdot M // Z_x) + \log a_{\text{SA}}$$

Where,

E_{salicy} is the potential measured in 10^{-2} M salicylic acid solution.

Ex is the potential measured in a 10^{-2} M solution of the interfering cations

Z_{salicy} and Z_x are the charges of salicylic acid and interfering ions respectively.

S is the slope of the sensor calibration plot.

The selective was determined in the presence of buffer acetate pH 5 prepared by dissolving 13.6 g of sodium acetate and 6 ml of glacial acetic acid in sufficient water to produce 1000 ml.

2.4. DETERMINATION OF SALICYLIC ACID IN ITS PHARMACEUTICALS PREPARATION

Five tablets of the drug were weighed in a small dish, powdered and mixed well. A portion equivalent to one tablets (i.e 10 mg of salicylic acid) was weighed and dissolved on 15 ml hydrochloric acid (1N) and completed to 1000 ml by distilled water, shaken well and filtered through glass crisible. One ml of this solution transferred to 25 ml volumetric flask, followed by buffer acetate of pH 5. The EMF of the test solution was directly measured and compared with the calibration graph.

3. RESULTS AND DISCUSSION

3.1. The performance characteristic of salicylic acid tungstophosphate –PVC-membrane sensor: Salicylic acid cations react with phosphotungstate anion to form water insoluble ion

association complex. The prepared complex was identified and examined as ion exchange in PVC membrane sensor for salicylic acid cation.

The electrochemical performance characterization of the sensor was according to IUPAC recommendation and the results are summarized in table (1) and figure 2. The proposed sensor showed near-Nernstian response for at four orders of magnitude of salicylic acid (10^{-5} - 10^{-2} M) with calibration slope of 57.46 mV/decade and lower limit of detection of 3.7×10^{-6} M. The proposed sensor showed fast response time at various drug concentration. By using the dipping method the electrode is instantaneously in to a solution of known activity of the tested ion simultaneously and the response record is started. In order to examine the dependence of the response time on concentration and the operation repeated with a series of separate solution.^[8] At a concentration level of 10^{-3} M salicylic acid, their response times defined and the time required to attain 95% of steady state potential, not exceed 5s.

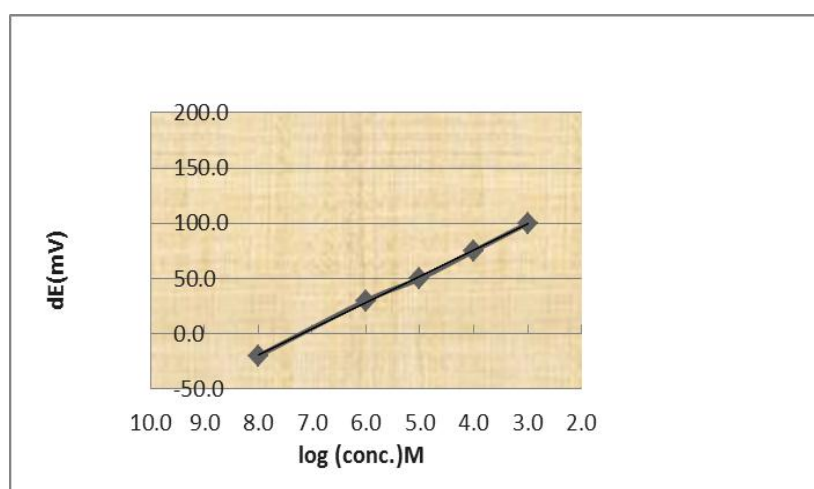


Figure-2. Calibration curve for Salicylic acid sensor

Table 1. Performance characterize of salicylic acid membrane sensor

Sr. No.	Parameter	Salicylic acid
1	Slope(mV/decade)	23.46±0.1
2	Linear concentration range(M)	1×10^{-3} - 1×10^{-1}
3	Life span(month)	2 months
4	Lower limit of detection (M)	3.4×10^{-6}
5	Working pH(pH)	3.5-8
6	Response time(s)	10
7	Correlation coefficient(r)	0.999
8	Slope(mV/decade)	23.46±0.1
9	Linear concentration range(M)	1×10^{-3} - 1×10^{-1}
10	Life span(month)	2 months

At lower concentration (10^{-4} - 10^{-5} M, the response time did not exceed 10 s. The response characteristics of the sensor did not change during 4 months of the continuous use. A study of the potential response of SA-PVC-PT membrane sensor as a function of change in the pH of the drug and no change occur over the pH range 4.5-8, See Figure 3. At lower pH the potential readings were decreased and at higher pH the disturbance happen in EMF reading due to interference of H^+ as shown in figure 3.

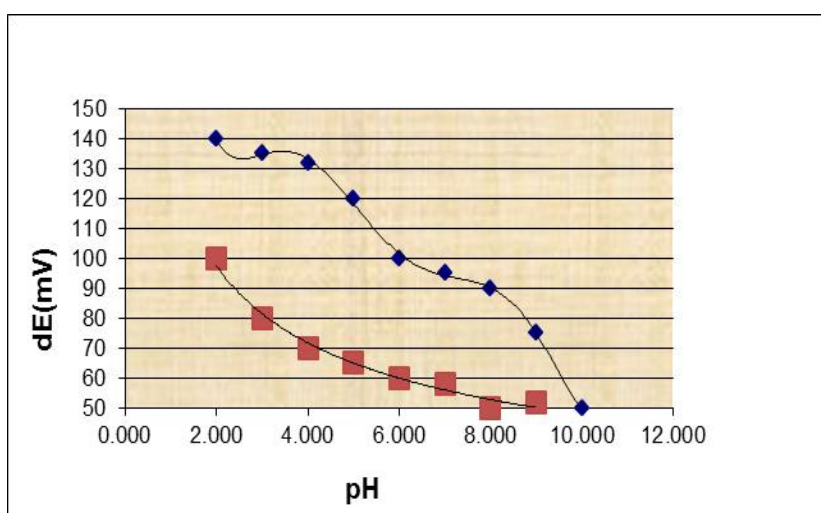


Figure. 3-Effect of pH on the response of (SAZ-PT (DOS) based membrane sensor.

3.2 Selectivity of SA-PT-PVC membrane sensor

The potential selectivity coefficients K^{pot} of salicylic acid sensor was evaluated using the separate solution.^[9] With 10^{-2} M concentration level of alkali, transition metal and some excipients in the drug such as Corn, Starch, aerosol and other (figure 4). The bulk of the excipient in a pharmaceutical tablets does not show any interference. This result supports the fact that selectivity is determine primarily by the partition coefficients of the prorogated amine between organic and aqueous phase.^[9] The inorganic cations do not interfere because of difference in ionic size and mobility.^[10] They showed a higher response for Salicylic ion than other interference (table 2).

Table2. Selectivity coefficients of sensors based on (SA) ionopore.

Sr. No.	Interferent (M)	K_{pot}
1	Corn	2.1×10^{-3}
2	Starch	1.9×10^{-3}
3	Aerosol	1.5×10^{-3}

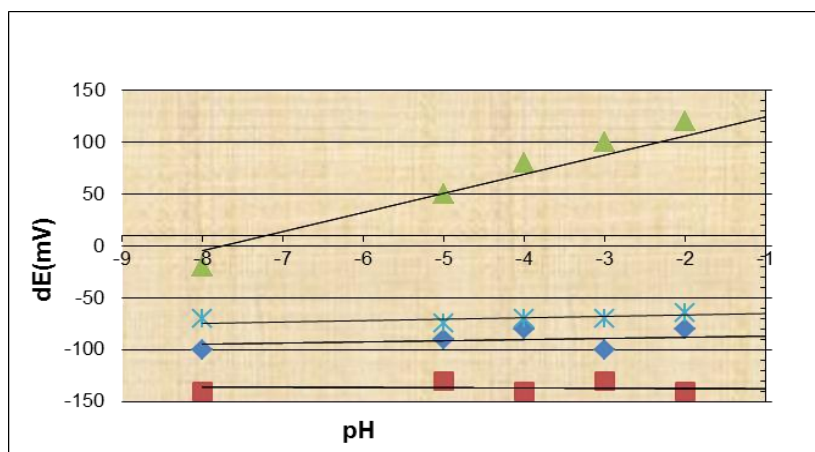


Figure 4. Selectivity characteristics of (SA) sensor

3.3 EFFECT OF IONIC EXCLUDERS

An effort was made to improve the response characterize of Salicylic acid^[11] sensor, by incorporating Nitron in the sensor cocktail to act as anion excluder to improve selectivity to reduce the activation barrier of the membrane /solution interface. The sensor gives a bad response and non Nernstian slope and no improvement of the sensor occurs. The deviation from linear ship might be attributed to the fact that not enough potential was built on the electrode membrane surface, PVC membrane used in this study contained enough anionic site even without addition of extrinsic additive.^[11]

3.4 ANALYTICAL APPLICATION

This membrane electrode can be successfully used for analysis of salicylic acid in pharmaceutical^[12,13,14], Drug delivery system^[15,16] and Derivative preparation.^[17,18] The results obtained to determine Salicylic acid in pharmaceutical preparation Alpyrin based on membrane sensor show average of 99.1% Given in table (3). No interference occurred from excipients used in pharmaceutical and used in pharmaceutical preparation. As literature survey shows most of drug are made from 1,4 dihydropyridine heterocyclics.^[19-20]

Table-3: Dermination of Salicylic acid in pharmaceutical preparation

Sr. No.	Trade name and source	Nominal content (mg tablet ⁻¹)	Recovery
1	Alpyrin (Lincoln)	100 mg tablets ⁻¹	99.1%

Table 4. Comparison between different methods for determination of Salicylic acid

Sr. No.	Method	Working range	Lower limit of detection	Accuracy
1	HPLC	50-1000	15 mg/l	NR
2	HPLC	10-1000	5 mg/mL	98-105%
3	Ion Selective Electrode	1x10 ⁻⁵	3.4x10 ⁻⁶	99.1% (This work)

4. CONCLUSIONS

Although ion selective electrode have found many successful application in pharmaceutical analysis mainly because of their low cost, ease of use, maintenance, the simplicity and speed of the assay procedure, It has been applied yet to the determination of salicylic acid. It is usually possible to develop procedure for the determination of drugs in pharmaceutical preparation that need only a pre dilution with suitable buffer. Turbidity due to the matrix is not usually a problem. Usually the potentiometer method can be simple and fast for pharmaceutical analysis when suitable sensor is available. Table (4) reported a comparison between the present work and those of the previously done by other sophisticated method. It was found that the proposed sensor has the advantage of high selectivity, fast response and direct application of drug samples without prior separation or treatments. On the other hand the suggested method is simple and reproducible [RSD=1.1-3.1 and 1.5-2.7 for pure and dosage forms respectively]. The proposed method can analyze Salicylic acid in its pharmaceuticals forms without interference from excipients.

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