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RESEARCH ARTICLE

AN ELECTROCHEMICAL CHARACTERISTICS OF PROMETHAZIE HCL USING ION SELECTIVE ELECTRODES

[1]Sharma, B.D. and [2]Seema Rani

[1]Department of Chemistry, Delhi University
[2]Department of Pharmacy, Mewar University

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ABSTRACT

The highly selective and sensitive PVC based membrane sensor was fabricated by using 1,3,5-tris [(2,3-dihydroxybenzylamino) amino methyl]cyclohexane (L) as a neutral membrane carrier for the potentiometric determination of Promethazine HCl. The membrane with the composition of33% PVC, 64% Plasticizer, 3% PM-PMD (Ionophore) and 1% NaTPB was found to be best in terms of response characteristics of sensor assembly. The proposed membrane sensor has very low detection limit of 2.0 x 10-8 M, within the concentration range of 5.0 x 10-8 – 1.0 x 10-2 M, and has fast response time of about 10s. The proposed sensor was used for the selective determination of Promethazine HCl. in different synthetic as well as real sample.

INTRODUCTION

Antihistamine (Histamine antagonist) is a pharmaceutical drug that inhibits action of histamine by blocking it from attaching to histamine receptors. There are several types of antihistamine drugs. H_1 antihistamines are used to treat symptoms of allergy, such as runny nose and watery eyes, H_2 antagonists (cimetidine), which are widely used for the treatment of acid reflux and stomach ulcers, because they decrease gastric acid production (Sade, 1980). The H_3 and H_4 do not yet have a defined clinical use, although a number of drugs are currently in human trials (*wikipedia.org/wiki/Histamine_antag*).

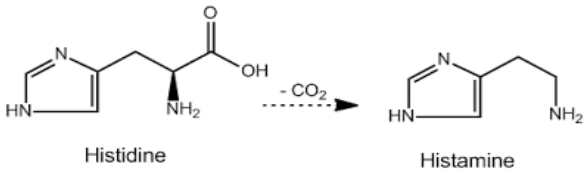

Fig. 1. Decarboxylation of histidine to histamine

The increasing use of ion sensors in the fields of environmental, agricultural and medicinal analysis is stimulating analytical chemists to develop new sensors for the fast, accurate, reproducible and selective determination of various species. In the past few decades, considerable efforts have led to the development of selective sensors for various medicinal compounds (Ni, 2001). Histamine is derived from the decarboxylation histidine (amino acid). The decarboxylation is catalyzed by an enzyme histiminase, which is also involved in the metabolism of the bioactive amines. They cause the tissues in our nose to swell, our nose and eyes to run and our eyes, nose and sometime mouth to itch. Sometime they also cause itchy rash on our skin, called (Wang, 1996).

Ion selective electrodes

An ion selective electrode (ISE) measure the activity of an ion in a solution by measuring the electric potential formed across a membrane when the electrode is submerged in the solution.

Corresponding author: Sharma, B.D.
Department of Chemistry, Delhi University

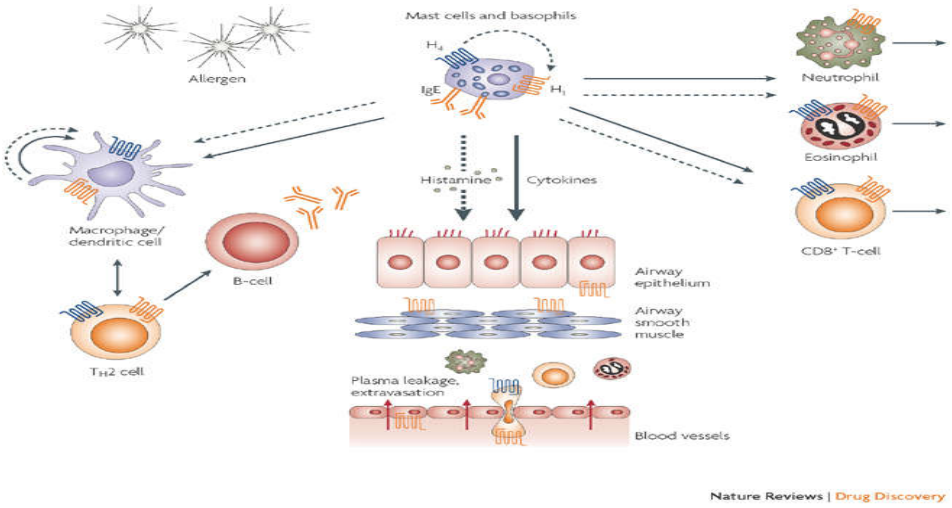

Fig. 2. Mechanism of action of antihistaminic drugs

In order to measure the electrode potential developed at the ion-selective membrane the ISE/pH electrode must be immersed in the test solution together with a separate reference system and the two must be connected via a millivolt measuring system.At equilibrium, the electrons added or removed from the solution by the ISE membrane (depending on whether it is cation or anion sensitive) are balanced by an equal and opposite charge at the reference interface. This causes a positive or negative deviation from the original stable reference voltage, which is registered on the external measuring system (Correia dos Santos, 2002). The relationship between the ionic concentration (activity) and the electrode potential is given by the Nernst equation:

$E = E^0 + (2.303RT/ nF) \times Log(A)$

Table 1. Ion selective electrodes in pharmaceutical analysis

DRUG	IONOPHORE	CONCENTRATION	REFERENCES
Tetracycline	Tetracycline silicotungstate	1.0×10^{-2} -3.0×10^{-5}	Yao et. al. (1989)
Benzyl penicillin	Benzyl penicillin & quaternary amine	5.0×10^{-1} -5.0×10^{-3}	Dumkiewics (1992)
Methadone	Dinonyl naphthalene sulphonic acid	1.0×10^{-5} -1.0×10^{-6}	Valsami et. al. (1989)
Naproxen	Tetraheptyl ammonium napronate in p-nitro cumene	1.0×10^{-1} -1.0×10^{-4}	Valsami et. al. (1989)

EXPERIMENTAL:(Determination of Promethazine HCl)

Reagents and Equipments

Ammonium phosphomolybdate
Promethazine HCl
PVC (Poly Vinyl Chloride)
DBP, DBBP
OA
CN
THF

Ion analyzer, pH meter and Saturated calomel electrodes

Preparation of ion pair- compound

Composition:

Promethazine HCl	20ml(0.01M)
Ammonium phosphomolybdate	20ml(0.01M)

Steps:1

20 ml solution of Promethazine Hcl+20ml of amm. Phosphomolidbate
↓
(at room for temp. 1hr)
Precipitate of (PM-PMD) was obtained
↓
Precipitate filtered off wash with water and dried

Step: 2

Promethazine Selective PVC Membrane Electrode (Ionophore)
PM-PMD:Plasticizers:PVC
3: 64: 3
↓
(dissolved in THF)Resulting solution transferred into glass dish of 2cm diameter
↓
Solvent was allowed to evaporate until conc. Mixture was obtained
↓
A pyrex tube dipped into conc. Mixture for 10sec
↓
A transparent membrane about 0.3mm thickness was formed
↓
Glass then pulled out and kept at room temp. for 5 hr
↓
Tube was filled with an internal solution of 0.001M Promethazine HCl solution
↓
The electrode was conditioned for 24h by soaking in a 1.0x10-2M of Promethazine solution.

Step: 3 Cell assembly for potential measurements:

Ag/AgCl, 0.1M │ Internalreferencesolution0.001M │ testsolution │ 1MKCl,(KCl)Ag/AgCl

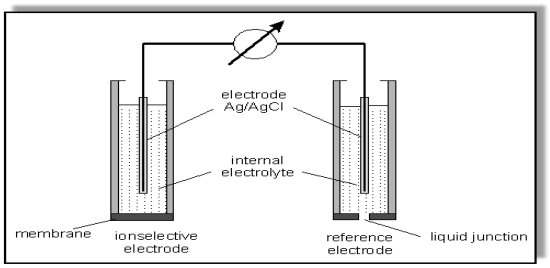

Figure 3. Cell assembbely

RESULTS AND DISCUSSION

The membrane electrode (no. 1) based on DBP as plasticizer has a detection limit of 1.0 x 10^{-6} M in a linear working concentration range of 1.0 x 10^{-6} M – 1.0 X 10^{-1} with slope of 50.5 ± 0.3 (mV/dec. of activity). It was observed that 62 – 65% of the plastcizer as membrane components gives the best posible response. It was observed that the ionophore more than 3% (w/w) as membrane component does not improved the detection limit and linear concentration range. pH effect: It was observed that the potential of electrode assembly remains almost same in a pH range of 2.5 to 6.0.

Conclusion

A promethazine phosphomolibdate (PM-PMD) ion-pair compound was used as electroactive material for construction of promethazine selective electrode. The electrode of the composition of PVC: PM-PMD: DBP of 33: 3: 64 (%, w/w) has a detection limit of 1.0 x 10^{-6} M in a liner concentration range of 1.0 x 10^{-6} – 1.0 x 10^{-1} M with a slope of calibration curve of 50.5 ± 0.3 (mV/decay of activity). The electrode can be used in a pH range of 2.5 – 6.0 for a period of 4 weeks and has fast response time of about 5 s. The selectivity coefficient calculated by MPM method indicates that the electrode can be alllied for the determination of promethazine in presense of other interfering ions.

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