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Potentiometric sensor for methylene blue based on methylene blue–silicotungstate ion association and its pharmaceutical applications

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Abstract

A methylene blue (MB) poly(vinyl chloride) membrane sensor based on MB–silicotungstate (SLT) ion association as electroactive material was described. The linear response covered the range 1×10^{-3}–1×10^{-6} mol dm^{-3} MB solution, with a slope 52.0 ± 0.8 mV decade^{-1} (pH range 3.0–10.0). The detection limit was 7.65×10^{-7} mol dm^{-3}. The electrode showed stability, good reproducibility and fast response. Interferences from common inorganic cations, some organic base were negligible. These characteristics of the electrode enabled it to be used successfully for the determination of MB in injection. There was a good agreement for the results of MB content in injection between potentiometric method and USP standard procedure. © 1999 Elsevier Science B.V. All rights reserved.

1. Introduction

Methylene blue, (3,7-bis(dimethylamino)phenothiazin-5-ium chloride trihydrate) was an antimethemoglobinemic agent and an antidote to cyanide [1]. Various methods had been used for its determination, e.g. complexmetry [2], spectrophotometry [3,4], ion-exchange chromatography [5], thin layer and high performance liquid chromatography [6], fast atom bombardment and tandem mass spectrometry [7], coulometric titration [8], reductimetric titration [9], polarography [10–12] and potentiometric titration [13–18]. Although potentiometry using a suitable indicator electrode was widely used in pharmaceutical analysis [19,20], no data had ever been reported about MB ion selective electrode (ISE).

The present paper describes the construction and performance characteristics of a MB ion-selective electrode based on the ion association MB–SLT embedded in a polyvinyl chloride (PVC) matrix. Application of the proposed electrode to the determination of MB content in injection would also be described.

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2. Experimental

2.1. Reagents

All reagents were analytical reagent grade and were used as received without further purification unless otherwise stated. All solutions prepared with distilled and deionized water. The MB injections (Jiangsu Taixing, Jiangsu, People's Republic of China) were purchased from local drug store.

2.2. Apparatus

All e.m.f. measurements were made at $25 \pm 1°C$ with an Orion microprocessor ionanalyzer (model 901). The electrode was used in conjunction with a model 801 double-junction calomel electrode (Jiangsu Electroanalytical Instrument Factory, People's Republic of China). The pH values of all solutions were measured with a model 231 glass electrode (Shanghai Dian Guang Device Works, People's Republic of China). The USP procedure [21] for the assay of MB injection was performed with a spectrophotometer (model 721–100, The Third Analytical Instrument Factory, Shanghai, People's Republic of China).

2.3. Preparation of the electrode

The ion-complex was prepared by mixing stoichiometric amounts of a 0.01 mol dm^{-3} aqueous solution of SLT with an equimolar aqueous solution of MB. The blue precipitation obtained was sedimented by centrifugation 3000 g, extensively washed with deionized water and dried over phosphorous pentoxide for 2 days in an evacuated disciccator.

The THF solution (5.0 cm^3) containing 11.9 mg ion association together with 150 mg of PVC and 300 mm^3 of DBP (dibutyl phthalate) were pored into small glass ring (diameter 46 mm) lying on glass cover slip. The ring was covered by a sheet of filter-paper and a second cover slip to obtain slow evaporation of the solvent over a period of 24 h at room temperature. It was ca. 0.3 mm for the thickness of the obtained PVC membrane.

The electrodes were prepared by gluing the cut out PVC membrane disc onto the cleaned ends of PVC modules by the means of a PVC–THF solution (62 mg of PVC in 1.0 cm^3 of THF). The modules were made from PVC tubes and had a length of 4 cm and a thread fitting to the electrode bodies. The complete electrodes were assembled by screwing the membrane modules onto the electrode bodies, which contained an Ag-AgCl internal leadout (laboratory made). The electrode body was filled with an inner filling solution containing 10^{-1} mol dm^{-3} NaCl and 10^{-3} mol dm^{-3} MB solution (saturated with AgCl). The schematic construction of the methylene blue selective electrode was presented in Fig. 1. The assembled electrodes were conditioned by soaking in a 4×10^{-3} mol dm^{-3} methylene blue solution for about 24 h. When not in use, the electrodes were stored in the same MB solution and thoroughly washed with deionized water between measurements. The assembled membrane modules were stored dry at room temperature before use.

2.4. Direct potentiometry

Standard solution of 1×10^{-2}–1×10^{-7} mol dm^{-3} MB solutions of pH 4.0 (citrate buffer) were prepared by serial dilution of a 1×10^{-1} mol dm^{-3} solution of MB. The electrode was placed in the well stirred solution and potentials were read at 30-s intervals. Calibration graph (E, mV versus pMB) was plotted in the usual way. The unknown concentration was determined from
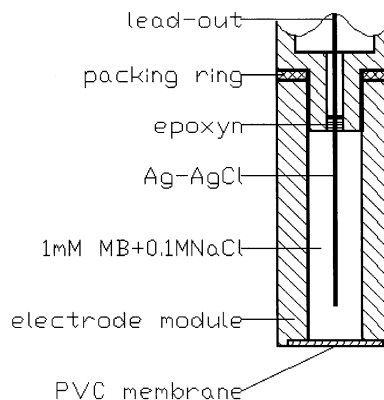

Fig. 1. The schematic construction of the methylene blue selective electrode.

the calibration graph. For more accurate results the standard addition method was recommended as following.

2.5. Standard additions method

Standard methylene blue solutions and methylene blue injection were analysed using the standard additions method [22]. Six batches of 5 cm³ methylene blue injection were each transferred into a calibrated flask (50 cm³) and diluted to the mark. The standard additions method was performed by spiking 200 mm³ of standard 2×10^{-3} mol dm⁻³ methylene blue solution into 20 cm³ of the test solution and measuring the change in potential.

3. Results and discussion

Typical calibration graph for the MB membrane electrode in Fig. 2 showed that the electrode was linear in the range of 1×10^{-3}–1×10^{-7} mol dm⁻³ for citrate buffer solution. The equation of the calibration graph was $E = E^0 + 52.0 \pm 0.8 \times \log[\text{MB}]$ with a correlation coefficient of 0.9998. The response characteristics of the electrode were shown in Table 1. The detection limit observed for the MB–SLT electrode, which was determined according to the IUPAC recommendations [23], were found to be 7.65×10^{-7} mol dm⁻³. The stability of the electrode response was checked over a period of 6 months. The response time of the electrode depended on the concentration of MB (< 1 min for 1×10^{-2}–1×10^{-4} mol dm⁻³ MB solutions and 1–2 min for 1×10^{-5}–1×10^{-6} mol dm⁻³ MB solutions). The electrode response displayed good stability and reproducibility over the test, as shown by the relative standard deviation values.

The effect of pH (1×10^{-3}–1×10^{-5} mol dm⁻³ MB solution) on the electrode potential was investigated by observing the changes in the potential readings with pH of the solution after the addition of small volumes of HCl and/or NaOH (0.1 or 1 mol dm⁻³). The investigated electrode gave a useful pH range from 3.0–10.0 as shown in Fig. 3. In alkaline media the measure-
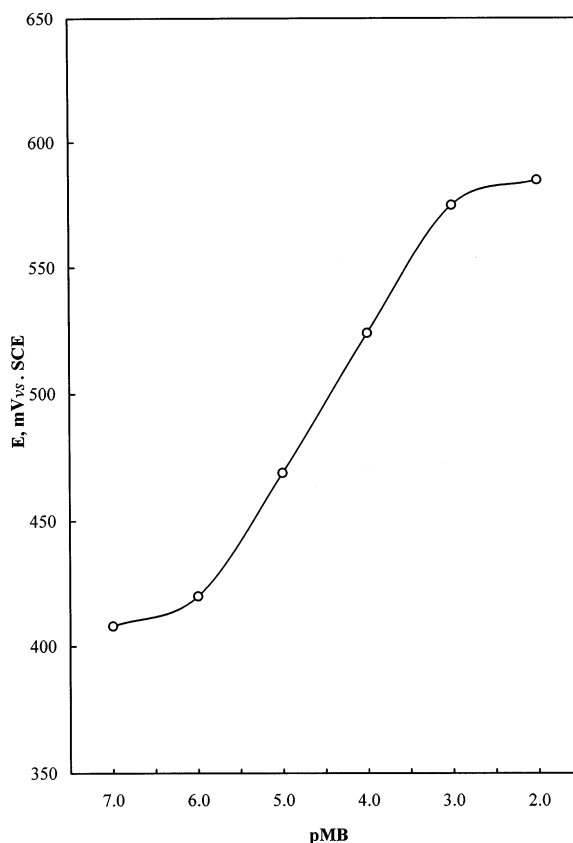

Fig. 2. Calibration graph for the methylene blue selective electrode.

ment were hindered owing to the formation of a precipitate in the test solutions.

The selectivity coefficients of the MB–SLT electrode determined against a number of dyes

Table 1
Response characteristics of methylene blue selective membrane electrode

Parameter	Response
Slope (mV pMB⁻¹)[a]	52.0 ± 0.8
Intercept E^0 (mV)[b]	731 ± 1.4
Linear range (mol dm⁻³)	1×10^{-3}–1×10^{-6}
Detection limit (mol dm⁻³)	7.65×10^{-7}

[a] Standard deviation of average slop values for multiple calibration ($n = 50$).
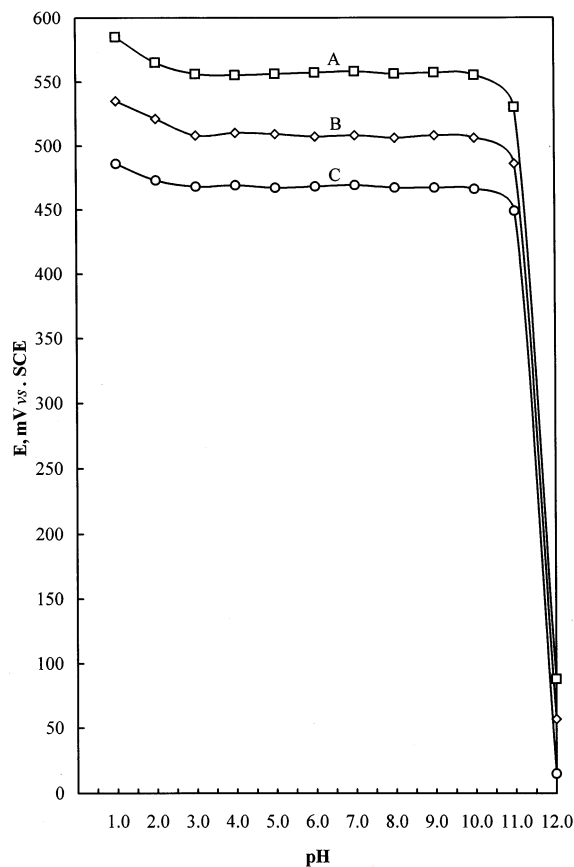[b] Standard deviation of values recorded over a period of 3 months ($n = 90$).

Fig. 3. Effect of pH on the response of the methylene blue electrode (A: 1×10^{-3} mol dm^{-3}; B: 1×10^{-4} mol dm^{-3}; C: 1×10^{-5} mol dm^{-3} methylene blue solution).

and alkaloids using the separate solution method [24] were given in Table 2. The results showed the electrode was reasonable selective towards MB. Interference from metal cations, glucose and fructose were generally negligible. However, with exception of acid chrome blue K and xylenol orange, other dyes such as methyl violet, crystal violet, brilliant and malachite green caused significant interference. Fortunately, these interferences were absent in MB injection.

The proposed electrode was employed for the assay of MB content in injection by the potentiometric method and compared with the USP standard procedure [21]. The results of the potentiometric methods compared with the USP standard procedure were shown in Table 3. As

could be seen in Table 3 high precision was obtained (RSD < 2%) by potentiometric method.

4. Conclusion

The MB-selective plastic membrane electrode, based on MB–SLT ion association in a PVC matrix, exhibited useful analytical characteristics for the determination of MB in pharmaceuticals.

Table 2
Selectivity coefficients for the methylene blue selective membrane electrode at 25°C

Interferent	$K_{MB,J}^{pot}$
Li$^+$	4.7×10^{-3}
Na$^+$	3.1×10^{-3}
K$^+$	2.6×10^{-2}
Ba^{2+}	3.6×10^{-4}
Mg^{2+}	5.8×10^{-4}
Ca^{2+}	6.2×10^{-4}
Cu^{2+}	9.7×10^{-4}
Fructose	6.3×10^{-3}
Glucose	4.9×10^{-3}
Maltose	7.1×10^{-3}
Acid chrome blue K	9.9×10^{-6}
Bromo cresol green	3.4×10^{-5}
Oxylenol orange	2.1×10^{-5}
Brilliant cresyl blue	1.72
Crystal violet	2.1×10^{3}
Methylene violet	9.8×10^{2}
Malachite green	1.7×10^{2}
Berberine	2.02
Brucine	6.6×10^{-3}
Caffeine	6.6×10^{-4}
Deoxyephedrine	2.7×10^{-3}
Phenacetin	9.4×10^{-4}
Theobromine	1.6×10^{-3}
Theophylline	9.4×10^{-4}

Table 3
Comparison of mean values of conventional and potentiometric methods for the assay of methylene blue injection

Sample	Potentiometric method		USP method	
	Recovery (% of nominal value)[a]	RSD (%)	Recovery (% of nominal value)[a]	RSD (%)
1	98.03	1.06	102.05	1.72
2	99.63	1.24	103.44	1.38
3	97.90	0.91	101.73	1.56
4	101.27	1.14	100.84	1.03
5	97.49	1.53	99.84	1.66
6	96.99	1.30	103.75	1.29

[a] All values are the average of 5 determinations.

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