Electrode Sensitive to Sulfa Drugs

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Abstract □ An electrode sensitive to sulfa drugs was constructed by using the iron(II)–bathophenanthroline chelate embedded in a liquid membrane. Rapid and Nernstian responses were exhibited against solutions of sulfamerazine and sulfisomidine ranging between 10^{-3} and 10^{-1} *M* in concentration. High selectivity was observed in the presence of urea, glycine, aminopyrine, or *p*-aminobenzoic acid. These chemicals are known to interfere in the usual colorimetric analysis of sulfa drugs.

Keyphrases □ Sulfamerazine—potentiometric analysis, liquid membrane electrode sensitive to sulfa drugs □ Sulfisomidine—potentiometric analysis, liquid membrane electrode sensitive to sulfa drugs □ Potentiometry—analysis, sulfamerazine and sulfisomidine, liquid membrane electrode sensitive to sulfa drugs □ Iron(II)–bathophenanthroline chelate—ion associations with sulfa drugs, used in preparation of electrodes for potentiometric analysis of sulfa drugs

Various ion-selective electrodes have been developed as electrochemical sensors in the last decade (1–8). These electrodes are able to respond to activity (or concentration) of specific ions rapidly and selectively in a complicated mixed solution. The attractive advantages of an analysis with an ion-selective electrode are the continuous determination of the concentration of respective ion species and the shortening of the analysis period.

It was desired to develop ion-selective electrodes for drugs in the field of pharmaceutical analysis. In the present study, liquid membrane electrodes sensitive to sulfisomidine and sulfamerazine were made by dissolving ion associations formed between an iron(II)–bathophenanthroline chelate and the sulfa drugs in nitrobenzene. The presence of a tenfold molar excess of urea, glycine, aminopyrine, or *p*-aminobenzoic acid, agents known to interfere in the usual colorimetric analysis of sulfa drugs, did not cause interference in the observed electromotive force (emf).

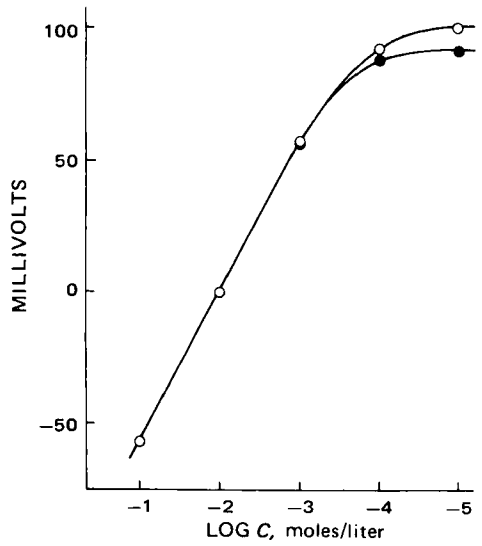

Figure 1—*Plots of the membrane potential against the concentration of sulfa drugs. The concentration of the ion association in the membrane was 5 × 10^{-5} M. Key: ○, sulfisomidine; and ●, sulfamerazine.*

Table I—Selectivity Coefficients of Various Substances for Sulfisomidine Selective Electrode

Substance	K_i
Urea	10^{-2}
Glutamic acid	3×10^{-2}
Glycine	2×10^{-2}
p-Aminobenzoic acid	10^{-1}
Aminopyrine	10^{-2}
Aspirin	5
Sodium chloride	10^{-2}
Sulfamerazine	4×10^{-1}
Sulfanilic acid	8×10^{-2}
Citric acid	4×10^{-3}
Sodium Trichloroacetate	17
Sodium borate	5×10^{-1}
Boric acid	10^{-2}

EXPERIMENTAL

The ion association existing between iron(II)–bathophenanthroline chelate and the sulfa drugs was determined by the same procedure as that employed previously (9). Bathophenanthroline (6×10^{-5} mole) was dissolved in 100 ml of nitrobenzene, into which 50 ml of ferrous sulfate aqueous solution (8×10^{-4} *M*) was added and shaken. Then 200 ml of aqueous sulfa drug (1×10^{-2} *M*), a large excess compared with the amount of iron chelate, was added and the mixture was shaken vigorously for 10 min. The nitrobenzene solution of the ion association was separated from the aqueous phase. The solution thus prepared was diluted to a desired concentration with nitrobenzene and was used as the liquid membrane.

The following cell was used for measuring the electromotive force (emf) across the liquid membrane:

SCE|reference solution|liquid membrane|sample solution|SCE

where SCE stands for the saturated calomel electrode. The electromotive force was measured at a room temperature (20 ± 2°) with an electrometer[1] connected to a penwriting recorder[2]. The sample and the reference solutions were separated by the liquid membrane, which was located in the bottom of a U-shaped glass tube. An aqueous solution (10^{-2} *M*) of sodium salt of the sulfa drug was used as the reference solution.

RESULTS AND DISCUSSION

The electrodes for sulfisomidine and sulfamerazine were used as the representatives of sulfa drugs. Steady potential was achieved within a few seconds and was reproducible to ±1 mv. The ion association used as the ion exchanger was positively charged and dissociated in the nitrobenzene. Then, the electrode could respond only to negative ions.

Since sulfa drugs are amphoteric, the effects of pH in the solution on the membrane potential were examined by adding sulfuric acid and sodium hydroxide to a sample containing 10^{-3} *M* sulfisomidine or sulfamerazine. The electromotive force observed was not affected by a pH variation in the media between 8.5 and 11 for sulfisomidine and between 8.3 and 10.0 for sulfamerazine. The electromotive force was not stable outside these pH ranges. In the

[1] Type TR-8651, Takeda Riken Co., Tokyo, Japan.
[2] Type VP-625 A, National Electric Co., Yokohama, Japan.

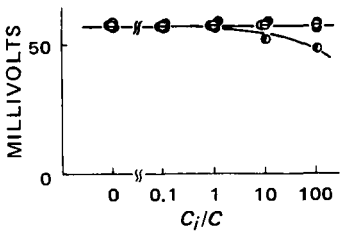

Figure 2—*Observed potential of the sulfisomidine electrode in various organic ions as a function of the relative concentration of added ions* (C_i) *against sulfisomidine* (C). *Key:* ◐, *glycine;* ⊖, *p-aminobenzoic acid;* ●, *aminopyrine; and* ○, *urea. These reagents interfere with the colorimetric method. The concentration of sulfisomidine in the test solution was fixed at* 10^{-3} M.

practical use of the electrode, the measurements should be made with solutions with these pH values. In the experiments described here, the pH value of the sample solution was adjusted at 9.0 by tromethamine and sulfuric acid buffer.

The electrodes were tested in solutions of sulfa drugs over a range of 10^{-1} and 10^{-5} M. As shown in Fig. 1, the response of the electrode was linear with a slope of 57 mv when the observed potential was plotted against the logarithm of the concentration of sulfa drug until the concentration decreased to 10^{-3} M. Although the electromotive force was not linear against log C in a dilute solution lower than 10^{-3} M, the electrode could be used down to about 10^{-4} M, since the potential response was stable and reversible.

The electrode responded to certain specific substances other than the sulfa drugs. When the sample solution contained both a sulfa drug and other interfering substances, i, the electromotive force observed was analyzed by the following equation (10):

$$E = E_0 - (RT/F) \ln (C + K_i C_i) \qquad \text{(Eq. 1)}$$

where E, C, C_i, and K_i are the membrane potential observed, the concentrations of sulfa drugs and of interfering substances i, and the selectivity coefficient, respectively, and E_0 is a constant dependent only on the concentration of the reference solution. For the sake of illustration, the selectivity coefficient, K_i, is determined for the sulfisomidine-selective electrode in the subsequent analysis. When the potential observed in a solution containing no interfering reagent is denoted by E', Eq. 1 is transformed to give:

$$K_i C_i = C \exp [F(E' - E)/RT] - C \qquad \text{(Eq. 2)}$$

If the right-hand side of Eq. 2 is plotted against C_i, the slope should give the value of K_i. The values of K_i thus obtained are listed in Table I. For some interfering substances (*e.g.*, glycine, sulfanilic acid, and sodium borate), the value of K_i depended on the concentration of the substance. In such case, the largest value of K_i is given in the table. As shown in Fig. 2, the potential was not affected noticeably by the presence of urea, glycine, aminopyrine and *p*-aminobenzoic acid. These chemicals are known to interfere considerably in the usual colorimetric analysis of sulfa drugs (11, 12). In contrast to these reagents, a small amount of sodium trichloroacetate and aspirin produced an appreciable effect in the measured potential. In spite of this restriction, the electrode developed here may be useful in the analysis of sulfa drugs.

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