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Potentiometric determination of sodium using a sodium ion responsive glass electrode

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A study to assess the feasibility of using a sodium ion responsive glass electrode in conjunction with a saturated calomel reference electrode to measure the sodium ion concentration of a wide range of electrolyte solutions used in clinical medicine has shown that the method is capable of giving results which are within acceptable limits. Direct measurement of solutions containing sodium chloride is possible by reference to a calibration based on the potential produced by the electrode pair as a function of pNa^+ defined as $-\log_{10}$ sodium ion concentration. For the measurement of the sodium content of solutions of sodium salts of weak acids and mixed solutions of electrolytes and dextrose it is necessary to use a calibration carried out in a buffer system (0·5M triethanolamine + hydrochloric acid to pH 7) and to dilute the preparations with buffer before measurement. It is also necessary to buffer dextrose and sodium chloride injection before measurement due to the effect of decomposition of dextrose during sterilization causing a shift in pH which must be corrected before making a determination. The advantages of the potentiometric method over conventional flame photometric and titrimetric methods are discussed and a brief review of the literature given, to indicate the applications of specific ion electrodes.

The early studies of Eisenman, Rudin & Casby (1957) using glass membranes highly selective to sodium ions have resulted in these electrodes being commercially available. Mattock (1962; 1967) has described the practical aspects and properties of these electrodes. Specific ion electrodes sensitive to other cations, K^+ and Ca^{2+}, and anions of the halide series are also available.

Applications of specific ion electrodes in analysis (Jacobson, 1968) can be extended to measure very low sodium concentrations as described by Hawthorn & Ray (1968) who measured sodium ion concentrations in water in the range of 0·004 to 25 ppm of sodium. These electrodes have also been used in solubilization studies involving micellar sodium dodecyl sulphate solution (Pearson & Lawrence, 1967). *In vitro* measurements have been made on a wide range of biological fluids, including blood, cerebrospinal fluid, sweat, urine, bile and brain extracts; work carried out *in vivo* has included the continuous measurement of plasma sodium levels of rabbit and dog (Friedman, Jamieson & others, 1958) and the intracellular measurement of sodium and potassium activities in the muscle cells of crab and lobster (Hinke 1959). Recent reviews of work in these and related fields have been given by Moore (1968) and Carr (1968).

We have used a sodium ion responsive glass electrode in conjunction with a saturated calomel reference cell for the measurement of the sodium content of a wide range of

electrolyte solutions. For some solutions the results are compared with those obtained using alternative conventional assay procedures. For solutions with sodium present only as chloride, direct chloride ion titration using standard silver nitrate has been used, and where sodium salts other than, or in addition to, chloride are present, flame photometry has been adopted.

EXPERIMENTAL

Reagents. For calibration and non-sterilized solutions, dry analytical grade chemicals were used. All sterilized infusions, injections and dialysis solutions tested were prepared with B.P. quality starting materials. The buffer solution was prepared using reagent grade materials.

Apparatus and operating conditions. The electrode pair consisted of a sodium ion responsive glass electrode [Electronic Instruments Ltd., (E.I.L.), Type GEA 33] in conjunction with a calomel reference electrode employing a saturated potassium chloride salt bridge (E.I.L. Type RJ23). Trial experiments were undertaken using an E.I.L. Model 46A pH meter for the measurement of potential output at a controlled temperature of 25 $\pm$ 0·1°; most measurements were made using a Pye Model 79 pH meter on solutions at room temperature within the range 21–28°. The electrodes were always kept moist. The sodium ion responsive electrode was stored in 0·1M sodium chloride and the calomel reference electrode in saturated potassium chloride solution between series of measurements. The electrodes when in use were lightly wiped with a tissue after a measurement and rinsed with the next solution before inserting the electrode pair into the bulk sample volume. Values of potential were recorded after approximately 3 min, although, owing to a rapid response time, equilibration was often complete before this time.

Procedure. Calibration was carried out before and after a series of measurements. For the initial calibration, standard solutions of 0·5, 0·1 and 0·01M sodium chloride in distilled water were used and a calibration graph plotted of electrode response in mV against pNa^+ ($-\log_{10}$ molar sodium ion concentration). Direct measurements of potential were made on 0·45% w/v, 0·76% w/v and 0·9% w/v sodium chloride test solutions without dilution, and on 28·8% w/v sodium chloride solution after diluting 1 in 32.

A second calibration graph was plotted of electrode response against pNa^+, using standard solutions of sodium chloride 0·1, 0·05, 0·01 and 0·001M in buffer solution (0·5M triethanolamine + hydrochloric acid to pH 7). Test solutions containing sodium salts of weak acids, mixed solutions of electrolytes with and without dextrose, and solutions of sodium chloride and dextrose were suitably diluted with the buffer solution before measurement. For dextrose 4·3% w/v with sodium chloride 0·18% w/v injection, four samples were diluted 1 in 10 with buffer, and the remainder by a factor of 5. Dilutions of the other solutions are given in Tables 2 and 4.

RESULTS

Calibration

Fig. 1 shows a full range calibration graph obtained at 25° for sodium chloride solutions made up using distilled water. The electrode response in mV is expressed both as a function of molar sodium ion concentration and activity, using literature values for the mean molal ionic activity coefficients (Scatchard & Prentiss, 1933). Ignoring the small error involved in using molal activity coefficients it can be seen from

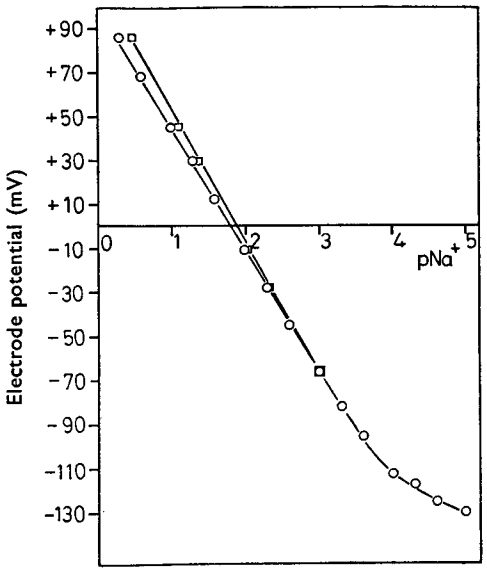

FIG. 1. Full range calibration graph based on unbuffered sodium chloride solutions showing potential of electrode pair (mV) as a function of pNa^+ defined as $-\log_{10}$ activity Na^+ (□) and $-\log_{10}$ concentration Na^+ (○).

Fig. 1 that the electrode response is a linear function of pNa^+ ($= -\log_{10}a_{Na^+}$) down to $pNa^+ = 3$ when deviation occurs. The experimental slope in the linear region for a ten-fold change in activity was 59·0 mV, in good agreement with the theoretical Nernst slope (2·303 RT/F) of 59·2 mV at 25°. Defining pNa^+ in terms of molar sodium ion concentration (i.e. $pNa^+ = -\log_{10}c_{Na^+}$) also results in a linear plot, of slope 56·0 mV in the linear region, and this plot has proved suitable for the direct analysis of sodium chloride solutions. Experience over a period of ten months has shown remarkable consistency in that potential values recorded for any given standard solution do not differ by more than about ±1 mV thus showing negligible long-term drift.

Using the buffer system the calibration plot was linear down to pNa^+ (concentration) = 3·5 with a slope of 59·2 mV. Diluting preparations with buffer before measurement ensured a medium of approximately constant ionic strength and pH, at least 10–20 times as strong as the sodium solution to be measured.

Products containing sodium chloride only

The sodium content of over 250 samples of sodium chloride solution 0·9% w/v (154 m-equiv/litre Na^+) was determined. All the recorded values fell within the range 148–159 m-equiv/litre Na^+ and this may be compared with a range of 147–156 m-equiv/litre Cl^- for the same solutions titrated using standard silver nitrate. Other simple products for which the method proved suitable included 0·45, 0·76 and 28·8% w/v sodium chloride solutions.

Injection of sodium chloride 0·18% *w/v and dextrose* 4·3% *w/v*

Preliminary attempts to analyse samples of this preparation for sodium content by reference to a calibration graph based either on aqueous sodium chloride solutions or sodium chloride in 4·3% w/v dextrose solution produced high results when compared

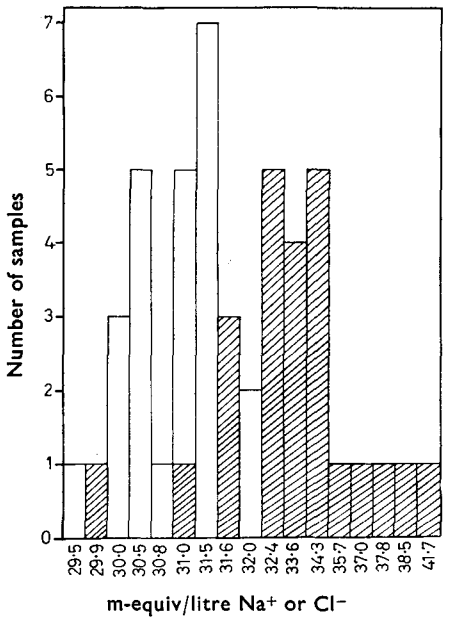

FIG. 2. Frequency histogram showing analytical results (m-equiv/litre Na^+ or Cl^-) for 24 samples of sodium chloride 0·18% w/v and dextrose 4·3% w/v injection as determined by the potentiometric method with reference to a calibration based on unbuffered solutions (shaded blocks) and by titration with standard silver nitrate (open blocks).

with the silver nitrate titration values. The results for 24 samples are given in Fig. 2 which indicates that over half of these are apparently above the 5% error limit by the electrode method, whereas all the preparations are acceptable by the silver nitrate titration method. Further investigation showed that the anhydrous dextrose B.P. used to prepare the solutions contained 0·0063% w/w sodium ion which would not be detected by silver nitrate titration. This would contribute about 0·1 m-equiv/litre Na^+ and is clearly not sufficient to account for the discrepancy.

The pH of solutions containing dextrose is known to decrease on autoclaving due to the production of decomposition products (Hudson & Tarlowski, 1947, Wing, 1960). Since the response of the sodium ion glass electrode is dependent on pH in certain regions, an experiment was undertaken to measure the pH and sodium ion content of solutions autoclaved for different times. A sample of the preparation was subdivided into four portions which were then autoclaved for the time intervals shown in Table 1. Samples were cooled as rapidly as possible after removing from the autoclave and the pH and sodium ion content measured by reference to a calibration graph prepared using unbuffered aqueous sodium chloride solutions. Mattock (1967) has shown that the observed pNa^+ may be expected to decrease as the pH drops below 5 for solutions in the region of 1·5 pNa^+; i.e. the solutions become apparently stronger in sodium ion content. (For stronger solutions e.g. sodium chloride solution 0·9% w/v with pNa^+ 0·81, variations in pH over this region do not affect the response.)

After the officially recommended sterilization time of 30 min, Table 1 shows that the observed sodium ion concentration is already about 3·5% greater than the theoretical value of 31 m-equiv/litre Na^+. Autoclaving times in excess of 30 min or prolonged cooling conditions will rapidly lead to results in excess of 5% of the theoretical value.

Table 1. *The effect of pH changes on the measured sodium ion content of sodium chloride* 0·18% *w/v and dextrose* 4·3% *w/v injection autoclaved for different times*

Autoclave time (min) at 115–116° C	pH	Observed Na^+ (m-equiv/litre)
0	6·1	31·6
15	5·2	31·6
30	4·9	32·1
45	4·5	33·3
60	4·3	35·5

To eliminate the effect of pH, calibration and measurements were made in buffer solution. The results of 30 determinations were within the range 30·0 to 31·9 m-equiv/litre Na^+ which are within ±5% limits. Silver nitrate titration results for the same samples gave values in the range 30·0 to 31·5 m-equiv/litre Cl^-.

Sodium salts of weak acids

Preliminary attempts to analyse salt solutions of this type using a calibration graph for aqueous sodium chloride gave results which were far greater than 5% below the theoretical values. However, using the buffer system, improved values were obtained and results for 15 samples are presented in Table 2; some figures are included for samples which were also analysed using standard titrimetric methods.

Table 2. *Analysis of the sodium ion content of sodium salts of weak acids.*

Product	Sample number*	Dilution with Buffer†	m-equiv/litre Na^+ Found‡	Theoretical
Sodium bicarbonate 2·5% w/v	1	1/50	301	298
2·5% w/v	2	1/50	288	
2·5% w/v	3	1/10	313 (305)	
2·5% w/v	4	1/10	309 (298)	
8·4% w/v	5	1/20	1026 (1005)	1000
8·4% w/v	6	1/20	1000 (1010)	
Sodium citrate 3·8% w/v	7	1/100	398	387
3·8% w/v	8	1/100	398	
Sodium lactate $\frac{1}{6}$ M	9	1/25	169	167
$\frac{1}{6}$ M	10	1/25	167	
1 M	11	1/20	1000 (1033)	1000
1 M	12	1/20	1000 (1000)	
1 M	13	1/20	1026 (1043)	
1 M	14	1/20	1000 (1043)	
Sodium thiosulphate 4% w/v	15	1/50	316	322§
4% w/v	16	1/50	316	

* Each sample number refers to a different batch of material.
† 0·5M triethanolamine + hydrochloric acid to pH 7.
‡ Values in brackets refer to results obtained using standard titrimetric methods.
§ Based on $Na_2S_2O_3.5H_2O$.

Mixed electrolyte solutions

The solutions examined showed a wide range of composition and the formulae are shown in Table 3. Results available at the present time for the determination of

Table 3. *Composition (% w/v) of complex electrolyte mixtures*

Component	Compound sodium lactate injection	Darrow's solution	Butler's solution (modified)	Intraperitoneal dialysis solution 1	Intraperitoneal dialysis solution 2	Intraperitoneal dialysis solution 3	Concentrated haemodialysis solution (32·08 ×)	Concentrated haemodialysis solution (25 ×)
Sodium chloride	0·6	0·4	0·06	0·56	0·56	0·56	18·75	14·6
Sodium lactate	0·34	0·56	0·22	0·5	0·5	0·5	—	—
Sodium metabisulphite	—	—	—	0·05	0·05	0·005	—	—
Sodium acetate	—	—	—	—	—	—	7·9	6·2
Potassium chloride	0·04	0·27	0·1	—	—	—	0·36	0·47
Potassium phosphate	—	—	0·05	—	—	—	—	—
Calcium chloride (hyd.)	0·04	—	—	0·039	0·039	0·039	0·532	0·16
Magnesium chloride	—	—	—	0·015	0·015	0·015	0·154	0·12
Dextrose (hyd.)	—	—	5·0	1·5	7·0	1·5	15·4	12·0
Distilled water	to 100 ml	to 100 ml	to 100 ml	to 100 ml	to 100 ml	to 100 ml	to 100 ml	to 100 ml

Intraperitoneal dialysis solution
1 = modified lactate formula, 2 = modified lactate formula, 3 = lactate formula B.P.C. 1968.

Table 4. *Analysis of the sodium content of complex electrolyte mixtures*

Product	Sample number*	Dilution with buffer†	m-equiv/litre Na+ Found‡	m-equiv/litre Na+ Theoretical
Compound sodium lactate injection	1	1/5	129	131
	2	1/5	129	
	3	1/5	126	
	4	1/5	129	
	5	1/10	132	
Darrow's solution	6	1/5	115	118
	7	1/5	112	
Intraperitoneal dialysis solution 1	8	1/5	144	141
	9	1/5	144	
	10	1/5	144	
	11	1/5	144	
Intraperitoneal dialysis solution 2	12	1/5	144	141
	13	1/5	141	
	14	1/5	144	
	15	1/5	148	
Intraperitoneal dialysis solution 3	16	1/10	146 (139)	141
	17	1/10	141 (142)	
	18	1/10	138 (139)	
	19	1/10	138 (142)	
Concentrated haemodialysis solution 1	20	1/50	130 (128)	130§
	21	1/50	130 (131)	
	22	1/50	130 (128)	
	23	1/50	130 (128)	
	24	1/50	130 (129)	
	25	1/50	130 (129)	
	26	1/250	132 (130)	
	27	1/250	132 (130)	
	28	1/250	132 (129)	
Concentrated haemodialysis solution 2	29	1/50	131 (132)	130§
	30	1/250	132 (134)	

* Each sample number refers to a different batch of material.
† 0·5M triethanolamine + hydrochloric acid to pH 7.
‡ Values in brackets refer to results obtained using a flame photometer.
§ Theoretical value based on final haemodialysis solution.

sodium ion content are shown in Table 4; results are also given for some of the samples in which the Na^+ content has been measured using flame photometry. Table 4 shows that the electrode method may be considered suitable for application to complex ionic mixtures without the need for detailed information on sodium ion activity coefficients in such systems; more work is currently being undertaken to gain further experience in these solutions.

DISCUSSION

Consideration of the results obtained for the analysis of sodium chloride solutions shows that the potentiometric method gives results which are within the demanded $\pm 5\%$ of the theoretical value. A calibration based on e.m.f. response against sodium chloride concentration in water is satisfactory, although in theoretical terms the electrode responds to sodium ion activity. Measurements made entirely using a buffer system throughout may be also expected to be satisfactory, although the present results indicate that this is not necessary for such simple solutions.

Previous workers have statistically compared the values obtained using a sodium ion responsive glass electrode with those obtained using a flame photometer on the same solutions. Moore & Wilson (1963) working with serum, urine and cerebrospinal fluid showed that the average difference between duplicate photometer measurements was 0·8 m-equiv/litre Na^+, while the average difference in similar electrode measurements was 0·3 m-equiv/litre Na^+; they also found that the electrode variability was less than half that of the flame photometer in each fluid. Annino (1967), in developing a method for the rapid routine measurement of sodium in urine, obtained excellent agreement in a blind comparison of sodium concentrations obtained by flame photometry and a sodium ion responsive glass electrode. Some of the results presented in this paper would seem to confirm these conclusions and although a complete statistical analysis has not yet been made, preliminary observations indicate a favourable comparison between electrode values and those obtained by standard titration techniques.

For solutions of 0·18% w/v sodium chloride and dextrose 4·3% w/v it was found rather unexpectedly that a calibration based on aqueous sodium chloride was not satisfactory. The effect of pH on the pNa^+ readings for these solutions drew attention to the effects of dextrose decomposition on autoclaving (Hudson & Tarlowski, 1947; Webb, Sperandio & Martin, 1958). Decomposition products may affect the sodium ion activity in addition to the direct effect of pH and future applications of the electrode in this area may be indicated. The observed pH range for this preparation is 4·2–5·0 which again emphasises the importance of sterilization conditions.

For the complex electrolyte mixtures, in addition to the possible effects of other ions on sodium ion activity, the decomposition of dextrose during autoclaving has been found to increase in the presence of sodium lactate and potassium phosphate (Griffen & Marie, 1958; Wing, 1960). The satisfactory results obtained by calibration of the electrode system on a pNa^+ (concentration) against e.m.f. basis in buffer would seem to make any reference to the question of sodium ion activity in complex electrolyte mixtures unnecessary. This also holds for the buffer method when applied to sodium salts of weak acids (Table 2) and it is likely that the range of compounds of this type could be greatly extended. For the solutions used in intermittent haemodialysis the sodium content has to be maintained within very narrow limits (Scribner, Fergus & others, 1965). Reference to Table 4 shows that preliminary results obtained for

haemodialysis solutions are well within $\pm 3\%$ of the theoretical value, inferring that the buffer was sufficient to swamp any possible interference effects due to pH changes or other ions. It may however be advantageous to study the electrode behaviour in buffer systems other than that used in the present work and at different dilution ratios.

The present work was undertaken with average pH equipment, the more sensitive E.I.L. instrument discriminating to about $\pm 0{\cdot}5$ mV; for greater precision however it is recommended that a more sensitive instrument is used. Although temperature effects within the quoted range appeared to have negligible effect on the measurements, determinations made on solutions at constant temperature would lead to greater accuracy; controlled temperature conditions would almost certainly be required for use with a sensitive meter.

The commercial development of electrodes sensitive to a wide range of cations and anions is rapidly leading to a new era in chemical analysis and it is suggested that the potentiometric method offers advantages in terms of convenience, ease of manipulation and speed of assay over conventional flame photometric and titrimetric methods. It is therefore anticipated that specific ion electrodes will find many future applications in the pharmaceutical sciences for example in official assay procedures, clinical investigations and general medical technology.

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