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The Presence of Potassium as a Source of Inaccuracy in the Chemical Estimation of Sodium in Urine

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Most methods for the chemical estimation of sodium in urine are based on precipitation of the metal quantitatively as the triple salt, sodium zinc uranyl acetate. This is subsequently estimated gravimetrically, colorimetrically, or by titration with alkali.

An early study of this method was made by Barber & Kolthoff (1928), and many subsequent modifications have been suggested (McCance & Shipp, 1931; Hoffman & Osgood, 1938; Bradbury, 1946; Albanese & Lein, 1948). In our hands, one version of the method, that of Dreguss (1939), has proved reliable and accurate for simple solutions of a sodium salt and for blood serum.

Difficulties were encountered, however, in applying the method to urine. The apparent sodium content was higher than expected on a basis of equivalence with the chloride, and higher than that obtained by flame photometry (Holiday & Preedy, 1953), especially in urines of low chloride content. This finding was investigated further.

EXPERIMENTAL

The method used was that of Dreguss (1939) with the following minor modifications. The solution was not heated after the addition of ethanolic zinc acetate; it was then centri-

fuged, not filtered. The volumes of supernatant fluid and of zinc uranyl acetate solution were 2 ml. each, instead of 1.5 ml. The solution in which precipitation took place was left for 3-24 hr. at room temperature. A filter stick with a tuft of asbestos was used for washing the precipitate, instead of repeated centrifuging.

Calculation. From the equation and calculation given by Dreguss, 1.0 ml. 0.1 N-NaOH used in titration is equivalent to 0.256 mg. Na. In our hands, this formula gave accurate results on the standard NaCl solution. (Dreguss used the formula 1.0 ml. 0.1 N-NaOH $\equiv$ 0.243 mg. Na, apparently on account of Na impurities in his samples of zinc uranyl acetate.)

Apparatus for flame spectroscopy. The flame photometer of Holiday & Preedy (1953) was used. The lens and filter system was dismantled, and a Hilger monochromator, Type D. 246, with glass prism, was interposed between the flame source and the image converter. Spectral analysis of the flame emission was carried out by scanning the spectrum between 400 and 800 m μ .

RESULTS

Accuracy of the chemical method

A standard solution of NaCl was prepared, containing 3 mg. Na/ml. Duplicate estimations of Na in this solution were carried out whenever a batch of urines was analysed. The relevant statistics of these

standard estimations and of the duplicate urine estimations are as follows:

Standard NaCl solution. Taking the calculated titration figure as 100, the mean of 54 estimations was 99.96 (S.D., 0.20).

Urine. The standard error of difference between 87 pairs of observations was 1.40 %. (Difference between duplicates, $(a-b)$, was expressed as a percentage of the mean, $(a+b)/2$. Standard error as percentage is $\sqrt{[\Sigma(a-b)^2/n]}$, where n is the number of pairs.)

Interference by other ions

Aqueous solutions of $(\text{NH}_4)_2\text{HPO}_4$, KCl, and CaCl_2 were prepared to contain 3 mg. of (NH_4) , K and Ca/ml., respectively. The (NH_4) , K and PO_4 concentrations in these solutions represent the approximate maximum values found in urine; the Ca concentration is much greater. The apparent Na content of each of these solutions was estimated, and the results are summarized in Table 1, column A.

Table 1. *Estimation of apparent sodium content of various solutions, separately, and in the presence of standard NaCl solution*

(Amount of each cation present at precipitation stage, 0.6 mg. in 4 ml. Values in column A for solutions of foreign ions alone (3 mg. each cation/ml.). Values in column B for these solutions in the presence of NaCl (3 mg. Na/ml.).)

Solution	A Na (mg./ 100 ml.)	B Na (mg./ 100 ml.)	Apparent increase over Na standard alone (%)
KCl	118	342	14
CaCl_2	Nil	300	0
$(\text{NH}_4)_2\text{HPO}_4$	Nil	300	0
$\text{CaCl}_2 + (\text{NH}_4)_2\text{HPO}_4$	Nil	300	0

No precipitate was formed from the $(\text{NH}_4)_2\text{HPO}_4$ or CaCl_2 solutions, but there was a considerable precipitate from the KCl solution. This was not due to Na impurity in the KCl sample used, since an approximate estimation by flame photometry showed a Na content of less than 0.02 g. Na/100 g. KCl.

NaCl (3 mg. Na/ml.) was then added to each solution, and the apparent Na content again estimated. The results in Table 1, column B, show that neither the presence of $(\text{NH}_4)_2\text{HPO}_4$ nor of CaCl_2 , separately or together, caused any increase in the expected reading of the solution. The presence of KCl, however, caused an increase of 14 %.

To the KCl solution (3 mg. K/ml.) varying quantities of NaCl were added to obtain solutions with a constant K concentration, but with Na/K ratios varying between 9:1 and 1:2. (All Na/K ratios quoted are w/w.) The percentage increase in apparent Na content of these solutions, as compared with NaCl solutions of equal Na concentration (but without KCl), was calculated. In Fig. 1 this per-

centage increase is plotted against the Na/K ratio for each solution. It will be seen that there is no increase in apparent Na content until the Na/K ratio falls below 5:1.

The apparent Na content of solutions of NaCl plus KCl of constant Na/K ratio (1:1), but of different concentrations, was determined. The percentage increase in reading of the mixed solutions over solutions of NaCl alone of equal Na concentration was estimated. For mixed solutions containing

Fig. 1. The effect of varying the Na/K (w/w) ratio by adding increasing quantities of NaCl to a solution of KCl (3 mg. K/ml.). The Na/K ratio is plotted against the percentage increase of apparent over expected Na content.

0.12, 0.30, 0.60 and 0.90 mg. of each cation in 4 ml. at the precipitation stage, the increase in reading was 15, 16, 14 and 17 %, respectively. These two experiments indicate that the apparent increase of Na content is independent of the absolute concentrations of Na and K.

The above findings were applied to urine. Thirteen urine samples were chosen in which analysis by flame photometry indicated that the Na/K ratio lay between 3:1 and 1.5:1. (Flame photometry was used in this and the subsequent experiment as an approximate indication of Na/K ratios only, no high degree of accuracy being assumed.) 3 mg./ml. K (as KCl) was added to each sample to produce Na/K ratios between 1:1.4 and 1:2.7. Sodium was estimated chemically in each sample, both before and after KCl addition. KCl addition increased the apparent Na content of the samples by a mean proportion of 33 %, with a range of 18–47 %.

The above findings suggested that K was being co-precipitated. Accordingly, precipitates were obtained from twelve urine samples in which, by flame photometry, the approximate Na/K ratios were found to cover a range between 1:1 and 1:3. Direct analysis of the washed precipitates was then carried out by flame spectroscopy. Strong emission lines were found in all specimens at 766 m μ ., as well as at 589 m μ .. Subsequent photography of the emission spectra, using a Hilger medium quartz spectrograph, showed that each line was a doublet, thus confirming them as the well known emission lines of Na (589.0, 589.6 m μ .), and K (766.4, 766.9 m μ .).

Exactly similar results were obtained with the washed precipitate from a solution of NaCl and KCl (3 mg./ml. of each cation), and from the solution itself. Precipitates from solutions of either NaCl or KCl alone showed emission lines at either 589 m μ .. or 766 m μ ., respectively. Solutions of zinc uranyl acetate showed no emission lines.

The relative intensities of the K emission lines obtained from precipitates of solutions of NaCl and KCl were found, by comparison with the lines obtained from KCl solutions of known concentration, to be approximately consistent with the degree of co-precipitation of K indicated by the chemical estimations.

DISCUSSION

The above studies indicate that, in Dreguss's modification, K interferes with the chemical estimation of Na, both in simple solution, and in urine. This is due to the co-precipitation of K.

High results due to K interference have been reported by Barber & Kolthoff (1928), Butler & Tuthill (1931) and Peters & Van Slyke (1932), but only when more than 25 mg. K was present in the volume taken for analysis. As the K content of urine rarely exceeds 5 mg./ml., this was not considered to be a source of inaccuracy in the urinary estimation. The possibility is, in fact, not mentioned in many subsequent modifications (Salit, 1932; Weinbach, 1935; Bradbury, 1946; King, 1946; Albanese & Lein, 1948).

McCance & Shipp (1931), however, in their modification obtained high results when more than 0.6 mg. K was present in the sample taken for

analysis (equivalent to 0.3 mg. in the 7 ml. of solution in which precipitation occurs). Harrison (1951), using this method for tissue fluid, obtained high results due to K co-precipitation, but was able to overcome this by precipitation at between 6° and room temperature, and not at 0°, as recommended by McCance & Shipp.

Using Dreguss's modification for urine, our results indicate that K interference depends on the Na/K ratio, and is independent of the absolute amounts of K present. At low Na/K ratios, K interference occurs even if K is present in smaller amounts than those recommended by McCance & Shipp. Furthermore, K interference is not prevented by precipitation at room temperature as recommended by Harrison, or by the modified precipitation conditions suggested by Van Loon, Likins & Seger (1952).

Methods for overcoming K interference, by removing the ion as KClO₄ before Na precipitation, as recommended by Butler & Tuthill (1931) and Dreguss (1939), have not proved satisfactory in our hands. A chance observation led to the finding that the addition of H₂SO₄ prevents the co-precipitation of K from simple solutions of NaCl and KCl. It was hoped that this method could be applied to urine, but consistent results have not been obtained.

As all methods relying on the quantitative precipitation of sodium zinc uranyl acetate are basically similar, it would appear advisable to investigate the possibility of K co-precipitation before using any modification for urine.

SUMMARY

1. A modification of the zinc uranyl acetate method of Dreguss (1939) for the estimation of sodium in urine is subject to interference from potassium.
2. This interference, which is due to co-precipitation of potassium, is dependent on low sodium/potassium ratios, and not on the absolute concentration of potassium.

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