LETTER TO THE EDITOR

A New Graphical Way to Indicate the Preparation of Solutions Isoosmotic with Blood, Tears and Tissue

SIR,—In the Danish Pharmacopœia and addenda graphs are given, which for a large number of compounds permit the preparation of solutions which are isoosmotic with blood, tears and tissue by indicating the addition of suitable amounts of sodium chloride or in a few cases of potassium nitrate. The curves are based largely on experimental evidence given by Lund, Peülicke Nielsen and Pedersen-Bjergaard[1], who have also proposed the graphical way in which the data are presented. For each compound the concentration of aqueous solutions is plotted as ordinate against the freezing point depression, together with a curve for sodium chloride (potassium nitrate) showing the concentration plotted against the difference between 0·52° C. and the freezing point depression. Several curves are drawn on the same graph in order to save space. A vertical line which meets the curve for a certain compound at the ordinate corresponding to a prescribed concentration will meet the sodium chloride (potassium nitrate) curve at an ordinate that indicates the concentration of a sodium chloride (potassium nitrate) solution in which the prescribed compound should be dissolved in order to obtain a solution isoosmotic with blood, tears or tissue.

Another way of presenting the same data in a pharmacopœia is to furnish the monograph of each substance from which eye-drops or injections are prepared with a graph, which directly shows the composition of solutions of any concentration of the compound in question, that are isoosmotic with blood, tears and tissue (Fig. 1). These graphs may be used in the following way.

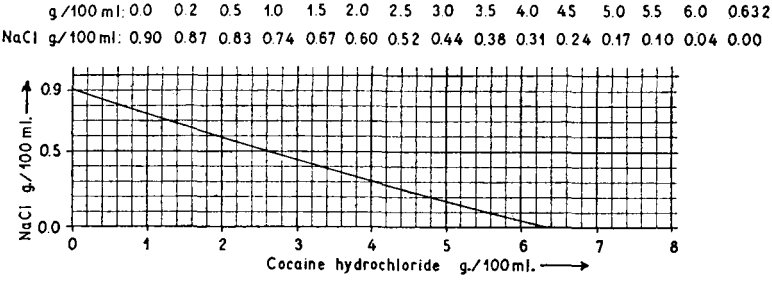

FIG. 1.

(*a*) *Solutions of a single prescribed compound.* The concentration of the described compound (in g./100 ml.) is sought along the abscissa. The ordinate of the curve corresponding to this abscissa gives the amount of sodium chloride (potassium nitrate) in g./100 ml. which has to be added to obtain a solution which is isoosmotic with blood.

(*b*) *Solutions containing more than one prescribed compound.* If the solution contains *n* prescribed compounds, the amounts of sodium chloride to be added in order to make a solution of each single compound in the prescribed concentration isoosmotic with blood, are found as described under (*a*). The sum of the found *n* amounts of sodium chloride in g./100 ml. minus (*n*-1) 0·9 g./100 ml. gives the amount of sodium chloride which renders the prescribed solution isoosmotic with blood.

The amount of sodium chloride (potassium nitrate) to be added to any

solution for which a curve is shown may also be given in an accompanying figure, such as that illustrated, though this is not imperative.

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REFERENCE

1. Lund, Peülicke Nielsen and Pedersen-Bjergaard, *The Preparation of Solutions Isoosmotic with Blood, Tears and Tissue.* Contribution from The Danish Pharmacopœia Commission, Vol. II, 1947.

(ABSTRACTS *continued from p. 966.*)

of choice in the treatment of pneumonia and that tetracycline should be reserved for cases that do not respond to penicillin or where the causal agent is penicillin-resistant. S. L. W.

Toxoids, Enhancement of Antigenic Activity by Sympathomimetic Drugs. J. Ungar. (*Brit. med. J.*, 1955, **2**, 20.) The investigation was conducted with purified diphtheria toxoid, the sympathomimetic drugs employed being (1) adrenaline hydrochloride, 1 : 1000 or 1 : 2000; (2) amphetamine hydrochloride, 1 : 250; and (3) ephedrine hydrochloride, 1 : 250. In addition, two amines with no vasoconstrictor action, β-phenylethylamine, 1 : 250, and phenylethylamine, 1 : 250, were tested but were found to be without stimulating effect on antigenicity. The method of testing the antigens was that used in earlier experiments (Ungar, *Proc. roy. Soc. Med.*, 1954, **47**, 355). The results were as follows:

MEAN ANTITOXIN TITRES IN GROUPS OF 10 GUINEA-PIGS AFTER GIVING PURIFIED DIPTHERIA TOXOID WITH VARIOUS SUBSTANCES

Group No.	Substance added to toxoid	Antitoxin Response (u./ml.) (Geometric mean of 10 animals)
1	Control, plain toxoid	0·25
2	β-Phenylethylamine, 1 : 250	0·17
3	Phenylethylamine acetate, 1 : 250	0·23
4	Amphetamine hydrochloride, 1 : 250	1·96
5	Ephedrine hydrochloride, 1 : 250	2·21
6	Adrenaline, 1 : 1000	2·87
7	Adrenaline, 1 : 2000	3·36
8	Histamine, 0·5 μg./ml.	0·70

Doses: 1 ml. of diphtheria toxoid (2·5 Lf./ml.) injected subcutaneously. Two doses with four-weeks interval. Animals bled 2 weeks after second dose.

The amount of vasoconstrictor added to the toxoid must be carefully chosen since higher concentrations of vasoconstrictors than those quoted may cause local tissue damage. The results show that vasoconstrictors have a considerable enhancing effect on the antigenic action of diphtheria toxoid. As adrenaline hydrochloride is stable only in an acid medium it cannot be kept in contact with the toxoid for any length of time. On the other hand, ephedrine and amphetamine, being stable at a neutral *p*H, can be mixed with the toxoid and stored at a suitable temperature. The addition of a vasoconstrictor to a toxoid may not only be useful for immunising children against diphtheria, but has the additional advantage that its anti-allergic action would be of value for children subject to allergic manifestations after injections of antigens. S. L. W.