

E. Sterilization of the Solutions.—The last important step in the preparation of intravenous medication is sterilization. Sufficient heat is necessary to kill organisms, yet excessive heat is undesirable since it causes decomposition of some organic compounds. Distilled water, solutions of inorganic compounds, and a few organic compounds may be sterilized in the autoclave; others should be boiled for ten minutes. For best results the solutions should not be kept for more than four days unless they are hermetically sealed.

REFERENCE.

- (1) Florence B. Seibert, *American Journal of Physiology*, 67, 83, 90, 105 (1923); 71, 621-652 (1936).

A READY METHOD FOR THE EXTEMPORANEOUS PREPARATION OF ISOTONIC COLLYRIA.*

BY MORRIS MELLEN AND LEONARD A. SELTZER.

WHY ARE ISOTONIC COLLYRIA PREFERRED?

The purpose of adjusting the osmotic pressure of solutions to be instilled into the eye is to obviate the discomfort, or even pain, which, depending upon the sensibility of the patient, results when the collyrium has a different osmotic pressure than that of the surrounding tissues: which discomfort continues until the equilibrium is restored.

This difference in pressure is due to the difference in the degree of concentration and the difference in the physical and chemical properties of the different substances comprising the solute. It is due to this difference in osmotic pressure that distilled water, for example, when instilled into the eye causes discomfort, while we are unconscious of the tear secretion because with it this difference in osmotic pressure does not exist.

Hence the discomfort attending the use of collyria is avoided by adjusting the osmotic pressures and rendering them isotonic with the lachrymal secretion previous to instillation.

Much research has been conducted for the purpose of developing a method for preparing isotonic solutions scientifically accurate. For the most part they involve technical procedure which would generally be considered inexpedient at the prescription desk.

The work of Dr. F. Nicola as given in Scoville's "Art of Compounding" (1927) in the chapter on Adjusted Solutions presents a method sufficiently accurate for the purpose intended and applicable at the dispensing counter.

According to Dr. Nicola, the elements which determine the osmotic pressure in any solution, collyria in particular, are, mainly, the degree of concentration, the degree of dissociation, and the molecular weights of the prescribed substances in solution.

The degree of concentration is expressed by the per cent, weight to volume, of the solute.

The molecular weight by that of the substance dissolved.

The degree of dissociation by the approximate dissociation constants determined as follows:

* Section on Practical Pharmacy and Dispensing, A. Ph. A., Dallas meeting, 1936.

For non-electrolytes and weak electrolytes	1.0
For substances dissociating into two ions	1.5
For substances dissociating into three ions	2.0
For substances dissociating into four ions	2.5

HOW ISOTONIC SOLUTIONS ARE PREPARED.

In order to render any solution isotonic with a given solution, it is necessary to determine (1) the tonic factor of each substance entering into the solution to be adjusted; (2) the total tonic factor of the solution to be adjusted; (3) the tonic factor of the solution with which tonicity is desired, usually referred to as the constant factor and (4) the differential factor.

The formula for determining the tonic factor is:

$$(a) \quad \frac{\% \text{ of substance} \times \text{dissociation constant}}{\text{molecular weight}} = \text{tonic factor}$$

Substituting the values of the members in the above equation using 1.4% as the degree of concentration of Sodium Chloride in the lachrymal secretion, we have:

$$(b) \quad \frac{1.4 \times 1.8 \text{ (dissociation constant)}}{58.5 \text{ (molecular weight)}} = 0.04307,$$

the constant factor of the lachrymal secretion, or tear factor.

METHOD FOR DETERMINING THE TONIC FACTORS.

Calculate the tonic factor for the medicinal ingredient by formula (a). If there are two or more ingredients in the prescription, calculate the tonic factors for each one separately, and add the factors to give the total tonic factor for the solution. Subtract this total tonic factor from the constant or tear factor (0.04307) to determine the differential factor. Substitute this differential factor for the tonic factor in formula (a) and transposing as follows:

$$(c) \quad \frac{\text{differential factor} \times 58.5 \text{ (mol. wt. of NaCl)}}{1.8 \text{ (dissociation constant of NaCl)}} = \% \text{ of NaCl}$$

to be added to render the collyrium isotonic with the lachrymal secretion.

Due to the length of time (10 to 20 minutes) involved in calculating the several equations above, the average dispensing pharmacist may find it inexpedient to follow the procedure necessary to compound an isotonic collyrium extemporaneously, and would, therefore, appreciate a method involving less time. Such a method, derived from Dr. Nicola's formula, is detailed below.

METHOD OF DETERMINING SODIUM CHLORIDE NECESSARY FROM TONICIC EQUIVALENTS.

From the foregoing it is evident that a solution of any single substance of such concentration as to have the tonic factor 0.04307 is isotonic with the lachrymal secretion (*i. e.*, with a 1.4% solution of Sodium Chloride).

To determine the quantity of a substance necessary to produce an isotonic solution, using boric acid as an example, substitute in formula (b) the values representing the molecular weight and dissociation constant of that substance (in this case of boric acid), and we have

$$(d) \quad \frac{\% \times 1 \text{ (dissociation constant of boric acid)}}{61.92 \text{ (molecular weight of boric acid)}} = 0.04307$$

Solving for %, we have 2.667%; multiplying by 4.54 we have 12.108 grains as the amount of boric acid required in one fluidounce of solution, to render this solution isotonic with the lachrymal secretion.

Since the lachrymal secretion contains 1.4% sodium chloride or (multiplying by 4.54) 6.356 grains per fluidounce, then

$$\left. \begin{array}{l} 12.108 \text{ gr. boric acid in 1 fl.} \\ \text{oz. of sol.} \end{array} \right\} \text{ is equivalent in tonicity to } \left\{ \begin{array}{l} 6.356 \text{ gr. NaCl in 1 fl. oz. of} \\ \text{sol.} \end{array} \right.$$

Dividing both sides by 12.108 we have 1 grain of boric acid as the equivalent in tonicity of 0.525 grain of NaCl. Hence it follows that if, from an isotonic solution of boric acid we remove 1 grain of boric acid and substitute for it 0.525 grain of sodium chloride (its tonic equivalent) the resulting solution remains isotonic.

TONICIC EQUIVALENTS.

In the table which follows, of substances most frequently employed in Collyria, the values were determined in the same manner as has just been shown in the case of boric acid.

1. The concentration % of the substance necessary to produce a solution isotonic with the lachrymal secretion. Col. I.
2. The number of grains per ounce accomplishing this concentration. Col. II.
3. The Sodium Chloride tonic equivalents of one grain of each substance. Col. III.

A solution is, respectively, hypotonic, isotonic or hypertonic with the lachrymal secretion, if and when the sum of the Sodium Chloride tonic equivalents given in Column III of the substances entering into the solution is less, equal to, or more than 6.356. Only in case this sum is less can adjustment be made to render it isotonic.

TO USE THE TABLE.

With the formula of the prescription written per fl. oz., add the sodium chloride tonic equivalents of the ingredients, subtract the total from 6.356, and the remainder represents the amount of sodium chloride per fluidounce to be added to render the solution isotonic.

EXAMPLES:

No. 1.

R

Zinc Sulphate	gr. 1
Boric Acid	gr. X
Aqua Dest. q. s. <i>ad</i>	fl. oz. 1

1 fl. oz. isotonic solution NaCl contains		6.356 gr. NaCl
Tonic equivalent of 1 gr. ZnSO ₄	0.1696 gr. NaCl	
Tonic equivalent 10 gr. H ₃ BO ₃		
(10 × 0.525)	5.25 gr. NaCl	

Total tonic equivalents of ingredients in R 5.4196 gr. NaCl

To make solution isotonic add 0.94 gr. NaCl

No. 2.

℞

Atropine Sulphate
Aqua Dest. *q. s. ad*gr. V
fl. oz. ss $\frac{1}{2}$ fl. oz. isotonic solution NaCl contains $\frac{1}{2} \times 6.356$ or
Tonicic equivalent of 5 gr. atropine sulfate is 5×0.0935 or3.178 gr. NaCl
0.4675 gr. NaCl
2.7105 gr. NaCl

To make solution isotonic add

TABLE OF TONICIC EQUIVALENTS.

Name.	Table of Concentration, %.	Concentration Grains per Ounce.	Sodium Chloride Tonicic Equivalent of 1 Grain.
Sodium Chloride	1.4	6.356	1.0000
Ammonium Chloride	1.5362	6.974	0.9113
Alum (Ammonium)	7.8103	35.459	0.1792
Antipyrine	8.1045	36.794	0.1727
Atropine Sulphate	14.959	67.914	0.0935
Borax	16.4424	74.648	0.0851
Boric Acid	2.667	12.108	0.525
Chloretone	7.6432	34.700	0.1831
Cocaine HCl	9.7548	44.287	0.1435
Dionin	11.0773	50.291	0.1264
Ephedrine HCl	5.79	26.287	0.2418
Ephedrine Sulphate	9.2257	41.885	0.1517
Eserine Salicylate	17.803	80.826	0.0786
Eserine Sulphate	13.9678	63.414	0.1002
Homatropine HBr	10.227	46.43	0.1364
Hyoscine HBr	12.5833	57.128	0.1113
Hyoscine HCl	10.7886	48.98	0.1298
Morphine HCl	10.7893	48.983	0.1297
Morphine Sulphate	16.3375	74.172	0.0856
Pilocarpine HCl	7.0253	31.895	0.1993
Pilocarpine Nitrate	7.7876	35.356	0.1797
Sodium Bicarbonate	3.618	16.426	0.387
Tannic Acid	13.8750	62.993	0.1009
Zinc Sulphate	8.256	37.482	0.1696

Another feature of the table is that the pharmacist will recognize immediately whether the collyrium is hypertonic or hypotonic. If, for example, it contains 15 grains of boric acid per fluidounce a glance at the second column of figures will show that it is hypertonic. Or, if the tonicic equivalents, as stated before, add up to more than 6.356 grains NaCl per fluidounce, the collyrium likewise is hypertonic.

A further suggestion for ready dispensing, if the quantity of prescriptions warrant it, is to have on hand isotonic solutions of single ingredients commonly prescribed such as Zinc Sulfate, Boric Acid, Sodium Chloride, etc., using the quantities specified in the second column of figures in the table. Then in dispensing, it is only necessary to measure the volume of the isotonic solution of each chemical named representing the number of grains of each required and add isotonic solution of sodium chloride sufficient to bring to the volume specified.

The solutions prepared in this manner are for all purposes required isotonic. With the table before him, the pharmacist finds the method simple, quick and readily applied at the dispensing counter. This use of the table eliminates all the bur-

densome work of calculation which has heretofore been necessary. The patient using these collyria is relieved of the discomfort attending the instillation of a solution of unnatural osmotic pressure, and physicians who have been supplied with collyria thus adjusted have found them indispensable.

The values of any substance which the pharmacist has occasion to use and which are not in the table may be computed by the same method as was used in the illustration computing the values of boric acid and included.

ADDRESS OF THE PRESIDENT OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

BY P. H. COSTELLO.

Ladies and Gentlemen of the American Pharmaceutical Association:

The ASSOCIATION has, throughout the years, been committed to the very definite policy of continued improvement in the selection, education and training of pharmacists, in the regulation of the practice of pharmacy, in the standards of drugs, medicines and medical supplies, and in the service which pharmacy renders to the people as an essential public health profession. Its activities have been confined, within reasonable limits, to the fulfillment of these aims and yet other problems which have had an indirect bearing upon the welfare of those engaged in Pharmacy have not been ignored. The ASSOCIATION has been ever ready to support legislative and all other efforts to improve the status of Pharmacy and of the individuals who practice it, with due regard to the public interest. It should be apparent to anyone who will review its record that our ASSOCIATION, from its inception, has been consistent in its aims, has acted carefully and wisely and has planned and progressed accordingly.



P. H. COSTELLO.

As we enter upon the Eighty-Fourth Annual Meeting of our ASSOCIATION, I am assuming for the purpose of this address, that every one interested in our work is more or less familiar with the greater part of all that has transpired since we last met which affects Pharmacy or has an important bearing upon it. The comprehensive and able addresses and reports already submitted or to be submitted at this meeting explain the activities of the year so thoroughly as to make a review of them unnecessary at this time. Each year in its history has been a period of activity and accomplishment for our ASSOCIATION and it is my privilege to report that the past twelve months have not been unusual in this respect.

As President of this ASSOCIATION one gains a full appreciation, as only those who have served similarly or on the Council are privileged to, of the broad field covered, the scope of the activities carried on, the fine understanding of its varied interests which Dr. Kelly possesses, and the influence he lends as secretary. It is