hemolytic index of 12 different fluidextracts varied from 1:1666 to 1:300.

For the assay of syrups, an aqueous dilution (1 to 10) of the syrup was used. The hemolytic index of 4 different syrups varied from 1:62.5 to 1:125.

DISCUSSION

If saponin increases the absorption of drugs, then sarsaparilla may be more than a mere flavoring vehicle and should be assayed for its saponin. The hemolysis method seems to give satisfactory results. If accepted as an assay method for the official preparations, further experimentation will be necessary to standardize the assay. The results reported upon give relative values of the saponins, and also the fluidextracts and syrups of sarsaparilla. We have shown by means of the "hemolytic index" the variability of the saponins, fluidextracts and syrups of sarsaparilla upon the market to be so great that, if the medicinal effect of the preparations depended upon it, physicians might easily lose confidence in them. Further study of the possibility of using the hemolytic index for this purpose is indicated, and also a study as to whether the hemolytic index parallels the degree to which absorption of standard drugs are increased by the saponin.

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A Monograph for Ringer's Solution as a Solvent*

By Norman Pinschmidt and John C. Krantz, Jr.†

The first work of note with physiological saline solutions was done by Sidney Ringer and his associates between the years 1882–1895. They advocated the use of the chlorides of sodium, potassium and calcium and discussed the physiological results obtained by the addition of each of these salts to physiological solutions. Shafer (1) studied the solution as a solvent for various salts. Fantus and Dynievicz (2) suggested the use of Ringer's solution as a solvent for tannic acid in the treatment of burns. At the suggestion of the National Formulary Committee the following monograph was prepared for Ringer's solution, suitable for use as a solvent for hypotonic solutions to be used parentally or when chlorides of sodium, potassium and calcium in the tissues have been diminished.

LIQUOR PHYSIOLOGICALIS SALINIS

Solution of Physiological Salts

Ringer's Solution

Solution of Physiological Salts contains in 100 cc. not less than 0.84 or more than 0.88 Gm. of NaCl, not less than 0.025 and not more than 0.035 Gm. of KCl and not less than 0.030 or more than 0.036 Gm. of $CaCl_2.2H_2O$.

* The expense of this investigation was defrayed in part by a grant from the National Formulary Committee.

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Sodium chloride	8.6 Gm.
Potassium chloride	0.30 Gm.
Calcium chloride (dihydrate)	0.33 Gm.
Recently boiled distilled water, sufficient to make	1000 cc.

Dissolve the three salts in a convenient quantity of recently boiled, previously cooled distilled water, to make up to 1000 cc. and filter. The solution may be sterilized by placing in an autoclave at 15 lbs. pressure for 15 minutes.

Description and Physical Properties.—Solution of Physiological Salts is a clear, colorless solution possessing a mild saline taste. The specific gravity of the solution at 25° C. is about 1.005. The hydrogen-ion concentration of the solution is about p_H 6.5. The solution gives a depression of freezing point not less than −0.54° C. and not more than −0.58° C.

Heavy Metals.—Ten cc. of Solution of Physiological Salts meets the requirements for the test for heavy metals.

Arsenic.—Twenty cc. of Solution of Physiological Salts meets with the requirements of the test for arsenic.

Tests for Sterility.—For bacterial contamination and for yeasts and molds proceed according to the methods given under Ampuls of Dextrose.

Assay for Calcium Chloride.—Evaporate 100 cc. of Solution of Physiological Salts accurately measured to 20 cc., heat to boiling and make alkaline with ammonia T.S., add ammonium oxalate T.S. dropwise until all the calcium has been precipitated. Heat on a water-bath for an hour, filter through hardened filter paper and wash thoroughly with warm distilled water. Puncture the filter and wash the precipitate into a beaker by means of a stream of hot distilled water followed by 30 cc. of dilute sulfuric acid. Heat to 60° C. and titrate with one-hundredth-normal potassium permanganate. Each cc. of one-hundredth-normal potassium permanganate is equivalent to 0.00074 Gm. $CaCl_2 \cdot 2H_2O$.

Assay for Potassium Chloride.—To 1.5 cc. of alcohol in a 15-cc. centrifuge tube add 5 cc. of Solution of Physiological Salts accurately measured, and mix thoroughly. Add dropwise, with continuous shaking, 2 cc. of potassium precipitating reagent. Allow to stand for one hour at room temperature. Centrifuge for about 10 minutes at about 2000 r. p. m. or until the precipitate is firmly packed in the bottom of the tube. Decant the supernatant liquid and allow the precipitate to drain for about five minutes. Wash the precipitate carefully with 5 cc. of 70 per cent alcohol, breaking up the bulk of the precipitate by forcing the wash solution in a fine stream from the pipette. Centrifuge for five minutes and drain as before. Dry the precipitate for one hour at 80 to 85° C. to remove all of the alcohol.

Add 5 cc. of two-hundredth-normal ceric sulfate and 1 cc. of sulfuric acid which has been previously diluted with an equal volume of distilled water. Heat on a water-bath until all the precipitate has disappeared. Cool to room temperature and titrate with ferrous ammonium sulfate solution using one drop of *o*-phenanthroline ferrous complex T.S. as indicator. Each cc. of two-hundredth-normal ceric sulfate used to oxidize the precipitate multiplied by 0.249 equals the weight of KCl in milligrams.

Assay for Total Chlorides.—Transfer 10 cc. of Physiological Salts Solution accurately measured to a 400-cc. beaker, add 50 cc. of distilled water and 4 cc. of diluted nitric acid; dilute to 200 cc. with distilled water, add 15 cc. of silver nitrate T.S., heat to boiling and allow to stand protected from direct light until the precipitate is granular. Filter onto a tared Gooch crucible previously heated to 150° C. Dry the precipitate to a constant weight at 150° and weigh. The weight of silver chloride obtained multiplied by 0.2474 equals the weight of total chloride. The chloride (Cl^-) calculated from the silver chloride is not less than 0.0520 Gm. or more than 0.0580.

Storage.—The solution should be kept in hard, glass-stoppered bottles.

TABLE I.—REAGENTS, INDICATORS AND STANDARD SOLUTIONS REQUIRED BUT NOT IN NATIONAL FORMULARY

I. Reagent:

Potassium Precipitating Reagent:

Dissolve 11.6 Gm. sodium cobaltinitrite, 4.75 Gm. sodium acetate and 4.5 cc. glacial acetic acid in 30 cc. of distilled water, allow to stand 48 hours and centrifuge at 2000 r. p. m. before using. Keep in a cold, dark place.

II. Indicators:

o-Phenanthroline Ferrous Complex:

See U. S. P. XI, Second Supplement.

III. Standard Solutions:

Ceric Sulfate, Two-hundredths-normal:

$Ce(SO_4)_2$ = 333.25

6.646 Gm. of $Ce(SO_4)_2$ in 1000 cc.

One cc. of 0.02*N* ceric sulfate is the equivalent of ceric sulfate, $Ce(SO_4)_2$..... .....0.0006646 Gram.

Preparation: See U.S. P. XI, Second Supplement.

EXPERIMENTAL

Table I shows the results obtained from assays on five different Solutions of Physiological Salts at optimum conditions.

In determining a suitable formula for the solution comparative studies were made of the large number of formulas available. It was decided after examination of the magnesium present as impurity in the salts of sodium and potassium to omit the magnesium from the formula.

TABLE II.—ANALYTICAL DATA ON SOLUTION OF PHYSIOLOGICAL SALTS

Bottle No.	Calcium Chloride Assay, Gm. (10 Cc. Aliquot)	Potassium Chloride Assay, Mg. (5 Cc. Aliquot)	Total Chlorides Assay, Gm. (10 Cc. Aliquot)	Depression Freezing Point, ° C.	p_H
1	0.0343	1.54	0.0532	0.56	6.5
2	0.0341	1.53	0.0533	0.57	6.6
3	0.0354	1.54	0.0538	0.56	6.0
4	0.0337	1.53	0.0532	0.56	6.4
5	0.0343	1.56	0.0529	0.56	6.4

The addition of sodium bicarbonate was not deemed advisable because of its alkalinity. Buffer salts were considered but in all probability unnecessary as the p_H of the solution is quite constant.

The sodium chloride suggested is of the U. S. P. grade. Comparative studies of several commonly used brands of the C.P. salt show that the U. S. P. standard was in most cases slightly alkaline whereas the C.P. standard was slightly acid. This sodium chloride alkalinity tends to combat the acidity found in all commercial samples of calcium chloride.

Concerning the calcium chloride used these observations revealed that all hydrates of calcium chloride ($CaCl_2$; $CaCl_2.2H_2O$; $CaCl_2.6H_2O$) seemed to impart a slight acidity to the solution. The hydrated gave a lesser degree of acidity than the anhydrous salt. Of the two hydrates the dihydrate is the better.

The solution has been made isotonic with blood serum and the isotonicity checked cryoscopically and through its speed of hemolysis of red blood cells.

In the assay for the potassium salt seven different procedures were tried with consistently low results and a high percentage error. The method suggested by Brown, Robinson and Browning (3), however, if followed carefully will give consistent and accurate results.

In the consideration of the use of Ringer's Solution as a solvent for the various ampul solutions of the National Formulary, there are only two ampul solutions in the group that are hypotonic, namely, emetine hydrochloride and mercuric succinimide. The latter, however, is decomposed in the presence of sodium chloride giving ionizable mercury and could not, therefore, be made isotonic by the addition of Solution of Physiological Salts.

The emetine hydrochloride, however, may be adjusted to isotonicity by the addition of 28.2 cc. of Ringer's Solution per 100 cc. of solution. This isotonic emetine hydrochloride in Ringer's Solution was prepared and checked cryoscopically.

CONCLUSION

A formula and monograph for a Physiological Salts Solution as a solvent for parenteral use have been proposed for the National Formulary.

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A Review of Tentative Changes in the Ampul Monographs of the National Formulary

By R. K. Snyder and E. N. Gathercoal*

INTRODUCTION

The Special N. F. Committee on Ampuls and Tablets[1] had their first meeting in January 1936 and laid the foundation for the work that has been done since that time. The ampul monographs, including the general monograph, were to be studied in detail and desirable changes were to be recommended to the N. F. Committee. This work has been completed and is set forth in a tentative form in the Bulletin of the National Formulary Committee (1).

The laboratory work involved was begun in the N. F. Laboratory in Chicago and completed in the A. PH. A. Laboratory in Washington. Collaboration on suggested assay methods was conducted in the Laboratories which the committee members represented. The results were discussed and decisions reached in the six semiannual meetings of the Committee (2).

GENERAL DISCUSSION

In a broad sense the work involved standards, methods of preparation, tests for identity and purity of the drugs used, methods of assay, sterilization procedures, and methods for testing the suitability of the glass containers.

To serve as a starting point a supply of the various official ampuls was obtained from each of five commercial houses.

The **tests of identity and purity** as listed in the monograph of each drug in the U. S.

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[1] The members of this committee are: E. N. Gathercoal, Russel A. Cain, F. E. Bibbins, F. O. Taylor, J. B. Fullerton, E. B. Carter and R. K. Snyder.