LABORATORY NOTES.*

BY GEORGE E. ÉWE.

A SODIUM HYPOCHLORITE SOLUTION STABILIZED BY NON-CAUSTIC ALKALI.

Neutral sodium hypochlorite solutions of about 0.5 percent NaOCl strength have proven very effective for the sterilization of wounds. But neutral sodium hypochlorite solutions are notoriously unstable, and as a consequence, must be freshly prepared. The labor of keeping available a supply of this solution of full strength would therefore be materially lessened if a stable or nearly stable product could be devised. Because of the bulkiness of this solution when of proper strength for application, it would be desirable for convenience in handling and storing to devise a product which, in addition to being stable or nearly stable, would be in a concentrated form permitting dilution just before use.

Sodium hypochlorite solution can be fairly well stabilized by insuring the presence of sufficient alkali. But this alkali must be of a non-caustic nature, so as not to cause irritation of the tissues upon which the solution is used. Lime, in proper proportion is an effective, non-caustic alkaline stabilizer for sodium hypochlorite solution.

Sodium hypochlorite solutions for wound irrigation can be prepared by reaction between chlorine and sodium hydroxide; chlorine and sodium carbonate; chlorine and a mixture of sodium carbonate and bicarbonate; chlorinated lime and sodium carbonate; chlorinated lime and a mixture of sodium carbonate and bicarbonate; etc. The most commonly employed methods are reaction between chlorinated lime and sodium carbonate and chlorinated lime and a mixture of sodium carbonate and bicarbonate. Of these two methods, it is probable that the last one is the most popular. The method outlined below of preparing a sodium hypochlorite solution stabilized by lime is applicable to all of the methods mentioned above, with the exception of that in which chlorine and sodium hydroxide is employed. Since the reaction between chlorinated lime and a mixture of sodium carbonate and bicarbonate is probably the most commonly employed one, only the product of this reaction will be considered in giving the details of the method of preparation of a sodium hypochlorite solution stabilized by non-caustic alkali.

The details of the method are as follows:

Sodium hypochlorite solution is prepared by reaction between chlorinated lime and a mixture of sodium carbonate and bicarbonate, then sufficient commercial calcium chloride is added to insure the presence of soluble calcium salt in the solution, which, at the same time deprives the solution of all carbonate. Instead of commercial calcium chloride, a sufficient quantity of a neutral or alkaline solution of calcium chloride made by dissolving in hydrochloric acid the precipitate of calcium carbonate and bicarbonate obtained in the manufacture of a lot of the solution, can be employed for elimination of carbonate. Sufficient dry slaked lime is now added by stirring until a filtered portion of the solution yields a precipitate when the breath is blown through it by means of a glass tube, indicating saturation with lime in the hydroxide state.

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It is not permissible to eliminate the treatment with calcium chloride and simply saturate the solution with lime for the reason that sodium hydroxide would be formed by reaction between the sodium carbonate and lime and thus result in a more irritating form of alkali than the carbonate originally present.

A formula taking advantage of these details would read as follows:

Chlorinated Lime ($32^1/_2$% available Cl)	100 Gm.
Water	127 Cc.
Sodium Carbonate, monohydrated	40 Gm.
Sodium Bicarbonate	41 Gm.
Water	379 Cc.
Calcium Chloride (Com'l) about	10 Gm.
Dry Slaked Lime, about	5 Gm.
Yield about	240 Cc.

Manufacturing Instructions.—Place the chlorinated lime in a jar with 127 Cc. water, agitate well and let stand tightly covered for 6–12 hours. Dissolve the Sodium Carbonate and Sodium Bicarbonate in 379 Cc. water and pour into the chlorinated lime mixture with constant stirring. Stir until the gelatinous mass which first forms is broken up and changes to a powdery precipitate. Let settle. Syphon off and strain roughly into dark glass bottles. Add the calcium chloride to the strained solution and stir for 10 minutes. Then immediately add the dry slaked lime and stir until a filtered portion yields a copious precipitate when the breath is blown through it by means of a glass tube. Filter into dark glass bottles, keeping tightly stoppered and in a cool dark place.

In order to save one filtration the calcium chloride and lime can be added before the solution is filtered from the original magma but this procedure results in the use of about 50 percent more calcium chloride because more carbonate is present due to the magma holding some of the solution.

Chlorinated lime of any other strength than $32^1/_2$ percent available Cl can be employed in proper proportion.

This formula will yield a solution assaying between 4 and 6 percent NaOCl and therefore is about 10 times the concentration required for use.

Five lots of concentrated solution were prepared by this formula from five different lots of chlorinated lime and were filed away in amber glass bottles closed with rubber stoppers and assayed periodically in order to determine their stability.

The following table shows the results of these tests:

Solution.	First assay.	Final assay.	Time between 1st and final assay.	Loss of total NaOCl per month.
1	4.49% NaOCl	4.38% NaOCl	6 months	0.5%
2	4.51% NaOCl	4.51% NaOCl	6 months	None
3	4.36% NaOCl	3.69% NaOCl	5 months	3%
4	4.02% NaOCl	3.91% NaOCl	1 month	3%
5	4.18% NaOCl	4.18% NaOCl	1 month	None

—Reported by George E. Ewe.

DETERMINATION OF PHENOL COEFFICIENT OF SUBSTANCES IMMISCIBLE WITH WATER OR CULTURE MEDIA.*

In the determination of the phenol coefficient of substances it is quite essential

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that the substance undergoing test be miscible with water or with the culture medium used in the test. This is essential because of the comparatively small sample employed and the necessity that it be brought into intimate contact with the organisms in the culture medium in order to insure that accurate results be obtained.

Very variable results attend the attempt to obtain the phenol coefficient of an oily substance by simply adding the sample directly to the culture medium. The difficulty lies in the inability to perfectly mix the sample with the medium.

Constant phenol coefficients instead of the usual discouraging variable results can be obtained by preparing the oily sample into a homogeneous emulsion by the following means:

Place the oily substance in a mortar and to each Cc. of it add 1 Gm. of powdered Acacia. Triturate together until a homogeneous mass results. Add water in small volumes, triturating after each addition, so as to maintain a homogeneous mixture. Finally wash the contents of the mortar into a volumetric flask and bring up to the required volume. The following proportions have proven convenient:

Oily substance	1 part
Gum Acacia	1 part
Water, qs	10 parts

The emulsion produced is stable and may be diluted with water to almost any degree without losing its homogeneity.

The above method of preparing samples is effective with practically all oily substances but the following modification has proven more satisfactory in a few cases:

Triturate one part of powdered acacia and one part of water in a mortar until a perfect mucilage results. Incorporate one part of the oily substance, then add water in small portions, triturating after each addition. Wash the contents of the mortar into a volumetric flask and bring up to 10 parts with water.

The accuracy of this method was tested on mixtures of purified cresols of known coefficient and it was found to yield results which agreed very closely with those given by the Hygienic Laboratory method.

This method was frequently employed during the past year in testing boring oils, refrigerants and other lubricating oils employed in the tool cutting industries. Some of these contained beta-naphthol, others paraformaldehyde and others cresylic acids and other phenolic substances.

The following table shows a few of the kinds of oils containing germicidal substances with which this method was effective:

Oil.	Germicide.	Phenol coefficient.
Sulphurized Lard Oil	1% Beta-Naphthol	4.89
Sulphurized Lard Oil	2% Paraform	9.68
Hydrocarbon Lubricating Oil	6% Cresylic Acid	0.07
Hydrocarbon Lubricating Oil	6% Liq. Cresolis Comp., U. S. P.	0.04
Lard Oil	6% Commercial Coal-Tar, Hydrocarbon Dip.	4.00
Lard Oil	6% Cresylic Acid	3.15
Lard Oil	6% Liq. Cresolis Comp., U. S. P.	3.30

Another method of preparing oily substances for phenol coefficient determinations is based on the fact that many oily substances can be made into a perfectly

clear or at least a homogeneous product which will emulsify perfectly or passably or form a clear solution with water by the following treatment:

Dissolve 40 Gm. rosin in 100 Gm. of the oily substance by aid of a little heat with stirring; add 20 Gm. of a 25% solution of sodium hydroxide, stir well, allow to cool and measure to obtain relation between the total volume of the mixture and the 100 Gm. of oily substance employed in making the mixture.

This method was compared with the Hygienic Laboratory method using 4 cresol samples for the tests. The following results were obtained:

Cresol.	Hygienic laboratory method.	Rosin-sodium hydroxide method.
1	1.75	2.11
2	2.21	2.60
3	2.28	2.90
4	2.29	2.72

It will be noticed that in every case the effect of the rosin and sodium hydroxide was to raise the coefficient a trifle. However, the error introduced by the use of these substances is infinitely less than would be introduced by the inability to obtain a homogeneous blending of an oily substance with the culture media.

The method has been applied to the determination of the phenol coefficient of some "Commercial Pine Oils" with the following results:

"Pine oil."	Phenol coefficient.
1	0.82
2	1.29
3	1.44
4	2.02
5	5.94

A commercial "Pine-tar Creosote" had a phenol coefficient of only 0.282 by this method and was found to be heavily adulterated with kerosene.

There appears to be no doubt that the two methods here outlined might be applied to many other oily substances and possibly to some insoluble germicidal substances in powdered form.

—Reported by Geo. E. Ewe.

BASES FOR IODINE OINTMENT.

The formula for U. S. P. Iodine Ointment reads as follows:

"Iodine	4 Gm.
Potass. Iodide	4 Gm.
Glycerin	12 Gm.
Benzoinated Lard	80 Gm.
Total,	100 Gm.

Triturate the iodine and potassium iodide in a glass mortar with the glycerin until dissolved, then gradually incorporate the benzoinated lard and mix thoroughly. All contact with metallic utensils and containers must be avoided. This ointment must not be dispensed unless it has been recently prepared."

This ointment has been a frequent source of annoyance to physicians because of uncertainty of results due to spontaneous reduction of the free iodine content in the ointment by reaction of the iodine with the benzoinated lard to form "iodized fat." Therefore the finding and adoption of an ointment base which would have a

minimum iodine absorption value under the conditions obtained in the manufacture of Iodine Ointment would result in an improvement of this important U. S. P. ointment.

The table below shows the comparative loss in free iodine suffered by iodine ointments prepared with various bases. In preparing the ointments no attempt was made to weigh the iodine with quantitative exactness, but only approximately, the ointments being accurately assayed for free iodine after manufacture.

Base.	Appear. of ointment.	First assay. Per-cent.	Date of first assay.	Second assay. Per-cent.	Date of second assay.	Loss of total free iodine per month. Per-cent.	Appear. of ointment after second assay.
Benz. Lard	Smooth	3.50	1–11–18	0.88	7–25–18	10	Granular
Benz. Lard	Smooth	3.53	1–11–18	1.002	7–25–18	9.7	Granular
Ammon. Stearate Vanishing Cream	Smooth	3.00	11–20–18	1.83	2–20–19	13	Granular
Yellow Petrolatum	Smooth	3.92	11–20–18	3.82	2–20–19	0.9	Smooth
Beef Suet	Smooth	3.91	11–20–18	2.83	2–20–19	9.2	Fairly smooth
Lanoline Anhyd	Smooth	4.19	11–20–18	2.61	2–20–19	12.6	Smooth
Lanoline Hydrous, water separated	....	..	....	...	...	..	.....
Benz. Lard, but Iodine increased	Smooth	5.59	12–20–18	4.67	2–20–19	8.2	Granular
Mutton Suet	Smooth	3.59	3–10–19	2.85	5–10–19	10.3	Granular
Eucerin, Anhyd	Smooth	4.25	11–20–18	4.02	2–20–19	1.8	Smooth
Eucerin, Hydrous	Smooth	3.72	11–20–18	...	2–20–19	..	Water separated
Cocoanut Oil	Smooth	3.63	11–20–18	3.34	2–20–19	2.7	Cryst. on surface
Hydrogenated Vegetable Oil	Smooth	3.48	11–20–18	3.10	2–20–19	3.6	Smooth
3% Ribbon Tragacanth Paste	Smooth	4.03	2– 8–19	3.11	5– 8–19	7.6	Smooth

Pullen[1] found a loss of free iodine of from 3.95 to 2.92% in 4 months, or an average of 6.5% per month when he used new lard, and a loss of from 3.38 to 2.26% in the same time, or an average of 8.3% per month when old lard was used.

Fried[1] found a loss of free iodine in U. S. P. VIII Iodine Ointment of from 3.89 to 2.81% in 1 month equivalent to 27.8% of the total free iodine, the loss remaining the same after 8 months.

Warren[2] found a loss of free iodine in U. S. P. VIII Ointment of from 3.32 to 2.99% in 7 days equivalent to a loss of 10% of the total free iodine and this loss was practically the same after 3 months, in one experiment.

In another experiment he found a loss of from 3.26 to 2.88% in 3 months or a total loss of 11.6%. In a third experiment the loss was from 3.30 to 2.88% in 3 months, or a total loss of 12.7%.

The satisfactory bases from the point of view of small loss of free iodine seem to be yellow petrolatum, anhydrous eucerin, coconut oil and hydrogenated vegetable oil.

Yellow petrolatum would probably be objected to unless supported by a large number of clinical trials because of the widespread difference of opinion regarding value of mineral bases in comparison with vegetable and animal fat bases.

Coconut oil is open to the objections of its great tendency to crystallize and its low melting point. These, however, can be corrected by an admixture of yellow bee's wax without decreasing the efficiency of the coconut oil in maintaining a fairly constant free iodine content.

Anhydrous eucerin has the one objection of comparatively high cost.

Hydrogenated vegetable oil, while showing a trifle lower efficiency than yellow petrolatum, anhydrous eucerin and coconut oil, seems to be the most practical base for iodine ointment.

Attention is especially called to the extreme cheapness of the 3 percent ribbon tragacanth base mentioned in the table. This paste showed quite as good keeping qualities as iodine ointment made with benzoinated lard and appeared to be somewhat more effective, physiologically, according to the following results:

Iodine ointment made with benzoinated lard and containing 4 percent free iodine caused cracking of the skin when applied to the shaved abdomen of a guinea pig every morning for 7 days.

An iodine paste containing 4 percent free iodine, prepared according to the U. S. P. process for iodine ointment, but with the benzoinated lard replaced by a 3 percent ribbon tragacanth paste caused cracking of the skin when applied to the shaved abdomen of a guinea pig every morning for 4 days.

—Reported by Geo. E. Ewe.

REFERENCES.

[1] *Pharm. Jour.*, 1912, 89, 610.
[2] *Rep. Chem. Lab., A. M. A.*, 1917, 10–38.

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A SUGGESTED CHANGE IN THE TECHNIQUE OF THE U. S. P. ASSAY OF OPIUM.*

BY H. W. JONES.

The method of assay for opium and its preparations given in the ninth revision of the United States Pharmacopoeia, while in general giving satisfactory results, contains certain directions, which, if followed specifically, may yield varying figures in the hands of different analysts, and indeed the results are apt to vary in the hands of the individual analyst unless he is unusually methodical in carrying out the details of analysis.

The directions for the extraction of the drug and for the crystallization of the alkaloid are quite definite and are scarcely capable of misconstruction, but the method directed for collecting the morphine crystals may allow a considerable variation in results even in the hands of the same operator. For this purpose the Pharmacopoeia directs that: "a small funnel, the neck of which has been previously closed with a pledget of purified cotton" be used. Through this pledget of cotton one is directed to pass the mother liquors from which the morphine has crystallized and which will contain fine crystals of morphine in suspension. I find that whether the pledget is thick or thin, pressed loosely or tightly will influence the quantity of these morphine crystals which will pass through with the mother liquors. That they do pass through has been observed repeatedly in this laboratory, for they may readily be seen upon allowing the filtrate to stand, and for this reason a second assay has been made on a number of samples already assayed by the U. S. P. method, using a quantitative filter paper instead of the

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