

I have prepared some of these creams, and have them here. They are very good indeed.

To replace glycerin in hair tonics, I find "turkey-red oil" recommended. This is sodium sulpho-ricinoleate. It is miscible with water. To replace glycerin in preparations where "body" is required, the London Pharmaceutical Committee recommends the following preparations:

Gum Tragacanth.....	30	grains	Picked Carragean.....	1	ounce
Chloroform.....	24	minims	Water.....	25	ounces
Water, to make.....	10	ounces			

And finally, another one:

For internal use, the following is claimed to be more suitable:

Gum Tragacanth.....	2	drachms
Alcohol.....	4	drachms
Chloroform Water.....	10	ounces

Washed Irish Moss.....	1/2	ounce
Water.....	24	ounces

Keep boiling for fifteen minutes, strain with pressure, make up to 19 ounces with boiling water and add 1 ounce of glucose. Mix and strain.

Another formula suggested is the following:

I have prepared some of these mucilages and, they are here for your inspection. Some of those used in Germany are also included.

The subject of war emergency formulae is certainly a very important one at this time. It seems to me to be even worthy of official consideration by the American Pharmaceutical Association. War emergency formulas might be worked out by a properly constituted committee, certain definite propositions made and duly legalized. Congress would surely not stand in the way, nor would State officers refuse to cooperate. By judicious effort of this nature, the American Pharmaceutical Association would make itself of great assistance to both the government and the profession. To the government such assistance would, no doubt, be most welcome, and it would be the carrying out, in a measure, of the promise of support made to President Wilson at the outbreak of the war. To the pharmacist, advice as to what he should do and can do in this emergency would be most valuable. When common substances become scarce, the pharmacist will do the best he can (which in many instances is the worst) and, furthermore, the temptation to illegal substitution becomes great.

Let us not wait until we are asked to do it, but let us be prepared. In our national emergency don't let us be followers, let us be leaders for the country's good.

THE PREPARATION OF DICHLORAMIN T. AND CHLORINATED EUCALYPTOL 1,2.*

BY ROBERT B. KRAUSS.¹

Para-toluol-sulphondichloramide was first prepared by Kastle, Keiser and Bradey² in 1896, who also prepared a number of related compounds. Since its introduction under the name of dichloramin T. by Dakin, Lee, Sweet, Hendricks and LeConte,³ the production of this substance on a large scale in pure form, as

EDITOR'S NOTE.—See also comment on this paper under Local Branches, this issue.

*Read before Philadelphia Branch A. Ph. A., December meeting, 1917.

¹ Henry Phipps Institute of the University of Pennsylvania.

² *American Chemical Journal*, 18, 491, 1896.

³ *Journal American Medical Association*, 69, 27, 1917.

well as that of suitable solvents for its application, have become problems of importance.

As originally used for this purpose dichloramin T. was dissolved in a prepared eucalyptol (chlorinated) and used in this condition or further diluted with prepared paraffin oil (chlorinated).

It was early recognized by the author that the products obtained by chlorination may vary considerably, according to the conditions of chlorination. By continued chlorination, under certain conditions, a chlorinated eucalyptol, specific gravity 1.2, is obtained, which has been extensively studied by surgeons. As a solvent for dichloramin T. it seems to have all the desirable qualities with the exception of the solution being definitely stable. There seems to be some reason to believe that chlorinated eucalyptol 1.2 itself has some therapeutic value.

This evening I will present an outline of the methods for preparing para-toluol-sulphondichloramide, and chlorinated eucalyptol 1.2, and the specifications for both as prepared for federal medical authorities.

1. PREPARATION OF THE SULPHONIC ACIDS.

Beginning with toluol, the sulphonic acids are formed by mixing equal parts of concentrated sulphuric acid and toluol. On shaking or even on standing the toluol dissolves in the acid. When the top layer of toluol has disappeared the sulphonation mixture is poured into water and neutralized with lime. After filtering, the solution of the ortho and para calcium sulphonates is treated with sodium carbonate and boiled to form the sodium salts and precipitate calcium carbonate. The filtered solution is evaporated to dryness and carefully dried.

2. PREPARATION OF THE SULPHOCHLORIDES.

The powdered sodium sulphonates are treated with an equal weight of phosphorus pentachloride. After the pentachloride has disappeared the semifluid mass is heated on the water bath to complete the reaction and then poured on ice. The para-sulphochloride crystallizes after a time while the ortho derivative is a liquid. They are separated by centrifuging.

3. PREPARATION OF THE SULPHONAMIDE.

The para-sulphochloride is melted on the water bath and treated with an excess of ammonium carbonate. The odor of sulphochloride should no longer be observable. The mixture of ammonium carbonate and sulphonamide is extracted with water and dried. If the sulphonamide is not pure white it should be recrystallized from hot water.

4. PREPARATION OF THE DICHLORAMIDE.

The toluol-para-sulphonamide is dissolved in ten parts of 1 : 10 caustic soda (39° Bé.) and diluted with twenty parts of water. The solution is filtered through glass wool and then through double filter paper. This removes iron hydroxide from the strongly caustic solution.

Chlorine gas from a cylinder is then passed through the solution, cooled externally by ice, until a voluminous white precipitate of para-toluol-sulphondichloramide is formed. This is filtered off, thoroughly washed twice with 5 to 8 parts of water and finally with enough 10 percent alcohol to make a thin paste. The dilute alcohol washing should be done very quickly and the substance filtered off with the aid of a vacuum filter. It is then dried at a temperature not exceeding 55° C. in a vacuum dryer.

The method has the advantage that it is very rapid and avoids the use of chloroform as a solvent. It was developed in order to produce a dichloramin T. which would be comparatively stable. The product has a negligible ash and a good chlorine content, but no free chlorine on standing.

Calculated: Cl = 21.54 percent. Found: Cl = 21.42 percent; 21.37 percent.

The very considerable work done in the chemical laboratory of the Institute on the preparation and distribution of dichloramin T. for surgical purposes has suggested the following specifications as most suitable for this material when used as a disinfectant:

PHYSICAL PROPERTIES.

White powder or crystals with slight yellow-green tinge. Melting point, 78–84° C.

CHEMICAL PROPERTIES.

Soluble in cold chloroform with slight to no turbidity. (Any turbidity must be removable by shaking with anhydrous calcium chloride.) Soluble in prepared eucalyptol, Dakin and chlorinated eucalyptol 1.2. Ash, not over 0.2 percent; chlorine content, 29.0 percent to 29.54 percent; calculated chlorine, 29.54 percent.

The solubility in chloroform or similar organic solvent is important in that it shows the presence of inorganic impurities, calcium salts, etc. The material should not have strong odor of chlorine, showing instability. The melting point may vary within the limits indicated, owing to moisture. Sharp drying will decompose the substance.

SOLVENTS.

The eucalyptol, as first proposed⁴ by Dakin and Dunham, was chlorinated with potassium chlorate and hydrochloric acid according to the following method:

Five hundred Cc. eucalyptol (U. S. P.) are treated with 15 Gm. potassium chlorate and 50 Cc. concentrated hydrochloric acid. After twelve hours the oil is well washed with water and sodium carbonate solution. Dry sodium carbonate is added to the oil and the mixture is allowed to stand twenty-four hours. It is then filtered and dried with a little calcium chloride.

This method has the disadvantage that no definite amount of chlorine enters the eucalyptol. The chlorination depends on the rate of adding chlorate and hydrochloric acid as well as the light in which the process takes place. Samples may have 1 percent chlorine present or scarcely any, depending on whether chlorination took place in sunlight or on a dark day. The specific gravity of this oil may vary from 0.930 to 0.935.

PREPARATION OF CHLORINATED EUCALYPTOL 1.2.

It was found that by passing chlorine gas from a cylinder into eucalyptol the reaction proceeded much further than by the chlorate method heretofore described. When a specific gravity of 1.20 was reached a comparatively heavy oil, much less volatile than eucalyptol, was obtained.

The results of the use of this oil are well known to-day; briefly, it was found that it is a good solvent for dichloramin T., that it can be used in full strength on the skin and in open wounds and that the use of paraffin oil either as a diluent or as a means of preventing sticking of dressings is unnecessary.

The following is a sufficiently detailed statement of the method by which this oil is obtained:

Through a glass tube reaching to the bottom of a five-gallon bottle containing about 10 kilos of eucalyptol is passed chlorine from a cylinder. The oil should have a boiling point of 176–177° C. and a specific gravity of 0.925 to start. The process should be carried on in good daylight.

During the chlorination the temperature rises and should be kept below 80° C. by regulating the chlorine stream. Hydrochloric acid is given off and may be absorbed in alkali.

When a specific gravity of 1.19 is reached the oil is chlorinated sufficiently and the process is interrupted. The oil is then washed with about four liters of water, then shaken thoroughly with 250 Gm. dry sodium carbonate and allowed to settle. After carefully decanting from the carbonate, about 500 Gm. fused calcium chloride are added and the whole again shaken. On standing preferably over night, the oil is filtered, bottled and is then ready for use. It is a white or slightly amber-colored oil, specific gravity 1.2, with a chlorine content of about 31 percent. Such an oil will readily dissolve 20 percent of dichloramin T. which solution may keep in an amber bottle without decomposition for a month.

FURTHER PRODUCTS OF CHLORINATION.

By further chlorination of the 1.2 oil, products may be obtained having a specific gravity of 1.5 and higher. This may be carried out by chlorinating directly at 100° C. or with a solvent such as chloroform at its boiling point. The oil of specific gravity 1.4 is amber colored and of the

⁴ Dakin and Dunham, *British Medical Journal*, June 1917.

consistency of molasses. The dichloramin is still soluble, although to a less extent. The future may find a use for this type of oil, since the increased viscosity presents an advantage in certain cases.

Dichloramin T. prepared as heretofore described is freely soluble in chlorinated eucalyptol 1.2. The solutions should be prepared about as follows:

PREPARATION OF 7½ PERCENT SOLUTION.

Measure off 150 Cc. of oil into a dry brown bottle, preferably one with a glass stopper. Add to this 11.5 Gm. powdered dichloramin T. This will dissolve, if shaken occasionally, in about an hour. It should *not* be warmed. This makes a 7½ percent solution, and is used for all dressings subsequent to the first two or three applications. This solution should keep for at least two weeks. If this is used in an atomizer, as directed, it has been found that one filling of the usual atomizer reservoir will dress from 100 to 150 cases.

PREPARATION OF 20 PERCENT SOLUTION.

This solution should be made up about 25 Cc. at a time, using 5 Gm. of dichloramin T. to 25 Cc. of oil. It is most quickly accomplished by trituration and the solution should be kept in a brown bottle. This is applied to fresh wounds and for the first treatment of infected wounds and focal infections. It is most conveniently applied with an ordinary medicine dropper. This solution is good until a crop of fine crystals appears in it, which may happen in three days, although it may remain in good condition for ten or more days.

When using the solution in an atomizer, the reservoir of which is of colorless glass, the solution should be protected against light as light greatly accelerates the decomposition of dichloramin T. in solution. The following points should receive consideration in its clinical use:

1. Surgical asepsis, as perfect as possible, should be used at both the primary operation and subsequent dressings.
2. At the primary operation all wound surfaces should be covered and all crevices filled with the 20 percent solution. Subsequent dressings are made with the 7½ percent solution.
3. Before the oil is applied the surfaces of the wound should be as dry as possible; free from blood and water.
4. Drainage should be avoided in all wounds closed by suture.
5. It has been suggested that with local infections, such as boils, carbuncles and abscesses, an incision be made somewhat earlier than usual and the 20 percent solution of dichloramin T. freely applied will very often sharply limit the progress of the infection.
6. This preparation is essentially non-irritating unless confined by unduly heavy or impervious dressings. If so confined, it may blister.

In conclusion I wish to acknowledge the coöperation of Doctors P. A. Lewis and W. E. Lee, and also the assistance of Miss Elizabeth Hill, in the chemical manipulations.

MAJOR D. A. COSSAR.

According to latest advice, Major D. A. Cossar, who was expected in this country, has been in Egypt; from there he will go to France. Mention was made in the JOURNAL, p. 922, October issue.