

of the drug shortly after collection in order to remove the soil. In fact, Van Fleet,¹ speaking of digging and curing the cultivated roots, suggests this procedure:

"The rootstocks and attached rootlets are washed clean of all soil and freed from sticks, pebbles, or other foreign matter lodged in the fibrous masses."

CONCLUSIONS.

It appears clear that a maximum limit of tolerance of 8 percent for total ash would be quite liberal, and the adoption of such a tentative limit by this country, producing the drug for domestic use and for export, as stated, has therefore been proposed.² A tentative limit of 3.0 percent of acid-insoluble ash is also suggested as a fair maximum limit of tolerance.

The findings with regard to the alkaloid content also indicate that the alkaloid requirement could well be raised to 2.75 percent, if the drug were in a properly cleaned condition.

SUMMARY.

It has been shown that:

- (1) The proportion of rhizome to roots varied considerably in the samples examined.
- (2) The alkaloid content was found to be higher in the rhizomes than in the roots. A previous report in literature is thus confirmed.
- (3) The raising of the required minimum alkaloid content to 2.75 percent of ether-soluble alkaloids is suggested.
- (4) Samples collected in interstate trade, while containing sufficient alkaloid, as required by the United States Pharmacopoeia, contained rather generally amounts of mineral matter greatly in excess of that naturally present.
- (5) The total and acid-insoluble ash in the roots was found to be higher than in the rhizomes.
- (6) A maximum limit of 8 percent for total ash, and 3 percent for acid-insoluble ash is proposed.

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PHARMACEUTICAL PROBLEMS PRESENTED BY THE DAKIN PRODUCTS.*

BY FRANK B. KIRBY, M. D.

Early in the World War it became evident that the economics of warfare demanded investigation of the problems of sepsis and antiseptics. Quick repair of wounds was a consideration of prime value as the return to the field of injured experts meant more for ultimate success and speedy victory than the training of recruit substitutes.

Attention was early drawn to the advantages presented by the hypochlorites and an investigating committee appointed under Col. E. F. Martin as chairman.

We shall pass the therapeutics of hypochlorites to emphasize the essential importance of using a calcium hypochlorite of known and definite free chlorine strength, as brought out by the fact that few if any products on the market could

¹ Walter Van Fleet, "Goldenseal Under Cultivation," U. S. Department of Agriculture, *Farmer's Bulletin* No. 613, 12, 1914.

² C. O. Ewing and A. Viehovever, "Acid-Insoluble Ash Standards for Crude Drugs," *THIS JOURNAL*, 8, No. 9, p. 725-730, September 1919.

* Read before Scientific Section, A. Ph. A., City of Washington meeting, 1920.

be depended upon. So-called "chloride of lime" for household purposes may satisfy the purchaser but for the fine results demanded by an exacting army and navy we had to have something different. This, with the fact that oxidation of sodium salt is very rapid, makes necessary a titration of the original Dakin solution at least once in every 24 hours, as a variance of .1 of 1% in alkalinity makes for the difference between success and failure.

The standard, while not impossible to accurate pharmacy, is impracticable in the every-day drug store and even in hospital dispensaries.

**ESTIMATION OF CHLORINE IN CALX-CHLORINATA,
PREPARATORY TO MAKING DAKIN'S SOLUTION.**

Take from various parts of the container small amounts of the Calx-chlorinata mix it thoroughly and accurately weigh 20 grains. Mix this 20 grains with one liter of water in a dark bottle and let it stand 12 hours. Then to exactly 100 ml. of the supernatant liquid add two ml. of ether, seven ml. of hypochlorous acid and 20 ml. of a ten percent solution of Potassium Iodide and distilled water up to 75 ml.

Next add 1/20 Sodium Thiosulphate drop by drop until complete discoloration takes place using starch T.S. to note the end-reaction. Let H represent the chlorine value and N the number of ml. used and solve the following:

$N \times 1775 = \text{the chlorine value of the calx-chlorinata in grams per 100 grains of the sample.}$

To make ten liters of Dakin's Solution when N=25 use calx-chlorinata 184 grains, anhydrous sodium carbonate 92 grams, and sodium bicarbonate 76 grams.

When the chlorine value varies calculate the amounts of each salt to use as follows:

$N \times 184 = N \times 92$ and $N \times 76$ and the product in each case will be the number of grams of each salt required.

The following reactions are of interest and a study of them will help the student understand the above procedure:

- ① $2\text{NaOCl} + 2\text{HCl} = 2\text{NaCl} + \text{Cl}_2 + \text{H}_2\text{O}$
- ② $\text{Cl}_2 + 2\text{KI} = 2\text{KCl} + \text{I}_2$
- ③ $\text{I}_2 + 2\text{Na}_2\text{S}_2\text{O}_3 = 2\text{NaI} + \text{Na}_2\text{S}_4\text{O}_6$

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PLATE I.

Chiefly because of this consideration, but also because of others of a therapeutic character, Dakin was led to investigate the possibilities offered by the synthetic chloramines. These are chlorine combinations with nitrogen releasing the chlorine radical in the presence of albuminoids and other organic material somewhat more slowly than the hypochlorites. The chloramines are more stable than the hypochlorites but in solution must be protected from strong sunlight and organic matter. Aqueous solutions keep relatively well but with the facility of solution we find stock solution objectionable because of possible contamination and deterioration.

The third of the Dakin products for consideration by the committee referred to is the dichloramine-T. This differs in every way from the chloramine-T. Dichloramine-T is oil soluble and instantly destroyed by the action of water. Dakin's first solvent was a chlorinated eucalyptol, which solution was diluted with chlorinated paraffin oil. The inconveniences and cost of the double solvent led to further investigations which developed into what he calls chlorcosane.

The chloramines are effective because of the free chlorine available for action as a germicide. They meet the therapeutic problem effectively only when rightly

prepared, and considering the delicate character of the di-chloramine-T solution must be properly carried out.

The solvent chlorcosane is made by melting paraffin and saturating with chlorine, which adds one-half the weight, replacing some of the hydrogen, part of which is driven off as hydrochloric acid.

To maintain full clinical efficiency it is necessary that the dichloramine-T solvent be saturated with chlorine, otherwise this element is robbed from the dichloramine-T.

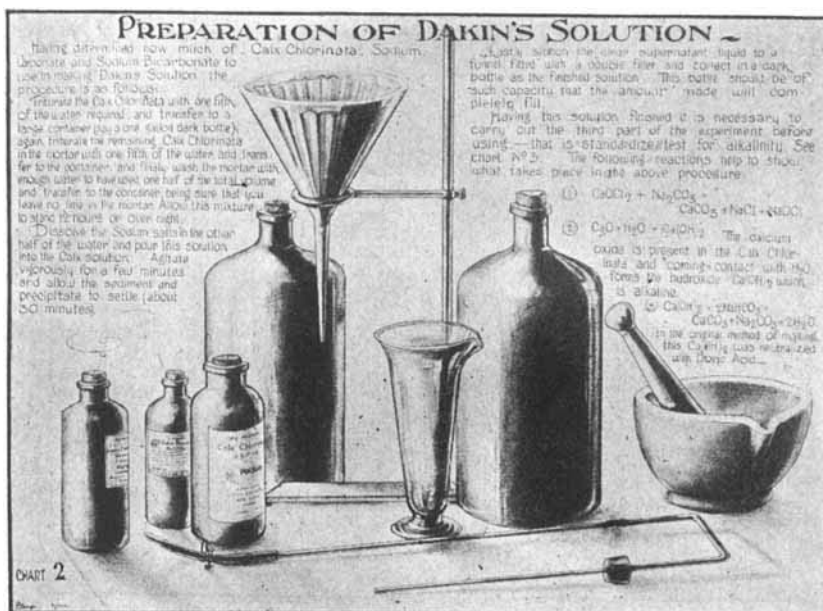


PLATE 2.

Solution is made by slight heat or a few drops of chloroform to be subsequently mixed with the chlorcosane. The dichloramine-T may be had in powder or tablet as preferred and must be protected from light, heat, chloroform, alcohol or organic matter.

For dispensing, solution must preferably be extemporaneous. Stock solutions will not do. Prescriptions should be filled in amber bottles, glass-stoppered, although if dispensed as it should be in, say, one-ounce bottles, a cork stopper has little disadvantage.

The reaction as to the chlorine loss has been accurately worked out, showing different losses for the various metals, wood, cotton and rubber, both hard and soft. Nothing but glass or porcelain should come in contact with dichloramine-T solution.

Unless the scientific work connect up with the commercial it has little value, and in presenting these facts it is with the intention to emphasize the necessity of presenting an accurate, full strength product for clinical use.

On this depends future business.

The commercial aspect of the problems presented is sufficient to warrant the care necessary, as three allied branches of applied medicine can and do make use of dichloramine-T. We refer to the general and special practice of human medicine and surgery, veterinary medical practise and veterinary surgery, and dentistry as well.

These are the channels of distribution and a well-made dichloramine-T solution is a subject on which the retail druggist should get a hearing from physicians, veterinarians and dentists who do not have the time, inclination or facilities for doing this work.

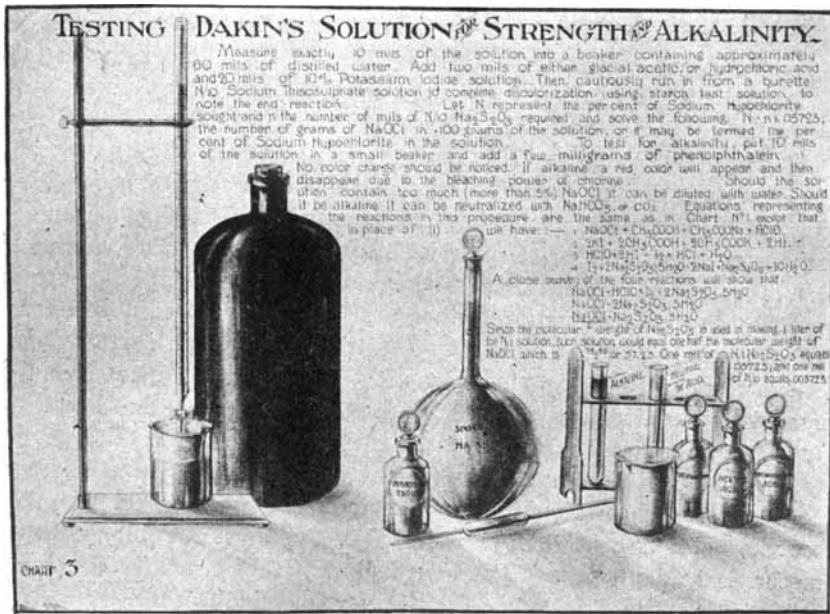


PLATE 3.

ABSTRACT OF DISCUSSION.

Albert Schneider inquired as to whether the average pharmacist was prepared to do the work necessary in connection with the preparation of Dakin's solution. William Gray stated that a solution of chlorinated lime, containing 4½ percent chlorine, of which a 1-10 dilution could readily be prepared would keep without material loss for a year. Lieut. Kennedy, U. S. N., stated that they had considerable trouble with the keeping qualities of chlorine solution; it kept better in large volumes; he also asked for a ready, accurate method of titrating the solution. Charles M. Hallum stated that the control of alkalinity was as troublesome as of chlorine, and it was important to have that just right.

In answering the questions the author of the paper replied that pharmacists were equipped for making Dakin's solution. The difficulties are the factors brought out by others and which induced Dakin to investigate the chloramines. He did not know of any more rapid method than that usually employed; the solution must be titrated every 24 hours to insure a suitable product. He did not encourage the making of a stock solution; it is essential to have the dichloramine-T properly made, so that there is no precipitate, and no excess of acid.

Doctor Kirby called attention to three charts of the Navy Department for use of the pharmacists, for their guidance in making Dakin's solution. These were published in the *Supplement to the U. S. Naval Medical Bulletin*, of January, 1919. The editor acknowledges the courtesy of the loan of these cuts; they are used in connection with this article.