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THE PREPARATION OF DILUTED HYDRIODIC ACID AND SYRUP OF HYDRIODIC ACID.*

BY WILLIAM J. HUSA.**

INTRODUCTION.

The purpose of this paper is to present some practical formulas for the preparation of Diluted Hydriodic Acid and Syrup of Hydriodic Acid by the retail pharmacist. In order that the problem may be viewed in the proper perspective, it will be well to begin with a brief summary of earlier work in this field which has a bearing on the present discussion.

HISTORICAL REVIEW.

Discovery of Iodine and Hydriodic Acid.—Following the discovery of the element, iodine, by the French pharmacist, Courtois, in 1811, hydriodic acid was first recognized by Clement and Desormes (1) in 1813. In the following year, Gay-Lussac (2) prepared hydrogen iodide by passing a mixture of hydrogen and iodine through a red hot tube.

Introduction of Iodine and Hydriodic Acid into Medicine.—Shortly after the discovery of iodine, Coindet (3) suspected that this element was the active constituent of the ashes of sponges, which had long been used empirically in the treatment of goiter and scrofula, and after proving this to his own satisfaction he introduced iodine into medicine. Due to its irritant action, iodine frequently caused severe gastric disturbances, and to overcome this undesirable effect, Dr. Andrew Buchanan (4) of Edinburgh, in 1837, introduced the use of hydriodic acid, which he prepared by the action of tartaric acid upon potassium iodide.

Official Recognition of Preparations of Hydriodic Acid.—Diluted Hydriodic Acid was introduced into the U. S. P. of 1860, was omitted in 1870 and 1880, but was again included in the 8th, 9th and 10th revisions. The method of prepara-

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tion first recognized by the U. S. P. consisted in passing hydrogen sulphide into a mixture of iodine and water; when the liquid had become colorless it was filtered to remove the sulphur which had precipitated and the filtrate was heated to drive off the remaining hydrogen sulphide.

In the U. S. P. of 1880, the Committee of Revision introduced Syrup of Hydriodic Acid, which was made by dissolving iodine in alcohol, mixing with syrup, passing in H_2S, filtering and driving off the H_2S at a temperature not exceeding 55° C. The first edition of the National Formulary, published in 1888, contained a formula for Colorless Syrup of Hydriodic Acid, which was prepared from potassium iodide, potassium hypophosphite, tartaric acid, water, diluted alcohol and syrup, this formula being a modification of Buchanan's original method. A similar formula was adopted by the U. S. P. of 1890. In these methods the hydriodic acid was made in the course of the preparation of the syrup, but later a method of preparation of the acid was given only under the title of Diluted Hydriodic Acid, and the syrup was directed to be made from the diluted acid. Thus the U. S. P. IX formula for Syrup of Hydriodic Acid was as follows: "Diluted Hydriodic Acid, 125 mils; Distilled Water, 300 mils; Syrup, 575 mils, to make 1000 mils." In the U. S. P. X, the syrup was replaced by 450 Gm. of sucrose, thus slightly reducing the percentage of sucrose in the finished preparation.

The British Pharmacopœia of 1914 recognizes a Diluted hydriodic acid containing 10% of HI and 1% of hypophosphorous acid. Exact details of preparation are not given but it is stated that "It may be obtained by the action of hydrogen sulphide on a solution of iodine, with the subsequent addition of hydrogen hypophosphite." The formula for the Syrup of Hydriodic Acid, B. P. is as follows: "Diluted hydriodic acid, 100 Gm.; Distilled water, 50 ml.; Syrup, q. s. 1000 ml."

Aside from the U. S. P. and B. P., no other pharmacopœias recognize hydriodic acid or its preparations.

DISCUSSION AND RECOMMENDATIONS.

The fact that Syrup of Hydriodic Acid becomes discolored in the course of time has led to a great deal of work by pharmacists and manufacturers on methods of improving the stability. Among the stabilizers tried are hypophosphites, thiosulphates, sulphites, sugar, rock candy, glucose and glycerin. It is now generally conceded that the brown color which appears is caused primarily by caramelization of the sugar, although free iodine may appear after the hypophosphorous acid has been completely oxidized. In some of the papers on the subject, statements are made to the effect that stable preparations of Syrup of Hydriodic Acid have been obtained by various expedients, but these statements must be largely discounted in view of the fact that in recent years a committee of the Scientific Section of the American Drug Manufacturers' Association has investigated this subject and has not been able to develop a formula that was very satisfactory over a period of time (5) (6).

If the retail pharmacists would prepare Syrup of Hydriodic Acid freshly when needed, or at least at frequent intervals, the problem would practically disappear. Even some of the manufacturers are of the opinion (5) that Syrup of Hydriodic Acid is one of the preparations that should be made in the drug store. By keeping Diluted Hydriodic Acid (which is very stable) in stock, the pharmacist could mix this with sucrose and water whenever the syrup was needed. By so doing, the phar-

macist would avoid loss by spoilage and would have the satisfaction of dispensing a first-class product. If it is too much trouble for the pharmacist to weigh out the sugar, then perhaps the U. S. P. should return to the U. S. P. IX formula, which involved no weighing, but only the mixing of measured amounts of diluted hydriodic acid, syrup and water. In fact this change has already been suggested for inclusion in the U. S. P. XI by a Committee of the Philadelphia College of Pharmacy and Science (7) and it is the method used in the British Pharmacopœia.

The retail pharmacist need not use the cumbersome and time-consuming U. S. P. method for preparing Diluted Hydriodic Acid, which may be purchased as such. The U. S. P. is the only pharmacopœia of the world which contains a method for the preparation of hydriodic acid. I am of the opinion that the method has outlived its usefulness and should now be deleted from the U. S. P. The reasons for this opinion are as follows. When hydriodic acid was introduced into medicine, in the days when pharmaceutical factories were unknown, it was necessary that such products be made by the individual pharmacist. At the present time, however, pure hydriodic acid of 45% strength is a recognized article of commerce. Usually the 45% acid is stabilized by the use of 1.5% of hypophosphorous acid. When thus stabilized the acid will remain colorless for years. However, the stabilizer is quite necessary; in the acid of one manufacturer, no stabilizer was used and on examining the product I found it consisted chiefly of free iodine. At present prices, the 45% acid is relatively cheaper than the official 10% product, and it would therefore be practical for the pharmacist to purchase the 45% acid and dilute it to 10%.

In view of the availability of pure, concentrated hydriodic acid, there is no reason why the pharmacist should prepare this acid in small quantities, any more than he would prepare hydrochloric acid. In order to put this matter on a sound basis, it would be advisable to include standards for hydriodic acid of 45% strength in the U. S. P. XI, just as is done in the case of hydrochloric acid of 31% to 33% strength. In setting the standards, it would be best to adjust the percentage of hypophosphorous acid so that when diluted with the proper amount of water, the resulting product would correspond exactly to the present U. S. P. Diluted Hydriodic Acid, with respect to both hydriodic and hypophosphorous acids.

My calculations show that the concentrated hydriodic acid (45%) should contain 3.15% of hypophosphorous acid. The formula for Diluted Hydriodic Acid would be as follows:

Hydriodic acid (45%)	163 cc.
Distilled water q. s.	1000 cc.

For this calculation the sp. gr. of Diluted Hydriodic Acid was taken as 1.100 as given in the U. S. P. However, the U. S. P. value for sp. gr. is based on the product containing some potassium bitartrate (8) and thus the sp. gr. of the more pure acid would be lower and a slight correction in the formula for the diluted acid would be in order when the requisite data becomes available.

Replacing the diluted acid in the U. S. P. X formula by the 45% acid, the formula for Syrup of Hydriodic Acid would be as follows:

Hydriodic acid (45%)	21.2 cc.
Sucrose	450.0 Gm.
Distilled water q. s.	1000.0 cc.

Using syrup in place of sucrose, the following alternative formulas result.

Formula 1.

Diluted hydriodic acid	130 cc.
Syrup	530 cc.
Distilled water q. s.	1000 cc.

Formula 2.

Hydriodic acid (45%)	21.2 cc.
Syrup	530.0 cc.
Distilled water q. s.	1000.0 cc.

By use of these formulas, a first-class product may be quickly prepared and the entire procedure is economically sound.

SUMMARY.

1. Since pure, concentrated hydriodic acid is commercially available in a stabilized form, it is scarcely advisable for the pharmacist to prepare this acid.

2. It is suggested that the process for the preparation of Diluted Hydriodic Acid be deleted from the U. S. P.

3. It is suggested that the U.S.P. XI adopt standards for a concentrated hydriodic acid containing 45% of hydriodic acid and 3.15% of hypophosphorous acid. The present official Diluted Hydriodic Acid would be made by diluting the 45% acid with water.

4. Syrup of Hydriodic Acid should be freshly prepared by the retail pharmacist as needed or at frequent intervals.

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PURIFICATION OF DYNAMITE AND SAPONIFICATION GRADE GLYCERINS.*

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The purification of glycerin obtained from fatty sources has always involved an expensive distillation process. Thus a single distillation of saponification grade glycerin yields the so-called dynamite glycerin and a redistillation of this dynamite glycerin finally yields a "chemically pure" or "double distilled" glycerin. During

* Scientific Section, A. PH. A., Baltimore meeting, 1931.