

## SCIENTIFIC SECTION

BOARD OF REVIEW OF PAPERS.—*Chairman*, F. E. Bibbins; H. M. Burlage, W. G. Crockett, E. V. Lynn, C. O. Lee, L. W. Rising, L. W. Rowe, Heber W. Youngken, F. V. Lofgren, J. C. Krantz, Jr.

### STABILIZED SYRUP OF FERROUS IODIDE.\*<sup>1</sup>

BY P. L. BURRIN, A. G. WORTON AND F. E. BIBBINS.

Syrup of Ferrous Iodide has long been recognized as an unstable pharmaceutical product. Because of its value as a therapeutic agent, however, the medical profession has continued to prescribe it for more than a century. Certainly its use would be more extensive were it more stable.

Various methods have been advanced for stabilizing the syrup and specific directions have been given for storage conditions to retard deterioration. Considering the instability of this syrup, it is remarkable that an effective method of preservation has not been adopted before now.

Beral (1) is credited as the first to attempt stabilization of solutions of ferrous iodide. He reported the use of simple syrup as a preservative in 1841. Beral is also credited with being responsible for the introduction of Syrup of Ferrous Iodide into the United States Pharmacopœia of 1860.

In 1888, England (2), endeavoring to produce a stable product, experimented with commercial glucose, and a mixture of glucose and dextrose. These materials were found to be unsatisfactory for they did not prevent oxidation of the ferrous iodide. He is said to be the first to use powdered dextrose in compounding Syrup of Ferrous Iodide. He reported this syrup to be stable.

Braford and Langenhan (3), in 1927, made an extensive report covering all published data pertaining to Syrup of Ferrous Iodide. They reported several authorities for the use of citric acid, as a stabilizer, in a syrup made with sucrose. They also pointed out that citric acid was included in the formula for Syrup of Ferrous Iodide in the Pharmacopœias of Holland, Austria, Belgium and Hungary.

Because of the unsightly appearance of the deteriorated product, it is the common opinion that its therapeutic efficacy has been reduced. Husa and Klotz (4), however, have reported this deterioration to be confined to the sugar. They claim the darkening and precipitation in the syrup is caused by hydrolysis of the sucrose, and the ultimate decomposition of the resulting fructose. As proof for their claims they have proposed a formula for a stable syrup, which is compounded with dextrose in place of the sucrose, and contains hypophosphorous acid as the antioxidant.

The authors prepared several samples of Syrup of Ferrous Iodide, as proposed by Husa and Klotz, substituting powdered dextrose for sucrose to the point of saturation. Except for a nearly imperceptible blue-green tint, these samples could be classed as colorless. Because of the low viscosity and intensified bitter taste of the samples prepared with dextrose, it was decided to try further experiments.

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<sup>1</sup> From the Control Laboratories, Eli Lilly and Company.

Seven samples were prepared containing from 28 to 56 per cent by volume of glycerin. This addition of glycerin was found not only to increase the viscosity to the desired point, but also to improve the taste. After aging for a year in half-filled, flint-glass bottles, all samples prepared with dextrose were in excellent condition; however, the control sample made without glycerin acquired a very slight yellow tint as did the samples made with the greater amounts of glycerin. The sample prepared with 28 per cent by volume of glycerin showed no discoloration whatever. The discoloration, beginning with the sample containing glycerin 36 per cent by volume, increased proportionately with the amount of glycerin. The discoloration in the control sample, prepared according to the formula proposed by Husa and Klotz, was equal to that of the sample containing 56 per cent glycerin by volume. The shade of difference in these samples after aging a year may be considered inconsequential, and is mentioned only to show that the results are not identical.

Following the work of Husa and Klotz in stabilizing solutions of ferrous iodide by raising its  $p_H$  to 3.2, an effort was made by the authors to raise the  $p_H$  of Syrup of Ferrous Iodide U. S. P. XI by using the absolute minimum quantity of hypophosphorous acid allowed in this formula. The U. S. P. XI formula specifies hypophosphorous acid containing 30 to 32 per cent acid; therefore, 30 per cent acid was used in compounding several samples. The  $p_H$  changed from 1.0 to 1.2, but the stability was not changed at all as compared to a sample containing 31 per cent acid.

In a further endeavor toward stabilization, varying amounts of citric acid were added to three samples made according to the U. S. P. XI formula. To one sample was added 0.25 per cent of citric acid, to another 0.5 per cent and to the other 1.0 per cent. The citric acid changed neither the  $p_H$  nor the stability of the product. Another sample was prepared at the same time in which 0.07 per cent of citric acid was substituted for the hypophosphorous acid. The  $p_H$  immediately after its preparation was 2.0. This sample, after aging for nearly a year, is in excellent condition, having discolored to only a pale yellow, and contains no precipitate.

At the time the samples were prepared with citric acid, another was prepared according to the formula of the U. S. P. XI with 0.5 per cent of sodium citrate added. It seems that the addition of sodium citrate evidently buffers the solution, preventing hydrolysis of the sucrose and decomposition of the hydrolytic product, fructose. This sample still retains its original light green color and is free from precipitate; consequently it may be classed as an elegant pharmaceutical after having aged for nearly a year.

In conclusion it may be said that substituting powdered dextrose for sucrose to the point of saturation in the U. S. P. XI formula for Syrup of Ferrous Iodide produces a very stable product with a low viscosity. The viscosity and the stability likewise may be increased advantageously by the addition of glycerin up to 36 per cent by volume. The chief disadvantage of this additional glycerin is the increased cost.

Stabilization of the U. S. P. XI product containing sucrose may be brought about by the simple addition of 0.5 per cent of sodium citrate or by the substitution of 0.07 per cent of citric acid for the hypophosphorous acid.

## REFERENCES.

- (1) Beral, *American Journal of Pharmacy*, 13, 74 (1841).
- (2) England, *Ibid.*, 64, 547 (1888).
- (3) Braford, C. J., Langenhan, H. A., *Jour. A. Ph. A.*, 16, 336 (1927).
- (4) Klotz, L. J., Husa, W. J., *Ibid.*, 23, 679 and 774 (1934).

## THE DECOMPOSITION OF SOLUTIONS OF SODIUM SULFIDE.\*

BY G. BULFER, A. J. BOYLE AND L. H. BALDINGER.<sup>1</sup>

## INTRODUCTION.

The decomposition of sodium sulfide in aqueous solution has long been a subject of interest. Thomsen (1) has reported that a solution of sodium sulfide is almost completely hydrolyzed into sodium hydrosulfide and sodium hydroxide. This agrees with the reports of Knox, Bauer, Kolbe and others (2). Küster and Heberlein (3) showed that the hydrolysis of sodium sulfide in a tenth-normal solution occurs to the extent of 86.4% and results in the formation of sodium hydrosulfide and sodium hydroxide. They further reported the hydrolysis of sodium hydrosulfide into hydrogen sulfide and sodium hydroxide to the extent of 0.14 per cent.

Aqueous solutions of sodium sulfide are also oxidized in air with the formation of sodium thiosulfate and sodium bicarbonate. Mitscherlich (2) states that half of the sulfide is converted to the thiosulfate and half to the bicarbonate in the oxidation. Mellor (2) reported that carbon dioxide reacts with aqueous solutions of sodium sulfide converting it to sodium hydrosulfide and sodium bicarbonate. Borntrager (4), while investigating the analysis for copper using sodium sulfide solution, found that increasingly large amounts of sulfide solution were necessary as the solution became older. One sample showed 66.6% decomposition in a period of one month.

Sodium sulfide in varying concentrations, both in water solution and in paste form, can be used as a depilatory. The effectiveness of the preparations, attributed to the sulfide ion, is impaired by the decomposition of the sulfide salt in aqueous solution. Organic compounds such as glycerol and carbitol (diethyl ether of ethylene glycol)<sup>2</sup> have been added to depilatory preparations to inhibit decomposition. The present problem was undertaken to study briefly the effectiveness of these two compounds as inhibitors of the decomposition of sodium sulfide solutions.

## ANALYTICAL PROCEDURE AND DATA.

A rapid method of analysis of alkali sulfides was desirable for the proposed work. The standard and approved method of oxidation of the sulfide to the sulfate, precipitation and determination as barium sulfate was ruled out because of the time involved. Calcott, English and Downing (5) found that a mixture of ammonium chloride and sodium chloride readily evolves hydrogen sulfide from sodium sulfide while other substances which may be present in the sodium

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