

(2) In the case of the average light-sensitive chemical, does light act directly or merely as an accelerator of oxidation or reduction?

(3) In certain cases, notably the halide salts of such metals as silver, mercurous mercury and iron, the reducing action of light is clearly discernible. Thus photographic studies have cleared up the situation as far as the silver halides are concerned. Will further investigations of other metallic compounds indicate definitely which deteriorations due to light are reducing and which are oxidizing phenomena?

(4) In rancidity, is not the deterioration due to presence of air and moisture rather than to light?

We hope in the near future to make further efforts toward answering these interesting questions.

COLLEGE OF PHARMACY,  
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## THE STABILIZATION OF SYRUP OF FERROUS IODIDE, U. S. P. X.\*<sup>1</sup>

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### INTRODUCTION.

Ferrous iodide was discovered by Courtois (1) who reported its preparation in 1811. It was introduced into medicine in 1824 by Dr. Pierquin (2) who used the chemical as prepared by Caillot (3), a French pharmacist. In 1831, Pierquin (4) published formulas for the administration of ferrous iodide in the form of a water, chocolate, pastille, salve, tincture and wine and added that 2 oz. of the salt in sufficient water might be used for bathing. The voluminous literature concerning Syrup of Ferrous Iodide has been adequately reviewed (5). The purpose of the present investigation was to evaluate previous work, determine the mechanism and rate of decomposition and effect a satisfactory method of stabilization.

### EXPERIMENTAL.

*Chemicals and Reagents.*—Two kinds of iron wire were employed, *i. e.*, card teeth and Merck's Reagent Iron. The former assayed 99.6% iron and contained 0.07% of sulphur as well as some carbon and silicon; the latter showed 99.9% iron and contained 0.05% sulphur as well as traces of silicon. Sulphur was determined by the cadmium acetate absorption method (6).

Mallinckrodt's U. S. P. and Merck's C.P. and Reagent Iodine were used. Mallinckrodt's U. S. P. Hypophosphorous Acid assaying 31.04%  $H_3PO_2$  was employed. Colgate's C.P. glycerin; Merck's C.P. dextrose and U. S. P. Honey were used. The sucrose satisfied all U. S. P. requirements; its specific rotation at 22° C. was 66.15 determined according to the U. S. P. method. Distilled water having a  $p_H$  of 5.7 was used throughout.

*General Methods.*—All volumetric and gravimetric work was carried out using calibrated weights and apparatus. The progress of decomposition was followed in most cases by titration of free iodine using approximately 0.01*N* solution of sodium thiosulphate and freshly prepared starch T.S.

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<sup>1</sup> This paper is based on a dissertation submitted by Lyell J. Klotz to the Graduate Council of the University of Florida in partial fulfilment of the requirements for the degree of Doctor of Philosophy, June 1934.

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Assays for total iodide were performed by the U. S. P. method using approximately 0.1*N* silver nitrate V.S. and titration with approximately 0.1*N* potassium thiocyanate V.S. according to the Volhard method.

Since ferrous iron cannot be determined in solutions of an iodide by means of permanganate and the dichromate method is tedious and unsatisfactory, a modified permanganate method was developed. This method consisted in the addition of excess silver nitrate to the sample, thus precipitating the iodide, and subsequent determination of ferrous iron with potassium permanganate V.S. The procedure was as follows: An accurately measured quantity of the solution to be assayed is placed in a flask and a slight excess of 0.5*N* silver nitrate solution added after dilution of the sample with distilled water. An excess of Diluted Sulphuric Acid is then added and the mixture titrated with potassium permanganate V.S. The validity of this method was established by standardization of a permanganate solution against weighed quantities of ferrous ammonium sulphate, separately and in mixtures containing iodine, iodides, ferric iron or combinations of these substances.

Hydrogen-ion concentrations were determined by means of a La Motte block comparator and color standards, the hydrogen electrode and the quinhydrone electrode being unsuitable for use with ferrous salts.

Storage of solutions and syrups was made in ordinary prescription bottles or in bottles of comparable alkalinity. A Freas thermostat maintaining a temperature of 30° C.  $\pm$  .01°, a Freas electric oven maintaining a temperature of approximately 50° C. and an electric refrigerator maintaining a temperature of about 6° C. were employed.

The effects of various spectrum bands were obtained by the use of a series of light filters obtained from the Corning Glass Works. Quartz flasks were used for determinations involving ultraviolet light.

*Variations in Reaction Time.*—It has been stated that despite the simplicity of this reaction, the direct union of iron and iodine in aqueous solutions does not proceed uniformly to completion in various instances (7). Solutions of ferrous iodide were prepared from card teeth and from iron wire (Reagent grade) using various grades of iodine, and the reaction vessel was maintained in every case at constant temperature ranging between 21° and 26° C. for various samples. Efficient, uniform mechanical stirring was provided and the end-point taken as the time at which the solution was free from iodine. In no case was there a significant difference in the time of reaction. Ten solutions were prepared, the time ranging from one hour and twenty-five minutes to one hour and fifty minutes. The addition of carbon to solutions prepared from Reagent iron did not alter the reaction time. Insoluble residues from card teeth solutions were invariably black in color; those from Reagent iron samples were light brown.

*The Effect of Variations in Manufacture.*—The U. S. P. X directions for the manufacture of Syrup of Ferrous Iodide allow considerable latitude in interpretation. The phrase "cooling the flask as necessary" implies that volatilization of the iodine should be prevented, but no definite instructions as to the reaction temperature are given. Similarly, the end-point of the reaction is not well defined. It was found in this investigation that the green color so eagerly sought in this preparation is due, not to the salt at the concentration present, but to the presence of minute traces of iodine. In the preparation of aqueous solutions, this is best avoided by allowing sufficient time for the reaction and testing for the end-point with starch T.S. before subsequent application of heat.

In this investigation, solutions of ferrous iodide were prepared by direct union using various grades of chemicals and by double decomposition. In the direct

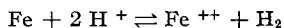
union reaction, various degrees of heat were used during the progress of the reaction and at its completion. No visible differences were apparent in the finished preparations. On the other hand, these solutions had different  $p_H$  values, contained different quantities of iron and left different types of residues upon filtration of the reaction mixtures.

Using card teeth as the source of iron, it was found that regardless of the amount of heat employed or the quality of the iodine used, the  $p_H$  varied between  $p_H$  3.2 and  $p_H$  4.2 with the usual value at  $p_H$  3.2 for the preparation of 2 liters of solution. On the other hand, a variation between  $p_H$  3.4 and  $p_H$  4.7 was noted in the case of samples prepared from Reagent iron. In this case, the usual value was  $p_H$  4.1. These values resulted from 30 determinations.

Solutions prepared by double decomposition between Mallinckrodt's barium iodide and Merck's Reagent ferrous sulphate varied between  $p_H$  3.2 and  $p_H$  4.7.

Residues from card teeth samples were invariably black in color while those from Reagent iron were light brown. The former residues were apparently carbon and the latter were ferric hydroxide.

The formation of ferrous iodide from iron and iodine has always been considered to be a simple direct union reaction. However, as the reaction proceeds, hydrolysis of the product occurs thus giving rise to hydrogen ions and iodide ions. Since iron reacts according to the equation:



it was thought that the solution might contain iron in excess of the quantity calculated from the iodide content. Gravimetric determinations of the amount of iron remaining unconsumed after expiration of the reaction indicated that more iron was used than could be accounted for upon the basis of the iodide content of the solution. Volumetric analyses of the solutions further indicated that this excess iron appeared in the solution. The excess amounted to approximately  $2 \times 10^{-3}$  mols/L. of ferrous iron in the case of card teeth solutions and approximately  $8 \times 10^{-3}$  mols/L. of ferrous iron in the case of the Reagent iron samples.

An analysis of the residues remaining after filtration of the reaction mixture indicated that nearly twice as much iron was present in the ferric state in Reagent iron samples as in card teeth residues. In solutions prepared from Reagent iron in an atmosphere of pure hydrogen, however, the quantity of ferric hydroxide formed was negligible.

The addition of carbon and ferrous sulphide to reaction mixtures of Reagent iron and iodine did not have any significant effect upon the  $p_H$  values of the resulting solutions.

Previous washing of the card teeth used with strong alkali solutions and dilute acid, did not alter the results as outlined above.

*The Evolution of Gases.*—It has been suggested that reduction of the carbon present as impurity in the iron results in the formation of unsaturated hydrocarbons. On the other hand, it appeared possible that if carbon acts as a reducing agent, carbon dioxide might be formed.

The gases were passed through standardized potassium permanganate solutions in certain instances and through lime water in others. Negative results were

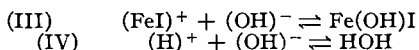
obtained in every case with both Reagent iron and card teeth. The addition of carbon to Reagent iron reaction mixtures was without effect.

*The Variation of Hydrogen-Ion Concentration with Time.*—As a result of 50 experiments, it was found that regardless of the form of iron or iodine used or of the original  $p_H$  value of the solution, the  $p_H$  dropped rapidly to  $p_H$  3.2. No further changes occurred during the observation period of 1 year. Precipitation accompanied this drop in  $p_H$  value although it continued after the hydrogen-ion concentration had reached stability. It was found that solutions of high  $p_H$ , *i. e.*, 4.1 or higher, remain at that point for some time before gradually becoming more acidic. Tests showed that ferrous sulphate solutions of comparable concentration exhibit a similar behavior.

*The Hydrolysis of Ferrous Iodide.*—Since ferrous iodide is the salt of a weak base and strong acid, it is logical to expect hydrolysis to occur. Despite this fact, the U. S. P. VIII specified that the preparation should be neutral in reaction. The ionization constant for the base concerned is not available in the literature, consequently, experimental determinations were necessary in order to determine the degree of hydrolysis. Obviously, it is possible for hydrolysis to occur in either of two ways:<sup>1</sup>



wherein the mechanism of equation (I) is represented by the ionic equilibria:



which may be combined in the simple equilibrium equation:



Applying the Law of Mass Action to equation (III), denoting concentrations by square brackets and neglecting activity coefficients,

$$\text{(VI)} \quad K_{b1} = \frac{[\text{FeI}^+][\text{OH}^-]}{[\text{Fe(OH)I}]}$$

Since  $(\text{OH})^- = K_w/(\text{H})$ , where  $K_w$  is the ion product of water, equation (VI) may be written:

$$\text{(VII)} \quad \frac{K_w}{K_{b1}} = \frac{[\text{Fe(OH)I}][\text{H}^+]}{[\text{FeI}^+]}$$

Upon making the simplifying assumptions that the salt and acid are completely ionized, letting  $v$  be the molar dilution of salt and  $z$  be the fraction hydrolyzed, then:

$$[\text{FeI}^+] = 1 - z/v; \quad [\text{H}^+] = [\text{Fe(OH)I}] = z/v$$

whence<sup>2</sup> we have from equation (VII),

<sup>1</sup> Similar expressions for salts containing multivalent ions were developed by Denham (8).

<sup>2</sup> This expression is true only if we neglect the hydrogen-ion concentration of the water used. The latter, however, is small compared with that furnished by the hydrolysis of the salt. Such an assumption is usually made in cases of this kind.

$$(VIII) \quad \frac{K_w}{K_{b1}} = \frac{z^2}{v(1-z)} = K_1$$

If, on the other hand, we treat equation (II) similarly, we have, using identical nomenclature,

$$(IX) \quad \frac{K_w^2}{K_{b1}} = \frac{[\text{Fe}(\text{OH})_2] [\text{H}^+]^2}{[\text{Fe}^{++}]}$$

In this case, however,

$$[\text{Fe}^{++}] = 1 - z/v; \quad [\text{Fe}(\text{OH})_2] = z/v; \quad [\text{H}^+] = 2z/v$$

and, substituting these values in equation (IX),

$$(X) \quad \frac{K_w^2}{K_{b1}} = \frac{4z^3}{v^2(1-z)} = K_2$$

Thus, since  $K_w$  may be taken as approximately  $1 \times 10^{-14}$ ,  $[\text{H}^+]$  can be determined experimentally and  $v$  is known, it is possible to calculate definite values for  $z$ ,  $K_1$  and  $K_2$ . A constant set of values for  $K_1$  is taken as evidence of the applicability of equation (VIII) and similar values for  $K_2$  indicate that equation (X) may be applied.

A solution of ferrous iodide was prepared in an atmosphere of hydrogen, using Reagent grade chemicals and recently boiled, distilled water. One-half of this solution was allowed to stand until  $p_{\text{H}}$  3.2 was attained; the other was immediately treated. Both solutions were subjected to a series of dilutions, the  $p_{\text{H}}$  values being determined at each dilution and the values of  $z$ ,  $K_1$  and  $K_2$  calculated in each case. These data follow in Tables I and II wherein the column 100  $z$  refers to the degree of hydrolysis on the basis  $z = v [\text{H}^+]$ , since equation (VIII) was found applicable.

TABLE I.—DEGREE OF HYDROLYSIS OF AQUEOUS SOLUTIONS OF FERROUS IODIDE.

Conc. Mols/L.	Freshly Prepared Solution.					
	$v$ .	$p_{\text{H}}$ .	$[\text{H}^+]$ .	100 $z$ .	$K_1 \times 10^7$ .	$K_2 \times 10^7$ .
0.235000	4.255	4.20	$6.31 \times 10^{-6}$	0.027	0.17	0.53
0.117500	8.511	4.35	$4.47 \times 10^{-6}$	0.038	0.17	0.38
0.058750	17.022	4.70	$2.00 \times 10^{-6}$	0.034	0.07	0.07
0.029375	34.044	4.95	$1.12 \times 10^{-6}$	0.038	0.04	0.02
0.014688	68.088	5.05	$8.91 \times 10^{-6}$	0.061	0.05	0.02
0.007344	136.176	5.15	$7.08 \times 10^{-6}$	0.096	0.07	0.02
0.003672	272.352	5.20	$6.31 \times 10^{-6}$	0.172	0.11	0.03

TABLE II.—DEGREE OF HYDROLYSIS OF AQUEOUS SOLUTION OF FERROUS IODIDE.

Conc. Mols/L.	Solution Allowed to Stand until Equilibrium at $p_{\text{H}}$ 3.2 Reached.					
	$v$ .	$p_{\text{H}}$ .	$[\text{H}^+]$ .	100 $z$ .	$K_1 \times 10^6$ .	$K_2 \times 10^{11}$ .
0.23600	4.238	3.15	$7.08 \times 10^{-4}$	0.30	2.12	75.23
0.11800	8.476	3.55	$2.82 \times 10^{-4}$	0.24	0.67	9.49
0.05900	16.952	3.80	$1.59 \times 10^{-4}$	0.27	0.43	3.38
0.02950	33.904	4.05	$8.91 \times 10^{-5}$	0.30	0.26	1.20
0.01475	67.808	4.30	$5.02 \times 10^{-5}$	0.34	0.17	0.43
0.00738	135.616	4.40	$3.98 \times 10^{-5}$	0.54	0.21	0.42

(To be continued.)