STABILITY OF SYRUP OF FERROUS IODIDE.*

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Preservation of Syrup of Ferrous Iodide is a problem which has been given considerable attention for many years and still gives evidence that it has not been successfully solved in the present U. S. P. X formula.

The earliest efforts at preservation of a Ferrous Iodide preparation were based on use of sufficient sugar as a preservative, hence the preparation of a syrup of Ferrous Iodide, the theory held being based on knowledge that saccharin solutions retard oxidation, and it is and has been held that oxidation is the cause of color change from light green to yellow, through amber to a dark brown.

In order to test out the theory that oxidation was the cause of darkening, a lot of U. S. P. X Syrup of Ferrous Iodide was prepared, using boiled distilled water, and further sub-divided in 2-oz. flint bottles, same being completely filled to exclude oxygen.

One-half of these completely filled bottles were evacuated by aid of a vacuum pump and the vacuum broken by means of nitrogen, and securely stoppered. The two sets of syrup so prepared were then stored under varying temperature conditions, room temperature and in a refrigerator (about 50° F.).

After a period of three months all the samples stored at room temperature showed decided darkening, even though oxygen had been removed from the product, whereas the set stored at ice-box temperature had maintained a light green color, but caused crystallization of sugar in the product.

An examination of the set stored in the refrigerator at the end of nine months showed slight discoloration; these samples were tested for free iodine, but none was found, hence it would seem the discoloration of the syrup of Ferrous Iodide may be due to caramelization.

Hypophosphorous acid has been used in preparation of Syrup of Ferrous Iodide throughout a number of revisions, and on the theory that its action on the sugar may cause discoloration, as a result of caramelization, two further series of comparative products were prepared.

A.—Strictly U. S. P. X product (with hypophosphorous acid).

B.—U. S. P. X product, except 3 Gm. of citric acid per 1000 cc. were substituted for the hypophosphorous acid.

The two above sets of samples were packaged in flint bottles which were then placed in card board containers and stored at room temperature in a laboratory cabinet in order that light influence might be avoided.

These two sets of samples have at this time been under observation for a period of four months and show that a definite change has taken place in the strictly U. S. P. X product, whereas the product prepared with citric acid is the characteristic light green of freshly prepared Syrup of Ferrous Iodide. A test applied to a sample of the U. S. P. X product gives no reaction for free iodine, indicating that darkening is not due to liberation of this element.

In a paper by John C. Krantz, Jr.[1] entitled: "A Study of the Relative Pre-

* Section on Practical Pharmacy and Dispensing, A. PH. A., Portland meeting, 1929.

[1] JOUR. A. PH. A., 12 (1923), 963.

servative Values of Glycerin and Sugar Solutions in Certain Official Preparations," the author cites an examination of Syrup of Ferrous Iodide in which Dilute Hypophosphorous Acid was used, that within ten days 94.2% of the sucrose showed inversion.

In the series of articles which have appeared in the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, during the past year by Braford and Langenhan[1] it is brought out in several instances that citric acid has been advocated at various times as a preservative for Syrup of Ferrous Iodide.

In the above-named article it is also pointed out that the pharmacopœias of Holland, Austria, Switzerland, Belgium and Hungary all prescribe the use of citric acid.

Some years ago Syrup of Ferrous Iodide, using citric acid instead of hypophosphorous acid, was successfully prepared in Squibb Laboratories, and experiments herein enumerated seem to point to the fact that greater stability of Syrup of Ferrous Iodide may be obtained through the use of citric acid instead of hypophosphorous acid, which seems to be a decided factor in discoloration of the preparation, and that the generally accepted theory, that darkening is due to oxidation is in reality a caramelization of the sugar.

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PHYSOSTIGMINE PHARMACOLOGY.

Contribution to the analysis of the action of physostigmine in warm-blooded animals. Zucker–Proc. German Pharm. Soc., Sept. 12, 1928; *Arch. exptl. Path. Pharmakol.*, 138 (1928), 139; through *Squibb Abstract Bulletin*, Feb. 6.

The results of the former and recent investigations with physostigmine in various animals and in neurological cases point to the misunderstood poisonous action of this drug, whose point of attack is supposed to manifest itself in the form of a purely muscular action. The author found the muscle reaction in only 1 out of 4 animals; nor was it evident in animals with infundibulum injury, indicating that the expected metabolic changes would have taken place were it not for the presence of the drug. Calcium injection obviated the muscle reaction to physostigmine, except for the increased irritation; with magnesium, the reaction appeared immediately. Rabbits subjected to 33° C. did not respond to the drug muscularly until after warming. Hydrocyanic acid which as physostigmine, increases the lactic acid content of the muscles, produced with an inferior dose of physostigmine, a definite but premature muscle reaction which disappeared as prematurely. The fibrillation spasms and tonic phenomena after nerve incision were still evident several days after the administration of the drug in carnivora; they decreased in rabbits and guinea-pigs after the 4th day; in birds, immediately after the injection. With serious spinal cord incisions, the muscle manifestations disappeared at the latest on the 5th day. It is believed that a relation exists between the physostigmine action and the increased lactic acid value in the muscles. As for the interpretation of the muscle reaction of physostigmine poisoning, the author gives evidence to the support of the hypothesis that the reaction is not due directly to the poisonous effect of the drug but, indirectly, to the changes in metabolism. For example, the muscle response appears 20–22 minutes after the administration of the drug. Already in 10–13 minutes the animal shows not only excitation but the effects of light percussion and severe convulsions and rigidity; yet when the muscle is examined kymographically at this time there is scarcely anything of significance to be noted.—J. P.

[1] JOUR. A. PH. A., 16 (1927), 561.