

Section on Practical Pharmacy and Dispensing

Papers Presented at the Fifty-Ninth Convention

THE COLOR OF TINCTURE OF IRON CITRO-CHLORIDE.

OTTO RAUBENHEIMER.

The writer does not wish to go into the chemical composition of iron citro-chloride, which has already been done by Prof. A. B. Stevens at the New York City meeting of the A. Ph. A. in 1907 (Proc. Vol. 55, p. 153), and again lately before the American Chemical Society.

Suffice it to state that the "tasteless tincture of iron" was introduced by Mr. J. L. J. Creuse, a Brooklyn pharmacist, in 1873, and after his death was manufactured for the widow by one of our members, Mr. J. D. Aug. Hartz, of College Point. Mr. Edw. Klein, the present owner of the Hartz pharmacy, was good enough to send me a sample of the Creuse preparation, prepared July 17, 1904, herewith submitted. I am also informed that Mrs. Creuse has discontinued supplying the market.

The color of tincture of iron citro-chloride (and this is the subject of my paper) is by no means uniform, as can be readily seen by the array of samples. As this tincture is mostly used in the preparation of elixir of iron, quinine and strychnine N. F., the very popular I. Q. & S., and as the beautiful green color of this elixir depends upon the color of the tincture, it is therefore a necessity to look into the cause of the variation. The N. Y. and Brooklyn Formulary ordered, for one pint of the finished product, 2100 grains of citric acid to be dissolved in boiling water, and 2270 grains of sodium bicarbonate to be gradually added, and when effervescence has ceased, 4 fluidounces of solution of iron chloride to be added. When cool sufficient water is added to make 12 fluidounces, and finally 4 fluidounces of alcohol.

In calculating the quantities, I find that sodium bicarbonate is deficient in this formula, as it takes 2534 grains (instead of 2270 grains) to form 3554 grains of U. S. P. sodium citrate. Perhaps this may have been intentional in order to have an excess of citric acid in the finished preparation.

In the N. F. I., 1888, the formula was changed by dissolving 7 troy ounces of sodium citrate with the aid of a gentle heat in a mixture of solution of iron chloride and water. The quantity of sodium citrate in this formula is only 3360 grains, quite a reduction from the theoretical 3554 grains. In the N. F. II, 1896, practically the same formula appears in the metric system; namely, 460 Gm. sodium citrate for 250 Cc. solution of iron chloride for 1000 Cc. finished tincture. However, the quantity of sodium citrate was again reduced to 410 Gm. in the later copies of the N. F. II. As the U. S. P. VIII decreased the strength of the

solution of iron chloride from 37.8 per cent. of crystallized ferric chloride to 29 per cent., consequently N. F. III, 1906, orders 350 Cc. of the solution representing the same strength as the 250 Cc. of the second edition.

The quantity of sodium citrate ordered by N. F. III is 410 Gms., which, however, has been increased to 425 Gm. in the Errata of March 15, 1907.

I will also mention that with all these changes, the strength of the "tasteless tincture of iron" has remained the same; namely 4 Cc. containing the equivalent of 0.5 Gm. of anhydrous ferric chloride.

When a formula is changed or modified in any edition of our standards as U. S. P. and N. F., then it proves beyond doubt that it does not produce a satisfactory preparation. And such is the case in tincture of iron citro-chloride. The submitted samples have been procured from retail pharmacists, from wholesale druggists, and also include some of my experiments. In order to facilitate comparison I have put them in bottles of the same size and shape. As can be readily seen, the color of this tincture ranges from a light or bright green to an apple green, to an olive green, a brownish and reddish green to a yellowish brown.

What is the cause of this great color variation? In order to determine it, and in order to get a uniform preparation, the writer has experimented for several years. The literature on this subject is very meagre indeed, as the books have nothing to say on it, and even that excellent "Digest of Comments on U. S. P. and N. F." does not mention "Tinctura Ferri Citro-chloridi" so far.

Dr. E. H. Squibb (Bullet. A. Ph. A., Sept., 1908, p. 280), recommends that the 425 Gm. of sodium citrate in the N. F. formula be replaced by 390 Gm. of potassium citrate, which will prevent the crystallization commonly complained of in making elixir of iron, quinine and strychnine. In answer to this criticism, I beg to state that during my own experience of manufacturing several hundred gallons of elixir I. Q. & S., and according to the experience of a number of other pharmacists, we have never had any precipitation in this elixir. Nevertheless, from the standpoint of economics, the substitution of potassium in place of sodium citrate should be considered as (1) it is about two cents per pound lower in price; (2) it requires about 10 per cent. less, because on account of containing only one molecule H_2O , its molecular weight is 322.08, while sodium citrate contains $5\frac{1}{2}$ molecules of H_2O , and has a molecular weight of 354.6.

In my experience it is immaterial, regarding the color of the tincture, if the potassium or the sodium salt is used, as frequently, in fact mostly, the desired apple green color is not obtained. Even by following the formula and using the chemicals of the very manufacturer who suggested potassium citrate, I failed to obtain in the proper color. During my many years of experiments I have also tried the following modifications of the N. F. formula:

1. Increase in quantity of sodium or potassium citrate, by taking from 10 to 50 Gms. more.
2. Instead of dissolving the citrate in the iron solution "by the aid of a gentle heat", as stated in the N. F., I have employed a higher heat up to boiling point.

While these two modifications will *sometimes* help to develop the apple green color, I came to the conclusion that the fault does not lay in the sodium citrate, which is a stable and uniform chemical, but in the solution of iron chloride.

The U. S. P. requirements are that Liquor Ferri Chloridi should contain 29

per cent. anhydrous FeCl_3 , corresponding to about 10 per cent. metallic iron, and furthermore, that nitric acid, which is used in the oxidation process, should be absent. In my experience, the solution also differs greatly as to its acidity; i. e., its excess of hydrochloric acid, of which a little is needed to prevent the formation of a basic or oxychloride.

From experiments which extended through several years, I found that when the acid solution of ferric chloride is partly neutralized, either before or after the addition of sodium or potassium citrate, then the beautiful apple green color will be developed.

My modus operandi is as follows: Heat the diluted solution of ferric chloride, and dissolve therein the sodium or potassium citrate. In case the apple green color is not brought out, then gradually add a little sodium bicarbonate, and heat to expel CO_2 before adding more, until the desired shade of green is obtained. When cool, add a sufficient quantity of water, and lastly, the alcohol. According to my experiments, from 15 to 25 Gm. NaHCO_3 are required for 350 Cc. solution of ferric chloride, or 1000 Cc. finished tincture.

Besides sodium bicarbonate, the carbonate or also potassium carbonate can be used with the same results. The iron in this preparation is in the ferric state, presumably as a double salt of iron and sodium citrate.

Care must be taken not to add too much alkali or an olive green color is developed. By the addition of still more alkali the green color will disappear entirely, and when neutral, then the preparation has a red color, and is now a ferrous salt instead of being in the ferric state.

In my opinion, our N. F. should recommend the addition of a sufficient quantity of NaHCO_3 to bring out the apple green color. It might also substitute 390 Gm. of potassium citrate in place of 425 Gm. sodium citrate. The N. F. IV might also give a short description as to color, taste and reaction, also tests for the absence of ferrous salt, and last, but not least, a statement of keeping this tincture in amber bottles protected from light which, as it is well known, will reduce iron preparations from the ferric to the ferrous state.

DISCUSSION.

A. B. STEVENS: "Mr. Raubenheimer has called your attention to the fact that in order to obtain the apple green on the addition of the citrate to the tincture of chloride of iron it is necessary to neutralize the mixture with sodium carbonate, but should you add too much sodium carbonate you will obtain a brown color. The neutral citro compound is green and does not respond to ordinary tests for iron, either ferrous or ferric, but on the addition of a few drops of acid it gives the characteristic tests for iron in the ferric condition. The first addition of the carbonate simply combines with the free acid in the tincture. Upon further addition of sodium carbonate ferric hydroxide is formed which redissolves in the chloride present. The depth of color depending upon the amount of hydroxide formed.

"The green solution may be separated into a crystallizable and a non-crystallizable substance. By adding alcohol to a concentrated solution of the citro compound you obtain a precipitate which may be washed with alcohol until free from chloride, but this is very tedious. A better method is to add alcohol to the concentrated solution until a permanent cloudiness appears, then pour this mixture into strong alcohol. In a short time, what at first appears to be a precipitate separates in the form of a dark green, thick liquid. Pour off the alcohol and add sufficient water to make the solution thin enough to pour easily, and again pour into strong alcohol, stirring constantly. If this operation is repeated several times the precipitate becomes a thick plastic mass, free from chloride. If this is covered with alcohol and left for

a few hours it assumes a solid amorphous mass, which, on removal of the alcohol and drying may be easily powdered. The powder is strongly acid and consists of iron, potassium and citric acid. The molecular formula has not yet been determined, but from the character of similar compounds I presume we will find that the iron has replaced the hydrogen of the citric acid radicle.

"If the alcohol, from the precipitation of the citro compound, be distilled or evaporated to dryness potassium chloride may be obtained. These experiments prove that the compounds which we have called citro-chloride and citro-iodide of iron are not true to name but are potassium iron citrates.

"Syrup of citro-iodide of iron manufactured strictly according to the National Formulary will always be brown, due to the presence of free iodine. It has been recommended to decrease the last portion of iodine or increase the first portion. This would give an excess of ferrous iodide, which would be objectionable, as it would soon oxidize and the syrup become brown. A better method would be to follow the formula and then remove the excess of iodine by shaking with starch and filtering."

MR. FORD: "The quality of sodium citrate on the market is not uniform as found in the Middle States. The quality of ordinary sodium bicarbonate is also quite different from the U. S. P. substance, and in the preparation of Tincture of Iron Citro-Chloride it is important to use the official article.

"I have always had good success using potassium citrate, as in the original Creuse formula, and believe that failure in the process is commonly due to the use of an inferior quality of alkali salts."

MR. RAUBENHEIMER: "Prof. Stevens' process for making Syrup of Iron Citro-Iodide by removing excess of iodine with starch, has been accepted for the new edition of the National Formulary.

"In developing the green color of citro-chloride tincture only a small quantity of the alkali should be added at a time, and the liquid should be heated to the boiling point, if necessary, to expel CO_2 and develop the desired apple green color. In the specimens submitted it required from 10 to 30 grams to develop that color. Experiments made together with Dr. Francis prove that by further addition of NaHCO_3 the green color is destroyed. As soon as the preparation is neutral a brown color will develop in the tincture. The iron is not detectable in these citro preparations unless they are first acidified with a mineral acid."

THINKING IN MONEY.

"There are some people that think so much of money for its own sake that they have learned to think only in the terms of finance and to talk only in the language of the counting house. They have no ear for any music except the clicking of the cash register. They can see nothing in all that God has created that is worth while, except as it may be converted into some marketable product.

"There are men who would gather up the rays of the sun and the glitter of the stars and coin them into gold. There are men who would convert the Mammoth Cave into a subway, the Natural Bridge into a toll-gate; that would plow up our parks and plant them in corn and potatoes; that would sell the Statue of Liberty and Bunker Hill for Marconi receiving stations; they would lease the Washington Monument for a billboard and stretch the equator in the back yard for a clothes line; but there are some men who earn their money, who get it honestly, who appreciate it because of the opportunity that it gives to serve themselves and their fellow men.—*Charles F. Moore*, Editor of "Paper."