AN ASSAY FOR ELIXIR OF IRON, QUININE AND STRYCHNINE, N. F.*

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It is the purpose of this paper to describe a method of assay for iron, quinine and strychnine in the elixir of iron, quinine and strychnine now official in the National Formulary. The facts that this preparation is one of the most generally used pharmaceuticals and that many samples examined by pure food and drug officials have indicated fraudulent quantities of active ingredients, make this assay one of importance to pharmacists.

THEORETICAL CONSIDERATIONS.

The estimation of the iron present in the elixir is the first problem to be considered. The iron in this preparation is present in the form of ferric chloride and ferric citrate, which are probably combined in the form of a double salt. If the elixir is evaporated to dryness and the residue ignited the organic matter present is readily oxidized, leaving a residue of ferric oxide and sodium carbonate. When this residue is dissolved in hydrochloric acid the solution contains ferric and sodium chlorides. Since ferric chloride liberates iodine from potassium iodide, the amount of iron present can be titrated with sodium thiosulphate solution in terms of liberated iodine. The quantity of iron present in a standard elixir may be seen by the following calculations:

$350 \text{ cc} \times 1.3 \times 0.105 = 47.775$ Gm. Fe in L. of Tr. fer. citro-chlor.

$\frac{125 \text{ cc} \times 47.775}{10{,}000} = 0.5971875$ Gm. Fe in 100 cc of elixir.

350 cc = the amount of ferric chloride solution used in L. of Tr. ferric citro-chloride.
1.3 = specific gravity of ferric chloride solution.
10.5% = the percentage of iron represented in ferric chloride solution.
125 cc = the amount of tincture of ferric citro-chloride used in a liter of the elixir.

The Pharmacopœia allows one per cent. variation in solution of ferric chloride, so the amount of iron present is obtained by substituting the percentage of iron present for 10.5% in the above formula. Thus if the sample of ferric chloride solution assays 11%, the quantity of iron in 100 cc of the elixir would be raised to 0.625625 Gm. If the percentage of iron were 10% the corresponding quantity of iron in the elixir would be 0.56875 Gm.

The next determination of the assay is that for total alkaloids. The quinine is present as hydrochloride and the strychnine as sulphate, so when the elixir is made alkaline with ammonia the liberated alkaloids are precipitated along with ferric hydroxide. The alkaloids can be obtained in a free state by several extractions with chloroform. When 100 cc of the elixir is used for analysis, the following calculations show the weight of the total alkaloids in an uncombined state:

$\frac{324.26 \times 0.875}{396.71} = 0.71505$ Gm. anhydrous quinine from 100 cc.

324.21 = molecular weight of anhydrous quinine.
296.71 = molecular weight of quinine hydrochloride.
0.875 = Gm. quinine hydrochloride used in 100 cc of elixir.

$\frac{668.4 \times 0.0175}{856.56} = 0.0136$ Gm. strychnine from 100 cc.

668.4 = twice molecular weight of strychnine.

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856.56 = molecular weight of crystallized strychnine sulphate.
0.0175 Gm. = strychnine sulphate used in 100 cc of the elixir.
0.71505 Gm. quinine
0.01360 Gm. strychnine
0.72865 Gm. = weight of total alkaloids from 100 cc of elixir.

The separation of quinine from strychnine is the next problem. In this attempt the old oxalate and dichromate methods were not tried because of the generally admitted inaccuracy of the methods. The first method employed had for its purpose the precipitation of the sulphuric acid in combination with strychnine as barium sulphate and the weighing of the latter. The difficulty of this method lies in the small amount of strychnine sulphate present and the relative difference in the molecular weights of strychnine sulphate and barium sulphate. Thus, 0.035 Gm. of the alkaloid sulphate yields only 0.0095 Gm. of barium sulphate. On account of the small weight of the precipitate the writer was unable to obtain concordant results by this method.

In consideration of the solubilities of quinine hydrochloride and strychnine sulphate in chloroform an attempt was made to extract the quinine salt with chloroform and leave the strychnine sulphate in the elixir to be estimated as free alkaloids. The results of these extractions showed that the quinine hydrochloride could not be totally extracted from the elixir medium with chloroform.

The final and successful method of separation depends upon the decomposition of strychnine with concentrated hydrochloric acid and diluted nitric acid, whereas quinine under the same conditions is not affected. If both alkaloids are extracted in a free state and weighed, then treated with hydrochloric and diluted nitric acids, the strychnine loses its alkaloidal state and is not precipitated upon the addition of ammonia water, whereas the quinine is precipitated and may be conveniently extracted with ether and weighed. The difference in weight represents strychnine as free alkaloid. The purpose of making the second extraction with ether is to prevent the dissolving of any strychnine that may not have been decomposed by the above treatment.

EXPERIMENTAL.

(1) *Iron.*—Transfer 10 cc of the elixir accurately measured into a 15–20 cc platinum or silica crucible and carefully evaporate to dryness. Tilt crucible and ignite until all the carbonaceous matter has been dissipated. Dissolve the residue in 10 cc of concentrated HCl, using 2 cc for each washing and diluting the HCl well before transferring to a filter. Wash crucible and filter until a drop of the washings does not react with potassium ferrocyanide, then add 2 Gm. of potassium iodide to the ferric chloride solution. Transfer to a tightly stoppered flask and heat to 40° C. for 30 minutes.

Add 100 cc of water and titrate the liberated iodine with $N/10$ $Na_2S_2O_3$ V. S., starch paste indicator. Each cc of $N/10$ $Na_2S_2O_3$ V. S. used corresponds to 0.005584 Gm. Fe.

Grams Fe present in 100 cc of elixir	0.5971
Determination I showed.....	0.5913 Gm.
Determination II showed.....	0.5930 Gm.

(2) *Total Alkaloids.*—Evaporate 100 cc of the elixir accurately measured to 75 cc on a water-bath. Transfer to a separator, rinse container with enough

distilled water to make the volume of the elixir about 100 cc. Make the elixir decidedly alkaline to litmus with ammonia water; extract the alkaloids with four portions of chloroform (20, 15, 10, 10) and evaporate the combined chloroform extractions to dryness on a water-bath. Dry the residue to a constant weight at 125° C. and weigh the strychnine sulphate and quinine hydrochloride from 100 cc of the elixir as free alkaloids.

Grams calculated to be present.....	0.72865
Determination I showed.....	0.7290 Gm.
Determination II showed.....	0.7289 Gm.
Determination III showed.....	0.7295 Gm.

(3) *Separation of Quinine from Strychnine.*—Dissolve residue in 5 cc to 7 cc of concentrated HCl with the aid of gentle heat. Add 3 cc of dilute nitric acid (1 cc concentrated HNO_3 and 19 cc water); heat until the solution becomes dark orange to red. Dilute with 75 cc water, transfer to a separator and slowly make the mixture alkaline to litmus with dilute ammonia water. Extract the precipitated quinine with four portions of ether (20, 15, 10, 10) and evaporate the combined ether extractions to dryness on a water-bath. If any of the quinine should remain clinging to the sides of the separator in an apparently insoluble form, it may be dissolved in a little dilute acid, precipitated with ammonia and extracted with ether; the ether extraction is added to the other ethereal extractions. Dry the residue to a constant weight at 125° C. and weigh as anhydrous quinine The difference between the above weighing and this weighing is equivalent to the amount of alkaloidal strychnine present.

The following factors convert the weights of the anhydrous alkaloids into terms of the crystallized sulphate and hydrochloride, respectively.

$$\text{Quinine } \frac{396.71}{324.26} = 1.223 \text{ factor}$$

$$\text{Strychnine } \frac{856.56}{668.4} = 1.28 \text{ factor}$$

The following results were obtained:

Quinine hydrochloride in 100 cc

Determination I showed.....	0.8720 Gm.
Determination II showed.....	0.8771 Gm.
Determination III showed.....	0.8762 Gm.
Determination IV showed.....	0.8757 Gm.

Strychnine sulphate in 100 cc

Determination I showed.....	0.0193 Gm.
Determination II showed.....	0.0170 Gm.
Determination III showed.....	0.0170 Gm.
Determination IV showed.....	0.0175 Gm.

The experiments carried out in this laboratory indicate that the above method of assay for elixir of iron, quinine and strychnine is practicable, simple in procedure and yields results sufficiently accurate for a determination of this type.

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