

surrounding tissues. Bands of bast fibers together with parenchyma and sieve elements occur between the lines of ray cells. Large thin-walled cells possibly concerned with the secretion of the aromatic constituent also occur in this part of the bark.

The most striking element in the powder is the fibrous tissue, and the fibers occur singly, are non-porous, non-striated and with a slightly roughened outer wall. The fibers are very long and measurements show many reaching one millimeter in length. The stone cells usually occur in groups and are yellowish in color. The individual stone cells are angled to irregular in form and are porous. Both thick- and thin-walled types occur although the former predominate. The cork and parenchymatic tissues are of types usual in barks and are not especially characteristic. The starch occurs in single and compound grains up to three, the single grains ranging between 5 and 10 microns. The crystals are small, narrow prisms not exceeding 15 microns in length and about one-third as broad. The powder is a dull brown color.

PHARMACOGNOSY LABORATORY,  
COLLEGE OF PHARMACY,  
COLUMBIA UNIVERSITY.

---

#### MISCELLANEOUS CHEMICAL PAPERS.\*

##### THE ACTION OF LIGHT ON SOLUBLE FERRIC PHOSPHATE.

BY N. R. MUELLER.†

The action of light on so-called Soluble Ferric Phosphate of the U. S. Pharmacopoeia (1900) and on the preparations into which it enters, has given rise to a number of disturbances that interfere more or less seriously with prescription practice. One of the most unsatisfactory classes of preparations in this respect are the elixirs into which this and similar compounds enter. Because of the unsatisfactory character of these, the Elixir of the Phosphates of Iron, Quinine and Strychnine was prepared a year ago<sup>1</sup> according to a number of formulas. Practically all of the formulas employed were modifications of an original formula, suggested for the purpose of overcoming the unsatisfactory character of the elixir when made according to the original formula. Nevertheless, practically all of the elixirs thus prepared, which differed more or less from each other, agreed in this particular that they were alike unsatisfactory, especially when exposed to light.

Inasmuch as the complexity of the elixir precludes the proper diagnosis of the case, it seemed fruitless to continue the study of improvement along the empirical lines heretofore pursued. It seemed much more rational to ascertain which ingredient or which combination of ingredients is affected by light. Leaving out the sugar and alcohol for the present, the first series of preliminary tests was made with aqueous solutions of soluble ferric phosphate. In the second series of preliminary

---

\* From the laboratory of Edward Kremers.

† Abstract of thesis submitted for the degree of Bachelor of Science (Pharmacy Course), University of Wisconsin, 1915.

tests various combinations of chemicals that enter into the composition of the soluble ferric phosphate were tried out. The first series of tests revealed that, whatever might be the effect of other ingredients of elixirs of this class, the fundamental difficulty might be looked for in the mixture of compounds known as soluble ferric phosphate. The second series revealed that at least part of the basal difficulties lies in the action of sunlight on citric acid in the presence of ferric iron. In how far the case has been diagnosed by these preliminary experiments will be explained in the following report.

*First Series.*

*Materials.*—Four samples of soluble ferric phosphate were used: one preparation from Merck, one from Squibb, and two preparations made in this laboratory.

1. The commercial preparation of Merck consisted of brittle scales. It was an old preparation and contained 14.26 percent of iron.<sup>2</sup>

2. The commercial preparation of Squibb consisted of thin, bright green, transparent scales. It was more recent and assayed 11.53 percent of iron, whereas the U. S. P. demands 12 percent.

3. This preparation was kept in form of a solution and from it No. 4 was prepared by scaling. Both of these preparations were made from electrolytic iron, the purest iron available. For the preparation of the ferrous sulphate, C. P. sulphuric acid and distilled water were used. The directions given in the U. S. Dispensatory, 9th revision, p. 511, were followed. About 3 Kg. of this pure sulphate were prepared as stock for the experiments hereinafter recorded.

Inasmuch as the U. S. Pharmacopoeia, 8th decennial revision, gives no directions for the preparation of soluble ferric phosphate, those given by W. A. Puckner<sup>3</sup> were followed, with the exception that the ferric sulphate was prepared according to the U. S. P., 8th revision, p. 264. Whereas Puckner suggests the use of potassium chlorate as oxidizing agent, the U. S. P. directs the use of nitric acid. About sixteen hours of heating were required to concentrate the solution of soluble ferric phosphate to the required weight (500 Gm.). A portion of this solution was kept as such, the remainder was scaled, the ratio of the two products being about 2:1. This solution assayed 6.38 percent of iron.

4. As already indicated, this scale preparation was obtained from the above solution (No. 3). Hence it was the most recent of the three scale preparations used. It assayed 10.96 percent of iron, whereas the U. S. P. demands 12 percent.

*Exposure of Solutions of Soluble Ferric Phosphate to Light.*—From the scale materials described (Nos. 1, 2 and 4) five percent aqueous solutions were prepared, of the solution (No. 3) twice the amount was taken in order to obtain a dilution of similar strength. In order to ascertain whether the heat of solution caused a difference in the behavior of the finished solution to light, solution was effected both at room temperature (about 20°) and with a "gentle heat."<sup>4</sup> The following solutions, 100 cc of each, were prepared in triplicate (A, B and C):

- I. Own scale preparation (No. 4) at room temperature.
- II. Own scale preparation (No. 4) with the aid of gentle heat.
- III. Own solution (No. 3) at room temperature.
- IV. Merck's scale preparation (No. 1) at room temperature.
- V. Merck's scale preparation (No. 1) with the aid of "gentle heat."
- VI. Squibb's scale preparation (No. 2) at room temperature.

Of these solutions, 100 cc each were transferred in triplicate to 100-cc glass-stoppered cylinders; one set was exposed to direct sunlight, the second set was exposed to diffused daylight in the same room, and the third set was kept in a dark cupboard, also in the same room. Observations were made every twenty-four hours. The tabulated detailed results may be consulted in the thesis deposited in the university library.

The data recorded in the table referred to reveal that the samples in direct sunlight began to decompose very soon after they were exposed, while the samples in diffused light became slightly darker only after the lapse of several days. The samples in the dark remained quite stable except for a mould which began to grow upon the solution of the soluble ferric phosphate sample about four days after it had been prepared. After about two months moulds also developed upon other solutions kept in the dark, and also upon the solution of soluble ferric phosphate.

As manifestation of decomposition in the samples exposed to sunlight the evolution of a gas was observed. The evolution began almost immediately after the samples were set out, and had completely ceased in about five days. The sample made with Squibb's Soluble Ferric Phosphate (No. VI) and the sample of our own salt made with the aid of heat (No. II) began to throw down a precipitate, while some gas was still being given off. The other samples began to throw down a precipitate about four days after gas had ceased to be evolved. Precipitation began, in most cases, with the formation of a "scum" on the top of the solution. After two weeks' exposure, the decomposition was completed in all but our own samples of salt (No. II) and of the solution made in the cold (No. I). These two samples showed no signs of precipitation after two weeks, but they were completely decomposed at the end of a month.

The color of the precipitate varied from a dark green to a pure white. The upper layer of the white precipitate had a green color. The solutions varied from a light brown, in the case of samples with a dark precipitate, through a milky to a very clear solution in the cases of a light green to white precipitate. Bottles having loosely fitting stoppers had a dark precipitate and a dark solution showing that the action of the air causes a change which presumably is of the nature of an oxidation.

Three samples each of solutions similar to No. II and No. VI were exposed under conditions similar to those of the original samples. The same action and results were observed in these check samples as in their originals.

*Precipitate.*—An endeavor was made to separate the fine white precipitate from sample No. II by means of filtering under a hydrogen cap. As soon as the precipitate was exposed, it turned to a blue-green color. The precipitate was dried in a desiccator filled with hydrogen.

*Gas.*—Three nitrometers were prepared by charging them with a solution of 1 Gm. of scale salt in 15 cc of water. The solutions, made with Nos. 1, 2 and 4, were kept in the nitrometer tube over chloroform. Observations were made twice daily and the results are shown in the following table:

Sample.	No of cc of gas evolved.					No. of cc after 2 months' exposure.	
	No. 1	0.0	0.0	0.0	0.05	0.05	0.10
No. 2	0.0	0.7	3.4	4.2	4.4	4.4	50+ (capacity of tube, 50 cc)
No. 4	0.0	0.6	1.9	2.8	3.0	3.5	2.93

It will be noticed that the fresh salts (Nos. 2 and 4) began to evolve large amounts of gas very soon after exposure, while the old sample (No. 1) did not evolve much gas, even after the lapse of several months.

The gas from another set of nitrometers was collected in an aspirator bottle. A few cc of the gas passed into freshly prepared lime water, gave a decided cloudiness, indicating the presence of a large amount of carbon dioxide. Other gases may be present but have not been identified.

Pure citric acid solutions 5 Gm. in 100 cc placed in nitrometers in direct sunlight did not decompose or evolve gas, although they were exposed for several months.

*Solubility of Ferric Hydroxide in the Three Sodium Ortho-phosphates.*—Three tests were made using ferric hydroxide (0.6 Gm.) and a different sodium ortho-phosphate, mono-, di-, and tri- (2 Gm.), in each case. The proportions were the same as in the scale salt. Enough water to make 100 cc was added.

After standing a day at room temperature, the excess of ferric hydroxide was filtered off, and the filtrate, which was clear and colorless, was tested for iron with potassium sulphocyanate T. S., hydrogen sulphide T. S., hydrogen sulphide gas, potassium ferrocyanide T. S.

No test for iron was given by any of the reagents in any of the samples.

From these tests it may be concluded that no iron is present in the solutions, and that none of the three sodium ortho-phosphates have any solvent or combining action with the ferric hydroxide in an aqueous medium at room temperature.

*The Action of Sunlight upon Several Different Solutions.*—The following solutions and partial solutions or mixtures were prepared and held over chloroform to 50 cc nitrometers.

- I.  $\text{Fe}(\text{OH})_3$ , from 1.56 Gm.  $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$  [0.6 Gm.  $\text{Fe}(\text{OH})_3$ ].
- II. Citric acid,  $\text{C}_6\text{H}_8\text{O}_7 \cdot \text{H}_2\text{O}$ , 1.2 Gm.
- III.  $\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$ , 2.0 Gm.
- IV.  $\text{Fe}(\text{OH})_3$ , 0.6 Gm.;  $\text{C}_6\text{H}_8\text{O}_7 \cdot \text{H}_2\text{O}$ , 1.2 gm.
- V.  $\text{Fe}(\text{OH})_3$ , 0.6 Gm.;  $\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$ , 2.0 Gm.
- VI.  $\text{C}_6\text{H}_8\text{O}_7 \cdot \text{H}_2\text{O}$ , 1.2 Gm.;  $\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$ , 2.0 Gm.
- VII.  $\text{Fe}(\text{OH})_3$ , 0.6 Gm.;  $\text{C}_6\text{H}_8\text{O}_7 \cdot \text{H}_2\text{O}$ , 1.2 Gm.;  $\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$ , 2.0 Gm.

In each case enough water was used to make 100 cc of solution or mixture.

The gasometers were charged with 25 cc of the above solutions or mixtures, and were then exposed to sunlight in a south window of the laboratory. Readings were taken every day.

For the details the original thesis may be consulted.

There appeared to be no change and no gas was evolved in the following experiments:

- I.  $\text{Fe}(\text{OH})_3$ , 0.15 Gm., in 25 cc water.
- II.  $\text{C}_7\text{H}_8\text{O}_6 \cdot \text{H}_2\text{O}$ , 0.3 Gm., in 25 cc water.
- III.  $\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$ , 0.5 Gm., in 25 cc water.
- V.  $\text{Fe}(\text{OH})_3$ , 0.15 Gm., and  $\text{Na}_2\text{HPO}_4$ , 0.5 Gm., in 25 cc water.
- VI.  $\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$ , 0.5 Gm., and  $\text{C}_6\text{H}_8\text{O}_7 \cdot \text{H}_2\text{O}$ , 0.3 Gm., in 25 cc water.

A decided change and decomposition took place in experiments Nos. IV and VII.

- IV.  $\text{Fe}(\text{OH})_3$ , 0.15 Gm., and  $\text{C}_6\text{H}_8\text{O}_7 \cdot \text{H}_2\text{O}$ , 0.3 Gm., in 25 cc water.

Evolution of gas began 24 hours after the nitrometer had been exposed to sunlight. The rate of evolution was proportional to the intensity of the light; that is, on cloudy and dark days, gas evolution almost ceased, while on bright sunny days gas evolution was almost continuous. After 10 days' exposure, about 24 cc of gas had been collected, and at this point the reaction appeared to be completed, since at the end of 22 days there were still only about 24 cc of gas, but this was a period of very little sunshine, which may account for the constancy of the volume of gas. After exposure for 22 days another evolution of gas took place, but was accompanied by an accident resulting in the loss of the experiment. During the first few days of the exposure the solution was almost colorless, and the precipitate had a brown color. After several weeks' exposure the solution had a greenish yellow color and the precipitate seemed to be partially changed to perhaps reduced iron (a black precipitate heavier than chloroform being formed).

VII.  $\text{Fe}(\text{OH})_3$ , 0.15 Gm.;  $\text{C}_6\text{H}_8\text{O}_7 \cdot \text{H}_2\text{O}$ , 0.3 Gm.; and  $\text{Na}_2\text{HPO}_4$ , 0.5 Gm., in 25 cc of water.

A partial solution of  $\text{Fe}(\text{OH})_3$  resulted. The color of the solution was a light green. The remainder of the  $\text{Fe}(\text{OH})_3$  went to the bottom as a precipitate and a day or two later several green layers of varying intensity were formed at the bottom of the solution. The evolution of gas began about 24 hours after exposure to sunlight. The evolution of gas again appeared to be proportional to the intensity of the light. At the end of 10 days about 8.3 cc of gas had been formed. Then ensued about a week of cloudy weather with very little sunlight, and it was found that the volume of the gas in the top of the gasometer remained constant. At the end of 20 days there were about 8.5 cc of gas, and the decomposition and evolution of gas was apparently complete. At the end of 30 days there were 14 cc of gas in the nitrometer, but this last increase in volume may have been due to the decomposition of the chloroform. Mercurous chloride again appeared to have been formed with the mercury in the trap as in the case of Experiment IV ( $\text{Fe}(\text{OH})_3$  and citric acid). The solution was practically colorless, and the precipitate had a light brown color.

In comparing the amount of gas evolved in Experiment IV and in Experiment VII, it will be seen that there was about  $\frac{1}{3}$  as much evolved in VII as in IV, although the amounts of the ingredients were the same except that  $\text{Na}_2\text{HPO}_4$  (0.5 Gm.) was added in Experiment VII. A conclusion can naturally be drawn, that the presence of  $\text{Na}_2\text{HPO}_4$  retards the decomposition and the evolution of gas.

EXPOSURE OF A SOLUTION (OR MIXTURE) OF CITRIC ACID AND FERRIC HYDROXIDE TO SUNLIGHT.

This experiment was a check on No. IV. The solution was held in the nitrometer over chloroform which was displaced through a mercury trap, as the gas was formed. Two nitrometers were charged with ferric hydroxide 0.15 Gm., citric acid 0.3 Gm. and water sufficient to make 25 cc.

Table showing amount of gas in cc evolved:

	12/14/14.	12/15/14.	12/16/14.	12/17/14.	1/11/15.
I.	0.0	2.0	4.2	7.0	22.3
II.	0.0	1.5	3.0	5.0	20.2

After about one month's exposure there had been 22.3 and 20.2 cc, respectively, of gas evolved in each nitrometer. Variations in temperature caused the gas

formed to contract, and air was admitted through the mercury trap, therefore the resulting gas volumes are contaminated with some air.

ACTION OF LIGHT UPON AN AQUEOUS SOLUTION OF CITRIC ACID AND FERROUS HYDROXIDE.

The ferrous hydroxide was prepared by treating a ferrous sulphate solution with ammonia water in molecular quantities and washing the resulting precipitate by decantation. The precipitate was protected from the air as much as possible, but some ferric hydroxide was formed. The product was assayed by converting the ferrous hydroxide to ferric chloride and then determining the amount of ferric iron according to the U. S. P. method for ferric chloride. (U. S. P., 8th revision, p. 152.)

Two nitrometers were charged with ferrous hydroxide (0.15 Gm.) and citric acid solution (0.3 Gm. in 25 cc H<sub>2</sub>O) held over chloroform.

A clear light green solution resulted. The nitrometers were exposed to sunlight for about a month, but no gas was formed. The solution became colorless and clear. Apparently there was no decomposition as in the case of ferric hydroxide and citric acid.

REFERENCES.

1. B. Chilson, U. W. thesis, 1914. (Under the direction of Dr. Langenhan.)
2. The iron assay was carried out according to the U. S. P., 8th revision, p. 161.
3. PROC. A. PH. A., 45, p. 231.
4. 'About 38° according to the U. S. P., p. LIII.

---

THE DIAGNOSIS AND TREATMENT OF HAY FEVER.\*

BY IVOR GRIFFITH.

Newer developments in the field of hay fever diagnosis and therapeutics have completely eclipsed the theories and practices indulged in when this field was first cultivated. This, of course, is the general turn of affairs when any new medical idea is promulgated, for it is only by experience and experiment that the true value of medical discoveries may be obtained.

Formerly it was held that hay fever or pollinosis was due to the unusual sensitiveness, or idiosyncrasy, of the sufferer to the pollen of a vast variety of plants out of Nature's garden. But Nature's garden is expansive, and the old conception of diagnosis meant that a large analytical botanical chart was followed in order to establish the sensitiveness of the person under examination. As time went on, however, it was found that a real majority of patients responded uniformly only to a small class of pollen proteins. Then, again, when closer study was made of pollination methods, it developed that comparatively few plants use the simplest way of broadcasting their pollen grains; namely, by trusting it to the wind. And it is wind-borne pollen that is responsible for most hay fever infections.

So we found, as time went on, that the diagnosis and treatment of hay fever causes became more simplified, and particularly so by the brilliant conception of a "grouping" of the pollen extracts. Investigation proved conclusively that patients who are sensitive to pollens may be "botanically" classified according to plant families.

---

\* Read before Section on Practical Pharmacy and Dispensing, A. Ph. A., Cleveland meeting, 1922.