

represents the total loss in weight of the sample, or, in other words, its water of crystallization.

TABLE II.—DETERMINATION OF WATER OF CRYSTALLIZATION OF QUININE SULPHATE AT VARIOUS HUMIDITIES.

Sample.	Original Water.	Lab. Hum. %.	H <sub>2</sub> SO <sub>4</sub> %.	3:1 H <sub>2</sub> SO <sub>4</sub> %.	2:1 H <sub>2</sub> SO <sub>4</sub> %.	1:1 H <sub>2</sub> SO <sub>4</sub> %.	20% Hum. %.	30% Hum. %.	40% Hum. %.	80% Hum. %.
A	0	+ 4.95 - 4.97	+ 1.15 - 1.33	+ 4.15 - 4.00	+ 4.63 - 4.61	+ 4.68 - 4.76	+ 5.15 - 5.15	+ 5.18 - 5.22	+ 5.11 - 5.17	+ 5.10 - 5.22
R	16.78	-10.60 - 5.00 -15.60	-11.90 - 4.78 -16.68	-11.85 - 5.08 -16.93	-11.68 - 5.20 -16.88	-11.15 - 4.96 -16.11	-11.12 - 5.01 -16.13	-11.70 - 5.14 -15.84	-10.52 - 6.28 -16.80	- 3.38 -13.50 -16.88
27-B	11.60	- 6.70 - 5.12 -11.82	- 6.98 - 4.59 -11.57	- 6.88 - 4.88 -11.76	- 7.00 - 5.18 -12.18	- 6.50 - 4.51 -11.01	- 7.20 - 5.25 -12.45	- 7.05 - 5.10 -12.15	- 6.66 - 5.76 -12.42	- 2.68 - 9.15 -11.83
28-B	4.66	- 0.04 - 5.30 - 5.34	- 0.03 - 4.80 - 4.83	- 0.07 - 5.06 - 5.13	- 0.005 - 5.03 - 5.035	- 0.002 - 5.21 - 5.212	0.00 - 4.05 - 4.05	0.00 - 4.48 - 4.48	0.00 - 5.34 - 5.34	0.00 - 5.48 - 5.48

+ Indicates increase in weight.  
- Indicates loss in weight.

#### CONCLUSIONS.

Although some discrepancies appear in the preceding table, these particular determinations have not been repeated, as our purpose at this time has only been to determine the trend of the dehydration or hydration.

Examination of the data in Tables I and II will indicate the tendency of this salt to form a stable dihydrate. The per cent of water in the dihydrate is 4.60, in the heptahydrate 14.43, and in the octahydrate 16.16. This tendency is in agreement with the U. S. P. description, which states that when exposed to dry air or when heated to 50° C. it loses all but two molecules of its water of crystallization.

The tendency of quinine sulphate U. S. P. to dehydrate is marked, and it behooves pharmacists to buy quinine sulphate only in small, tightly closed containers, to store them in a cool place, and to keep the packages tightly and imperviously stoppered between the occasions of their use.

Quinine sulphate of less than U. S. P. water content may be easily converted to the dihydrate by exposure to dry air or by heating at 50° C.

PITTSBURGH, PA.,  
September 19, 1933.

#### THE DETECTION OF SMALL QUANTITIES OF CARBON MONOXIDE IN MEDICINAL OXYGEN.\*

BY JACOB E. SCHMIDT AND JOHN C. KRANTZ, JR.

#### INTRODUCTION.

The detection and quantitative determination of small quantities of carbon monoxide in air and blood have been the subject of much investigation during the last three decades. However, little attention has been centered on the detection

\* The expense of this investigation was defrayed in part by a grant from the Research Fund of the AMERICAN PHARMACEUTICAL ASSOCIATION.—Scientific Section, A. PH. A., Madison meeting, 1933.

of this dangerous impurity in medicinal oxygen. Owing to the fact that the principal source of medicinal oxygen is through the fractional distillation of liquefied air, the presence of small quantities of carbon monoxide is indeed a possibility.

The principal methods employed for the determination of carbon monoxide in air are the Orsat (1), Blood Colorimetric (2), Blood Spectroscopic (3), Blood Pyroannic Acid (4) and Teague's (5) Iodine Pentoxide Method. Those methods involving the use of blood are well established and simple in manipulation. However, the sensitiveness of these methods is materially reduced when the dispersion medium of the carbon monoxide is pure oxygen and not air as shown by the following considerations.

When equilibration is established between CO and O<sub>2</sub> in the presence of hemoglobin the factors controlling the amount of carbon monoxide hemoglobin formed are the partial pressures of the two gases and the respective affinity (*a*) of the gases for hemoglobin.

Therefore

$$\frac{\text{HbCO}}{\text{HbO}_2} = \frac{p\text{CO} \times a\text{CO}}{p\text{O}_2 \times a\text{O}_2}$$

Prince (6) setting the affinity of O<sub>2</sub> for hemoglobin at unity found the affinity of CO for hemoglobin to be 300, then

$$\frac{\text{HbCO}}{\text{HbO}_2} = \frac{300 p\text{CO}}{p\text{O}_2}$$

With air  $p\text{O}_2 = 20.93$  per cent or 2093 parts per 10,000 but with oxygen the equation becomes

$$\frac{\text{HbCO}}{\text{HbO}_2} = \frac{300 p\text{CO}}{10,000}$$

This indicates that the sensitivity of the test is reduced approximately fivefold when oxygen is the dispersion medium.

Teague's modification of the iodine pentoxide method as further modified by Martinek and Marti (7) was studied. The latter investigators were forced to use many scrubbing bottles to free the air from hydrocarbons and other contaminating substances from the exhausts of internal combustion engines. The present authors found it possible to obviate much of this scrubbing as these impurities do not occur in medicinal oxygen. In this manner the test was simplified for Pharmacopœial purposes.

#### EXPERIMENTAL.

The iodine pentoxide method depends upon the passing of the dry gas containing the carbon monoxide over purified iodine pentoxide heated to 150° C. The gas bubbles, then, through a potassium iodide solution containing starch T.S. The iodine formed by the reduction of the iodine pentoxide is vaporized and passes into the potassium iodide solution.

The assembled apparatus is shown in the illustration.

A and B are made of glass tubing having an internal diameter of about 3 mm. They are filled to a height of about 5 cm. with iodine pentoxide which has been heated at 215° C. for 3 hours. Each tube is heated by the paraffin baths E and F which are kept constant throughout the test at a temperature of 145° to 155° C. by means of the heaters G and H. C and D are drying tubes filled with calcium chloride. I is a tube having a capacity of about 50 cc. and con-

taining about 25 cc. of potassium iodide T.S. J and K are two-way stop-cocks by means of which the gas to be tested may be made to pass through the tubes D, B and I or through tube M. N is a 25-cc. beaker containing 10 cc. of potassium iodide T.S. and 3 drops of starch T.S.

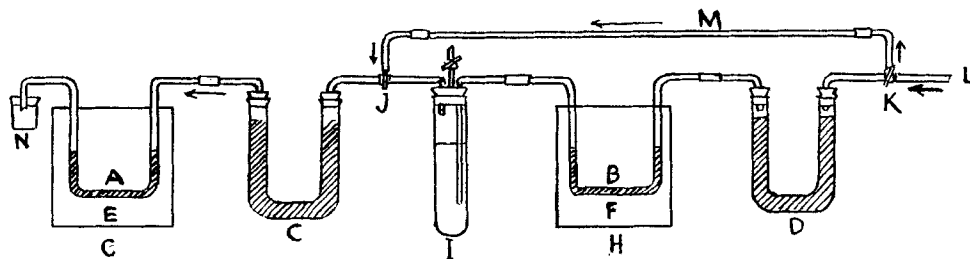


Fig. 1.

#### PRELIMINARY TREATMENT OF THE IODINE PENTOXIDE.

When the apparatus is assembled first or when it has not been in use for some time, a preliminary treatment of the iodine pentoxide prior to proceeding with the test is often necessary in order to prevent its spontaneous decomposition with the liberation of iodine, which may lead to erroneous conclusions.

Connect the oxygen supply with the inlet L, and adjust the stop-cocks J and K so as to include tube M. Heat bath E to about  $215^{\circ}$  and bath F to about  $150^{\circ}$  and pass oxygen through the apparatus allowing it to bubble through the solution in N at the rate of about one bubble every two seconds. Continue for about three hours. Reduce the temperature of bath E to about  $150^{\circ}$  and pass 10 liters of oxygen in from 50 to 60 minutes allowing it to bubble into a fresh solution in N. If the solution in N is colored blue or purple, raise the temperature of bath E to  $215^{\circ}$  and proceed as before. If no coloration is produced in N, the test may be begun.

#### THE TEST.

Connect the oxygen supply with the inlet L, and adjust the stop-cocks J and K so as to exclude tube M. Heat the paraffin baths to from  $145^{\circ}$  to  $155^{\circ}$ . Pass the oxygen through the apparatus, allowing it to bubble through the solution in N at such a rate that 10 liters will pass in from 50 to 60 minutes. At 10-liter intervals replace the solution in N, if it has acquired a blue or purple color. Continue the passage of the gas until a 10-liter volume produces no coloration in a fresh portion of the solution in N. Turn the stop-cocks so that the oxygen will pass through tube M, and, having poured a fresh solution into N, pass 5 liters of the gas (at the same rate). The solution in N is not colored blue or purple (carbon monoxide).

In this laboratory carbon monoxide was generated by the action of sulphuric acid on C.P. formic acid. One-tenth-cc. and 0.05-cc. quantities, respectively, were collected over water in an especially designed capillary pipette. The pipette containing the gas was transferred to a flask containing 5 liters of oxygen and agitated vigorously using about a liter of water to afford intimate mixing.

#### RESULTS.

- (a) Seven trials showed definite positive tests 1-50,000.
- (b) Five trials showed definite positive tests 1-100,000.

(c) Blank trials showed no liberation of iodine.

The test was conducted using pure nitrogen as the dispersion medium instead of oxygen. This apparently did not augment the amount of iodine liberated.

#### CONCLUSION.

1. A simple test, requiring no gas free from carbon monoxide for scrubbing purposes, for the detection of carbon monoxide in medicinal oxygen has been devised.

2. The sensitivity of the test is in the order of 1-100,000.

The authors wish to express their indebtedness to the Linde Air Products Company of Buffalo for the supplying of oxygen and nitrogen, and also to their chief engineer, Dr. Leo I. Dana, for his criticism and advice during the course of this investigation.

#### REFERENCES.

- (1) W. W. Scott, Standard Methods of Chemical Analysis, D. Van Nostrand (1917), page 697.
- (2) J. B. S. Haldane, *J. Physiol.*, 22 (1897), 139.
- (3) "Vogel's Spectroscopic Method in Technical Methods of Chemical Analysis," edited by George Lunge, through Martinek and Marti.
- (4) R. R. Sayers and W. P. Yant, Bureau of Mines, *Technical Bull.*, 373.
- (5) M. C. Teague, *J. Ind. Eng. Chem.*, 12 (1920), 964.
- (6) A. I. Prince, "The Combination of Carbon Monoxide and Hemoglobin and Its Analytical Application," N. Y. State Bridge and Tunnel Comm., Sec. 9, App. 4 (1921), 188, through Sayers and Yant.
- (7) M. J. Martinek and W. C. Marti, *Am. J. Pub. Health*, 19 (1929), 293.

BUREAU OF CHEMISTRY,  
STATE OF MARYLAND,  
DEPARTMENT OF HEALTH.

---

## LICORICE FERN AND WILD LICORICE AS SUBSTITUTES FOR LICORICE.\*

BY LOUIS FISCHER AND E. V. LYNN.

A preliminary study reported by one of us three years ago (1) indicated the possibility of using the rhizomes of licorice fern, *Polypodium vulgare* L. var *occidentale* Hook, in place of the official licorice. We have now completed that study and find increasing evidence for this substitution.

In the meantime attention was called to the common occurrence of wild licorice, *Glycyrrhiza lepidota* (Nutt.) Pursh. Apparently as an outcome of suggestions made at the annual convention of this ASSOCIATION in 1887, McCullough (2) reported an examination of the rhizomes. He found 8.53 per cent of ammoniated glycyrrhizin and 6.39 per cent of the crude acid, which differed considerably from taste from the compound as obtained from licorice.

From the published citations, one would conclude that the rhizomes are similar to those of licorice. Furthermore, we learn that they have been used as a

---

\* Scientific Section, A. Ph. A., Madison meeting, 1933.