CONCLUSIONS.

1. Approximately 2.5 times as large a quantity of tincture of aconite is required to kill rats as to kill guinea-pigs subcutaneously. A different ratio seems to hold for fluidextract (for a stabilized sample, about 1.0; for a sample not stabilized, about 5).

2. With increasing age, aconite preparations become less toxic to rats and to guinea-pigs. This is interpreted to mean that the hydrolytic cleavage products of aconitine are less toxic.

BIBLIOGRAPHY.

(1) "Bioassay of Aconite and Its Preparations. I. Lethal Dose of Aconitine to Rats," James C. Munch and G. S. Gittinger, JOUR. A. PH. A., 18 (1929), 17–24.

(2) "The Pharmacopœia of the United States of America," Tenth Decennial Revision (1925).

ABSTRACT OF DISCUSSION ON THE FOREGOING PAPERS.

Frank O. Taylor stated there was much misinformation in the literature and if coöperative investigation of drugs is undertaken as advocated in the Chairman's address, aconite deserves early consideration. He also commented on the difference in the toxicity of the tincture and fluidextract.

C. K. Glycart requested information regarding the identification of the true species by the number of stars; he was informed that this was not entirely adequate as a criterion.

H. A. Langenhan inquired relative to the number of aconite species and the extent of their pharmacological study. He was informed that of the 150 species only seven had been studied pharmacologically; different species differ in toxicity, and no pharmacological studies have been filed upon the native American species.

L. W. Rowe commenting on the last paper, stated that tests upon white mice had not shown the divergencies reported upon rats.

E. E. Swanson commented on the effect of alcohol upon the toxicity of aconite solutions.

THE PHYSICAL PROPERTIES OF GUAIACOL.

BY T. S. CARSWELL.

I. INTRODUCTION.

A study of the literature on the physical properties of guaiacol shows wide discrepancies in the data given, particularly in that regarding the melting or crystallizing point. The United States Pharmacopœia X, states that "solid guaiacol melts about 28°" and the Japanese Pharmacopœia (1922), also states that "guaiacol has a melting point of about 28°." The Nederlansche Pharmacopee (1915) gives a melting point of 27.6° to 27.8°. The Pharmacopee Francaise (1927) says that the melting point is 32° and the boiling point 205°. Hager, in "Handbuch der Pharmazeutischen Praxis," Vol. I (1925), 391, states: "Perfectly pure guaiacol forms large, colorless, prismatic crystals with melting point (crystallizing point) 33°, and boiling point 205°." Perkin (*J. Chem. Soc.*, London, 69, 1188) gives the crystallizing point as 28.3°. Behal and Choay (*Bull. de la soc. chim.* (3), 11, 703) give 28.3° and the same value is given by Pushin (*J. Chem. Soc.*, London, 125, 2628–30 (1924)). Denecke (*Z. anorg. allgem. Chem.*, 108, 1–44 (1919)) gives 28.4°. Jaeger (*Z. anorg. allgem. Chem.*, 101, 1–214 (1917)) gives 32°, and the same value is mentioned quite recently by Waser and Sommer (*Helv. Chim.*

Acta, XII, No. 3, 418 (1929)). The latter authors give the boiling point as 203–205°. The International Critical Tables for 1926 give the crystallizing point as 28.0° and the boiling point as 205.1°.

In order to clear up these discrepancies, pure guaiacol has been prepared and its properties determined.

II. EXPERIMENTAL WORK.

The guaiacol used as a starting material was a synthetic commercial product with a Cr. Pt. of 27.6°. 1820 Gm. of this product were dissolved in a hot solution of 650 Gm. of NaOH in 2000 cc. of water. The resulting solution was cooled to room temperature, when long needle-like crystals of sodium guaiacolate separated out. These crystals were filtered off, sucked as dry as possible, and then acidified. The guaiacol layer was washed with water and fractionated in vacuum. The first fraction which contained a little water was rejected, and the remainder was collected; 960 Gm. of product were recovered, with a Cr. Pt. of 28.0°. A small middle fraction, taken during the course of the distillation, showed Cr. Pt. 28.2°.

This product was then purified through the magnesium salt, as described by Ullman ("Enz. der tech. Chem." 2nd Edition, Vol. II, 0p. 657); 950 Gm. of the product which had been purified through the sodium salt were dissolved in 27 L. of water with 330 Gm. of NaOH. To the solution was added 845 Gm. of $MgCl_2.6H_2O$. A fine white precipitate formed, which was filtered off and washed. The filter cake was acidified and the guaiacol washed and fractionated as before. The main fraction, 650 Gm., had Cr. Pt. 28.0°, and a small middle fraction had Cr. Pt. 28.2°.

The main fraction from the Mg salt purification was then fractionally crystallized; 650 Gm. were cooled overnight in an insulated bath; 430 Gm. or 66%, was obtained as crystals with Cr. Pt. 28.1°. The crystals were melted and again fractionally crystallized; 65 per cent were recovered as crystals with Cr. Pt. 28.2°. These were again fractionally crystallized, when no change resulted. The product from the final crystallization was fractionated in vacuum and a small middle fraction was collected. This final product still had Cr. Pt. 28.2°.

This product was used to determine the boiling point. The boiling point was found to be 204.65° at 746.4 mm.

In making the above determinations, the thermometer used for taking crystallizing points was checked against one standardized by the Bureau of Standards; the thermometer used for taking the boiling point had been standardized by the Bureau of Standards.

III. LOW CRYSTALLIZING FORM.

It had previously been observed in this laboratory that another form of crystalline guaiacol could be prepared, with a crystallizing point much lower than the prisms usually obtained. This second crystalline form can easily be prepared by super-cooling molten guaiacol to —10° in a freezing mixture, and scratching the sides of the container to induce crystallization. Under these conditions the product crystallizes in the form of needles. The final purified product as described above showed, when cooled and seeded with the needle form, a Cr. Pt. of —3.2°. This form has not previously been mentioned in the literature.

IV. DISCUSSION.

Guaiacol has been purified by crystallization of the sodium salt, precipitation as the magnesium salt, repeated fractional crystallization and fractionation. The maximum observed crystallizing point was 28.2°. It seems certain that such varied methods of purification would remove an impurity present in an amount sufficient to lower the Cr. Pt. from 32° or 33° to 28.2°. It was thought possible that there might be another crystalline form with a higher Cr. Pt. However, during several years manufacturing experience at this plant, during which time guaiacol has been repeatedly crystallized, no such form has ever been observed. It must therefore be concluded that those authorities who give 32° or 33° are in error, and that the true Cr. Pt. of the usual form is 28.2°.

V. SUMMARY.

Guaiacol has been purified and the physical properties of the pure product determined. The usual prismatic crystals have Cr. Pt. 28.2°, and a needle-shaped form has Cr. Pt. —3.2°. The boiling point is 204.65° at 746.4 mm.

LABORATORIES: MONSANTO CHEMICAL WORKS,
ST. LOUIS, MISSOURI, August 8, 1929.

ASSIMILATION OF VITAMIN A WHEN DISSOLVED IN LIQUID PETROLATUM.*

BY E. MONESS AND W. G. CHRISTIANSEN.

Dutcher and his collaborators[1] claim that vitamin A in the form of butter fat is ineffective when fed to rats in mineral oil solution. The authors rather expected this result, since mineral oil is not absorbable in the gastro-intestinal tract, yet is a good solvent for vitamins A and D. However, according to their findings only vitamin A seemed to have been so affected; vitamin D, in the form of cod liver oil dissolved in liquid petrolatum, retained its full anti-rachitic properties.

The claim that vitamin A was made inactive by the presence of mineral oil caused an editorial expression of apprehension in the *J. A. M. A.*[2] lest the use of mineral oil should divert some of the vitamin A present in foods and prevent its alimentary absorption.

On account of the importance of this subject the effect of liquid petrolatum on vitamin absorption from the alimentary canal was carefully checked, using as a source of vitamin A a cod liver oil concentrate. This concentrate was dissolved in liquid petrolatum (Squibb) and in olive oil, the latter serving as a control. In both cases the proportion of oil and concentrate used was such as to yield a solution equal in volume to the original cod liver oil from which the concentrate was derived.

When white rats were fed a vitamin A deficient diet and carried to Xerothalmia and growth arrest as outlined in the U. S. P. test for vitamin A, the curative

* Scientific Section, A. PH. A., Rapid City meeting, 1929.

[1] R. A. Dutcher, J. O. Ely and H. E. Honeywell, vitamin studies: "XV. Assimilation of Vitamins A and D in Presence of Mineral Oil." *Proc. Soc. Exptl. Biol. Med.*, 24 (1927), 953.

[2] Editorial, *J. A. M. A.*, 89 (1927), 694.