in coloration has not been determined. It is uncertain whether it may be a direct action upon the pigment cells, or a secondary effect resulting from the cardiac derangement under the influence of the drugs.

SUMMARY.

Ouabain, scillaren B, coumingine hydrochloride, or cymarin, when injected into the lymph sac of the nebulous toad, *Bufo valliceps*, causes noticeable blanching of the dorsal skin. The reaction is definite with the minimal systolic dose of each cardiac drug.

REFERENCES.

(1) Chen, K. K., and Chen, A. L., *J. Pharmacol.*, 47, 295 (1933).

(2) Chen, K. K., Hargreaves, C. C., and Winchester, W. T., JOUR. A. PH. A., 27, 307 (1938).

THE CHEMISTRY OF PASSIFLORA INCARNATA.*

BY EDWIN J. FELLOWS[1] AND CLAYTON S. SMITH.**

INTRODUCTION.

Passiflora incarnata, one of about 125 species comprising the passion flower family, is a perennial climbing shrub found thriving in dry soils from Virginia to Florida and westward to Missouri and Arkansas. This drug has been used in medicine for almost one hundred years. While the drug is not found in either the current U. S. P. or N. F. it was recognized by N. F. V. There are at the present time, however, numerous hypnotic and sedative preparations of *Passiflora incarnata* on the market.

Fisher (1), the first to report on the clinical use of *Passiflora incarnata* stated that it was to be preferred to the bromides and chloral as a sedative, antispasmodic and hypnotic because the sleep it induced more closely approximated natural slumber. Sayre (2) in 1902 reported that passiflora had gained favor among practitioners in the treatment of insomnia, although there was some controversy as to its value. Three years later Stapleton (3) reported the successful use of tincture of passiflora in cases of insomnia from hysteria, neurasthenia and neuralgia. Leclerc (4) later reported the use of a tincture containing 50 per cent alcohol as a hypnotic and sedative with some degree of success. In the same year Hinsdale (5) reported demonstrations of a sedative action by means of reaction time experiments on human subjects. In the following year Hinsdale (6) reported diminution of acuteness of hearing of a number of human subjects after administration of tincture of *Passiflora incarnata*.

Discussions (7) concerning the components of passiflora are either to the effect that nothing is known about its chemical composition or that it is supposed to

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** We are indebted to Eli Lilly & Co. for their generous coöperation in furnishing the crude drug used in this investigation.

[1] Abstracted from a dissertation submitted June 1935, by Edwin J. Fellows in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Ohio State University.

contain an alkaloid. A search of the literature has failed to disclose satisfactory evidence that the drug contains an alkaloid. Ott (8) in 1898 reported that the drug was a depressant to the motor side of the cord, increased the respiratory rate and momentarily lowered blood pressure in experimental animals. Pilcher (9) reported that the drug has no effect on excised uteri of guinea pigs. DeNito (10) investigated several species of passiflora other than incarnata and it was his belief that they contained an alkaloid. The same author (10) also carried out a number of biological tests on a fluidextract of passiflora. Very little has been done toward standardization of *Passiflora incarnata*. In 1916 the Committee on Standards of the AMERICAN PHARMACEUTICAL ASSOCIATION stated that passiflora should not contain over 12 per cent ash. In N. F. V the standard was fixed at not more than 5 per cent of stems over 8 mm. in diameter.

This survey of the available literature on the subject discloses the fact that *Passiflora incarnata* has received wide-spread clinical application and that its continued use rests solely on an empirical basis. There also is a lack of reliable information concerning the chemical components of the drug. In order to secure some definite information concerning the chemical constituents of this drug the work described in the present paper was undertaken.

Analysis of Crude Drug.—To serve as a guide in subsequent experiments a proximate analysis was made. The results of these determinations have been summarized in Table I.

TABLE I.

Determination.	Per Cent.
Moisture (1)	7.60
Total ash (2)	15.60
Water-soluble ash	3.70
Water-insoluble ash	11.90
Acid-soluble ash	10.33
Acid-insoluble ash	5.25
Water-soluble constituents	25.40
Crude fiber (3)	29.20
Protein (4)	11.30
Petroleum ether extract	1.80
Ethyl ether extract	2.20
Absolute alcohol extract	1.79

Method Used: (1) Crude drug dried to constant weight at 100° C.; (2) Woodman Food Analysis, 2nd Edition, page 16; (3) U. S. P. X, page 465; (4) total nitrogen × 6.25.

Extraction of Drug with Organic Solvents.—Approximately 30 kilos of finely ground drug were completely extracted at room temperature with diethyl ether for a period of two weeks. This extract was reduced to a solid by distillation under reduced pressure and the residue so obtained completely extracted with petroleum ether. The portion of the crude drug insoluble in ethyl ether was air dried and then completely extracted with absolute alcohol.

The petroleum-ether extract was distilled under reduced pressure until practically all of the solvent had been removed and then the residue remaining in the distilling flask steam distilled. A volatile oil was obtained but the amount was insufficient to permit purification or a detailed examination. The constants obtained for this oil are listed in Table II.

TABLE II.

Specific Gravity, 27° C.	Specific Rotation, 27° C.	Refractive Index, 27° C.
0.810	+16	1.4382

The material not volatile with steam was saponified and after adding a large volume of water to insure complete solution of the soaps, extracted with ethyl ether. The ether extract was set aside for future investigation. The acids obtained by hydrolysis of the saponified material were esterified by heating under a reflux condenser for 18 hours with a large excess of methyl alcohol containing 2 per cent dry HCl gas. The esterified material was decolorized with Norite and the esters subsequently distilled at 5-mm. pressure, separated into two fractions and the following constants determined.

	B. P. (5 Mm.). °C.	Mean Mol. Wt. (Acids).	Iodine Number (Esters).
Fraction I	170–200	259	126
Fraction II	200–255	283	109

These two fractions were combined, fractionally distilled three times at 15-mm. pressure and fractions collected at each 5° interval between 185° and 220° C. Throughout the distillations a constant pressure was maintained by a device similar to the one described by Huntress and Hershberg (11) and the distillates collected in a modified Pauly receiver (12). The analytical data for the various fractions are to be found in Table III.

TABLE III.

Fraction Number.	B. P. Me Esters, 15 Mm. ° C.	M. Mol. Weight (Acids).	Iodine Number (Esters).	Fraction Weight (Gm.).
1	185	254	29	2
2	185–190	262	38	8
3	190–195	266	66	10
4	195–200	272	92	18
5	200–205	274	131	12
6	205–210	276	149	28
7	210–215	287	169	13
8	215–220	305	161	3
9	Above 220	574	118	8

The data in the above table indicate two things: *First*, that acids of the C_{18} series predominate (Mean Mol. Wt., B. P. and fraction weights); *second*, that unsaturated fatty acids are present in all fractions (iodine numbers). Each of the fractions in this table was subjected to the lead salt ether method described by Jamieson (13). The data obtained by analysis of the acids resulting from the decomposition of the lead soaps insoluble in ether are to be found in Table IV.

TABLE IV.—SATURATED ACIDS OBTAINED BY LEAD SOAP ETHER SEPARATION.

Fraction Number.	M. Mol. Weight.	Iodine Number.	Fraction Weight (Gm.).
1	240	10	0.8
2	242	11	5.0
3	247	13	6.0
4	253	15	7.0
5	257	16	4.0
6	262	15	7.0
7	279	14	1.0
8	...	..	0.1
9	362	36	0.7

Since the molecular weight of palmitic acid (C_{16}) is 256, it is probable that an acid or acids of lower molecular weight are present in Fractions 1, 2 and 3 of Table IV. The presence of acids of the C_{16} series appears to be clearly indicated from the mean molecular weight data for fractions 4, 5 and 6. Fraction 7, however, probably contains a mixture of acids of the C_{16} and C_{18} series. The data for Fraction 9 indicate the presence of an acid above the C_{18} series or of material other than fatty acids.

Fractions 1, 2 and 3 were combined and fractionally crystallized from acetone. After repeated crystallization a compound melting at 54° C. and having a mean molecular weight of 235

was obtained. This should establish the presence of myristic acid, m. p. 53.8° C., molecular weight 228.

Fractions 4, 5 and 6 in Table IV were combined and repeatedly crystallized from acetone. A product was obtained which melted sharply at 62.2° C. and had a mean molecular weight of 257. The following data indicate that the product is palmitic acid:

	M. P. ° C.	M. Mol. Wt.	Ultimate Analysis, Per Cent. C.	H.
Palmitic acid	62.6–63.0	256.3	75.00	12.00
Sample	62.2	257.0	75.21	12.40

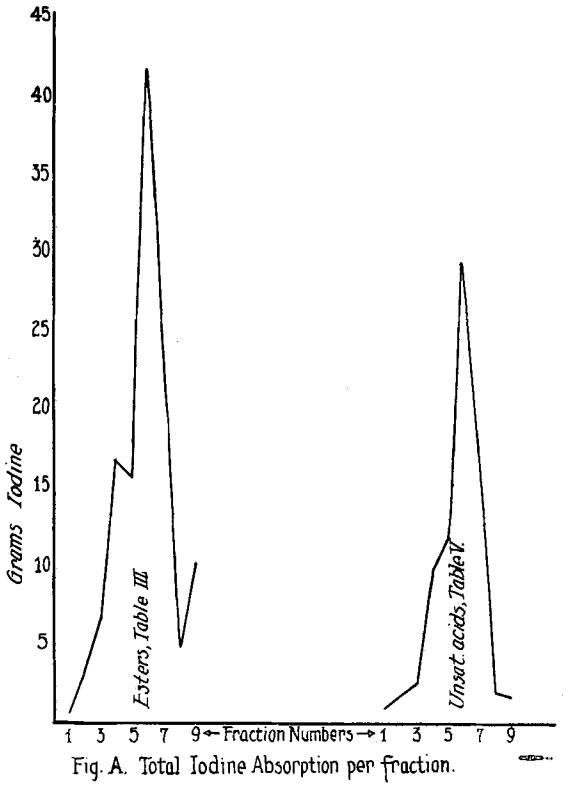

Fig. A. Total Iodine Absorption per fraction.

No depression of the melting point was observed when the product was mixed with an authentic sample of palmitic acid. The small amount of material available in Fractions 7, 8 and 9 prevented further attempts at purification.

The acids obtained by decomposition of the lead soaps *soluble* in ether next were examined. The results are to be found in Table V. The mean molecular weight data for Fractions 3, 4, 5, 6 and 7 of Table V indicate that they are made up almost entirely of acids of the C_{18} series. The iodine numbers of these fractions show the presence of acids with more than two double bonds. The mean molecular weights for Fractions 1 and 2 indicate the possible presence of unsaturated acids below the C_{18} series.

The total iodine absorption values for the fractions in Table III as well as for those in Table V have been plotted against the fraction numbers in Fig. A. These values have been calculated by the formula

$$\text{Iodine absorption} = \frac{\text{Wt. of Fraction} \times I_2 \text{ number}}{100}$$

TABLE V.

Fraction Number.	M. Mol. Weight.	Iodine Number.	Fraction Weight (Gm.).
1	266.0	98.6	0.3
2	267.0	114.0	1.4
3	273.0	183.0	1.3
4	276.5	192.2	5.0
5	279.5	193.0	6.0
6	282.0	194.0	15.0
7	284.5	183.0	7.0
8	292.0	167.0	1.0
9	352.5	150.0	1.0

Inspection of the curve shows a peak for Fraction 6 of both Tables III and V. The mean molecular weight for Fraction 6, Table III, is 276; and for Fraction 6, Table V, 282. This indicates the presence of unsaturated fatty acids containing 18 carbon atoms. Likewise lesser peaks at Fraction 4 in each table indicate the presence of unsaturated fatty acids containing 16 carbon atoms.

Each of the fractions of Table V was subjected to the barium-soap benzene method of separation for unsaturated fatty acids. Only traces of barium soaps insoluble in benzene were obtained. Table VI contains the analytical data for acids obtained by decomposing the barium soaps *soluble* in benzene. It is to be noted that the iodine numbers of several of the fractions have been slightly raised. Fractions 1–3, inclusive, contained insufficient material to warrant a satisfactory separation by the barium soap benzene method. Inasmuch as Fractions 4, 5, 6 and 7, of Table VI, showed no very marked differences in their analytical constants, they were combined and the polybromide number determined and found to be 26.2. The amount of bromine in the insoluble bromide was determined by the Parr bomb method and found to be 62.92 per cent. The melting point of this compound was 179.5–180.5° C. When these data are compared with similar data for hexabromostearic acid they are in close agreement indicating that the fatty acid before bromination was linolenic acid.

	M. P. ° C.	Bromine, Per Cent.
Hexabromostearic acid	180–181	63.3
Sample	179.5–180.5	62.92

TABLE VI.

raction Number.	M. Mol. Weight.	Iodine Number.
4	282	201
5	280	203
6	279	209
7	284	190
8	295	170
9	349	153

The ether solution and washings from the insoluble bromide were combined and the excess bromine removed with sodium thiosulfate solution. An ether-soluble petroleum-ether insoluble compound was eventually obtained and found to melt at 114° C. Its bromine content by the Parr bomb method was 54.35 per cent. These data compare favorably with those for tetrabromostearic acid as noted in the table below.

	M. P. ° C.	Bromine, Per Cent.
Tetrabromostearic acid	114–115	53.30
Sample	114	54.35

It may, therefore, be concluded that linoleic acid was present in the original fat. The final petroleum ether filtrate from the bromine precipitation may contain some oleic acid since the barium soap benzene method is far from quantitative. In order to establish the presence or absence of oleic acid in the original fat, 5 Gm. of the fatty acids from Fractions 4, 5, 6 and 7, after saponification with NaOH, were oxidized with $KMnO_4$ according to the method of Lapworth and Mottram (14). That oleic acid was present in the original fat is shown by the constants obtained for the oxidized compound.

	M. P. ° C.	M. Mol. Weight.
Dihydroxy-stearic acid	131–132	316
Oxidized compound	130	317

Non-Saponifiable Material.—Any non-saponifiable material present in the fixed oils of the drug would be found in the ether extract after saponification (page 567). After removing the ether from this extract by distillation under reduced pressure a deep red-colored residue remained in the

distilling flask. An attempt was made to dissolve this residue in 95 per cent alcohol. A portion of this material was soluble in cold alcohol, part of the cold alcohol-insoluble material was soluble in hot alcohol and the remainder insoluble in both hot and cold alcohol.

An orange-colored precipitate was obtained on allowing the *hot alcohol-soluble fraction* to cool. After repeated recrystallization from hot alcohol and after drying in a vacuum desiccator over sulfuric acid a nearly white substance melting rather imperfectly between 70–75° C. was obtained. A portion of this purified solid was soluble in hot acetic anhydride, the remainder floated on top the anhydride in the form of oily droplets. On cooling, the hot acetic anhydride soluble material settled out. This suggests the presence of an alcohol (or sterol) and a hydrocarbon in the mixture. Since the substance soluble in hot acetic anhydride gave negative Lieberman-Burchard and Salkowski tests the absence of unsaturated alcohols or sterols is indicated. From this it may be presumed that the material was a mixture of a saturated alcohol and a hydrocarbon. The amount of material available was too small to permit further purification.

The cold alcohol-soluble portion of the non-saponifiable material was subjected to distillation under reduced pressure. After the liquid had been reduced to about one-half its volume and cooled, a mass of rusty colored crystals appeared. After numerous recrystallizations from alcohol white crystalline material was obtained and found to melt at 139° C. This substance had a specific rotation of −34.9. The acetyl derivative (17) of this compound was prepared and after purification was found to melt at 130° C. The following data indicate that the purified precipitate was the sterol sitosterol.

	Salkowski and Lieb.-Burch.	M. P. ° C.	M. P. of Acetate ° C.	$[\alpha]_D^{30}$.
Sitosterol	#	138–139 (16)	130–131 (16)	−36.6 (16)
Precipitate	#	139	130	−34.9

The non-saponifiable material insoluble in hot alcohol (page 569) separated as a heavy red liquid when suspended in hot alcohol but on cooling hardened into a waxy mass. This was dissolved in acetone from which it crystallized as a light fluffy mass. After numerous recrystallizations from ethyl acetate a nearly white product was obtained which melted at 65–67° C. and when heated with acetic anhydride floated on top the mixture as an oily layer. This material was subjected to the treatment recommended by Leys (18) for hydrocarbons. A compound was obtained by this method which after purification melted between 67–68° C. The purified compound was insoluble in cold concentrated sulfuric acid and was unaffected by fuming nitric acid, did not react with acetic anhydride nor did it give positive tests for sterols. Furthermore, it did not decolorize 1 per cent $KMnO_4$ nor absorb bromine. From these data it may be concluded that a hydrocarbon was present. The following hydrocarbons have been found in plants: Triacontane, m. p. 67° C.; hentriacontane, m. p. 68° C.; dotriacontane, m. p. 70° C.

It will be recalled that the crude drug was first extracted with ethyl ether, the ether removed and the residue remaining extracted with petroleum ether. The portion of the residue insoluble in petroleum ether now will be considered. This residue was extracted with several liters of ethyl ether. Some of the material, which had apparently been carried along in the original extraction of the crude drug, failed to go into solution. After repeated washing with 95 per cent alcohol a nearly white solid was obtained. This was saponified with alcoholic KOH and the saponification mixture extracted with ether. An ether-soluble compound was obtained and purified by recrystallization from ethyl acetate. It was found to melt at 86° C. The compound was completely soluble in acetic anhydride and according to Lewkowitsch (15) should be classified as an alcohol. An acetyl derivative melting at 73° C. was prepared. The analytical constants for this non-saponifiable lipid indicate the presence of melissyl alcohol. The latter substance melts between 85–88° C. and its acetyl derivative at 73° C. An attempt was made to isolate and identify a fatty acid from the saponification mixture. A small amount of material was recovered but due to the inadequacy of the sample the nature of the acid or acids could not be determined. Although a fatty acid was not isolated the presence of melissyl alcohol suggests that the original substance may have contained a wax.

The *original ether extract of the crude drug* insoluble in petroleum ether was extracted with hot water and the aqueous extract steam distilled. A distillate which was acid in reaction was ob-

tained. This was extracted with ether and after evaporation of the ether a residue was obtained which gave all the tests (19) said to be indicative of formic acid. The material remaining in the distilling flask (water-soluble-non-volatile) gave a negative Molisch test and failed to reduce Fehling's solution. After hydrolysis with HCl the solution again failed to reduce Fehling's solution. This eliminates glucosides or other carbohydrate material.

The portion of the *original ether extract* of the crude drug *insoluble in hot water* next was examined. This was extracted with ethyl alcohol in which it was only partially soluble. The *soluble portion* was concentrated to a small volume and allowed to stand in a refrigerator over night. A small amount of material, insufficient for chemical identification, settled out. The *alcohol-insoluble* portion was fused with 8 times its weight of KOH and a portion of an aqueous extract of the fusion mixture extracted with ether. After removal of this solvent a residue was obtained, the odor of which was suggestive of formic and butyric acids. Tests (19) for formic acid confirmed its presence. No attempt was made to verify the presence of butyric acid. A number of color reactions (20), indicative of catechol, were obtained for another portion of the residue dissolved in distilled water. A small amount of the residue suspected of containing catechol was brominated in chloroform and a compound obtained which after purification melted at 189° C. Tetrabromocatechol (21) is said to melt at 192–193° C. All attempts to isolate catechol itself were unsuccessful. This concludes the investigation of the ether-soluble petroleum ether-insoluble fraction of the crude drug.

The ether-insoluble portion of the *original crude drug* was extracted with alcohol. The alcoholic extract was concentrated to a small volume, added to distilled water and filtered. Color tests made on this filtrate disclosed that tannins were probably present. Precipitation with basic lead acetate and removal of the precipitate thus formed next was undertaken. The lead-free, acid filtrate was extracted with petroleum ether, benzene and chloroform in the order named. These volatile solvents were removed in each case by distillation under reduced pressure. The respective residues were taken up in water. Portions of these aqueous solutions were tested with Fehling's and Molisch's reagents. Each of these tests was negative in every case. The remainders of the respective aqueous solutions were boiled with HCl for six hours. After neutralization, the various solutions failed to give either a positive Molisch or Fehling's test. Glucosides may be assumed to be absent from any of the extracts made by the various volatile solvents. The lead-free, acid solution was then made alkaline with NH_4OH and extracted with chloroform in the usual manner for the detection of alkaloids. The residue obtained by evaporation of the chloroform failed to react with either Wagner's or Mayer's reagent. This indicates the absence of alkaloids.

Another portion of the alcoholic extract of the crude drug was concentrated to a solid and divided into two parts. One part of the solid extract was mixed with a small amount of glycerol and heated at 190–200° C. for 20 minutes. After cooling, the glycerol mixture was diluted with water, acidified and extracted with ether. The ether was removed and the residue so obtained taken up in a small amount of water. No satisfactory evidence for the presence of phenolic compounds could be obtained from this solution although one or two qualitative tests suggested the presence of pyrogallol. The other part of the solid alcohol extract failed to reduce Fehling's solution. This extract then was heated with 10 per cent HCl on a boiling water-bath for two hours, allowed to cool, filtered and the filtrate extracted with ethyl ether. The residue obtained by evaporating the ether gave color reactions (22) said to be indicative of gallic acid. The acid-hydrolysis mixture after extraction with ether as just described was made slightly alkaline with KOH and basic lead acetate added. After filtration the filtrate was acidified and the lead removed by precipitation with H_2S. After filtration the excess H_2S was removed by aeration. This last filtrate gave a positive Molisch test and reduced Fehling's solution. A phenylhydrazine derivative was prepared from the filtrate. This derivative after purification had a melting point of 203° C.* Mulliken (23) records the melting point of glucosazone (fructosazone) at 204–205° C. Another portion of the solid alcohol extract was hydrolyzed and Seliwanoff's test applied. This test was negative. The optical rotation of the solution before hydrolysis was $[\alpha]_D^{20} + 46.3$. It appears that the compound is glucose resulting from the hydrolysis of a more complex substance. The identification of glucose and gallic acid in the alcohol-soluble portion of the drug suggests the presence of a glucosidic tannin.

As recorded earlier in this paper two investigators (8), (10) have claimed that passiflora contains physiologically active material. DeNito (10) found that intravenous injection of fluid-extracts of certain species of passiflora produced a fall in blood pressure and stimulated the respiratory center of anesthetized dogs. He found, however, that oral administration of the drug failed to produce any observable effects.

In order to ascertain whether any of the various extracts of the plant contained physiologically active material a series of bio-assays was made. The ethyl ether, the petroleum ether and the alcohol-soluble constituents of the crude drug were examined. The volatile solvents were removed by distillation under reduced pressure and in each case three Gm. of the residue were suspended in 20.0 cc. of 1.0 per cent acacia solution. Carotid blood pressure and respiratory tracings were recorded for dogs under ether anesthesia. All injections were made into the femoral vein. The alcohol-soluble residue produced a sharp transient fall in blood pressure but the other residues were physiologically inert when injected.

Due to the fact that all available material was exhausted another alcoholic extraction of the crude drug was made. The solvent was removed by distillation under reduced pressure and the residue obtained extracted with water. This material was only partially soluble in the distilled water. After filtration the filtrate and residues were assayed separately. The injection of 5.0 cc. of the filtrate into a dog produced a decided fall in blood pressure. A suspension of the water-insoluble residue was made in 1.0 per cent acacia solution. When 5.0 cc. of this suspension were injected no change in blood pressure could be detected. The water-soluble portion was treated with a slight excess of 20 per cent aqueous solution of lead acetate, the solution filtered and the precipitate decomposed with sodium carbonate; after filtration the lead-free filtrate from this decomposition mixture when injected into anesthetized dogs had no effect on blood pressure. The *filtrate from the lead acetate precipitation* was next examined. The excess lead remaining in the filtrate was removed by precipitation with H_2S and the excess H_2S removed by æration. Intravenous injection of this lead-free filtrate into anesthetized dogs produced a fall in blood pressure. A portion of the filtrate was made acid and extracted successively with benzene, ethyl ether, chloroform and amyl alcohol. Another portion of the filtrate was made alkaline and extracted with a fresh portion of the above-named solvents. The volatile solvents from both the acid and alkaline extractions of the filtrate were evaporated and the residue in each case taken up in distilled water. Distilled water was used because experiments already described showed the active principle to be water soluble. No change in blood pressure was observed when aqueous extracts of the residues from the volatile solvents were injected. The aqueous solution, which had been extracted by the volatile solvents, however, still contained depressor material.

The fact that the active principle could not be removed from an acid or an alkaline solution by means of immiscible solvents would seem to indicate the absence of alkaloids, although DeNito expressed the opinion that an alkaloid was probably present. In the present experiments *with the anesthetic used* no change in respiratory rate or amplitude was observed after injection of the physiologically active material. Oral administration to non-anesthetized dogs of relatively large quantities of the aqueous extract containing the active principle failed to produce any observable effects. Further work on the pharmacology of passiflora is in progress and will be reported later.

SUMMARY.

1. The chemical constituents of *Passiflora incarnata* were separated by means of differential solvents.

2. In the lipid fraction the following substances were identified and their analytical constants recorded, myristic, palmitic, oleic, linoleic and linolenic acids; melissyl alcohol and sitosterol.

3. A small quantity of a hydrocarbon was isolated from the petroleum-ether fraction.

4. Other organic constituents identified were catechol, gallic acid and glucose.

5. The catechol was probably derived from a resin while the presence of glucose and gallic acid probably indicates that a glucosidic tannin was present in the crude drug.

6. The plant contained water-soluble depressor material.

REFERENCES.

(1) Fisher, *Int. Med. Mag.*, 7, 929 (1899); from *Pharm. J.*, 64, 246 (1900).
(2) Sayre, *Western Druggist*, 24, 242 (1902); from *Pharm. J.*, 68, 529 (1902).
(3) Stapleton, *Apoth. Ztg.* (1904); from *Pharm. J.*, 74, 20 (1905).
(4) Leclerc, *Ibid.*, 105, 220 (1920).
(5) Hinsdale, A. E., *J. Am. Inst. Homeopathy*, 12, 887–891 (1920).
(6) Hinsdale, *J. Am. Chem. Soc.*, 16, 3515 (1922).
(7) Culbreth, "Materia Medica and Pharm.," 418 (1927); Kraemer, "Scientific and Applied Pharmacognosy," 524 (1928); Rusby, Bliss and Ballard, "Properties and Uses of Drugs," 425 (1930). United States Dispensatory, 22nd Edition, 1510.
(8) Ott, I., *Medical Bulletin* (Dec. 1898), from U. S. Dispensatory, 22nd Edition, 1510.
(9) Pilcher, J. D., *J. Pharmacol.*, 8, 110–111, Proc. (1911).
(10) DeNito, *Rassegna di Terapia e Patologia clinica*, Anno III (April 1931), (9), N. 4.
(11) Huntress and Hershberg, *Ind. Eng. Chem., Anal. Ed.*, 2, 144 (1930).
(12) Brown, J. B., *Ibid.*, 1, 160 (1929).
(13) Jamieson, *Veg. Fats and Oils*, 58, 289 (1932).
(14) Lapworth and Mottram, *J. Chem. Soc.*, 127, 1629 (1925).
(15) Lewkowitsch, *Chem. Tech. and Analysis of Oils, Fats and Waxes*, 6th Edition, 1, 613 (1921).
(16) Anderson, R. J., *J. Am. Chem. Soc.*, 48, 1450 (1924).
(17) Lewkowitsch, 6th Edition, 1, 600 (1921).
(18) Leys from Lewkowitsch, 6th Edition, 1, 615 (1921).
(19) Mulliken, 1st Edition, 1, 79–83 (1904).
(20) *Ibid.*, 94.
(21) *Ibid.*, 109.
(22) Allen, *Commercial Organic Analysis*, 4th Edition, 3, 528–531 (1910).
(23) Mulliken, 1st Edition, 1, 30 (1904).

A NOTE ON THE VOLATILE OIL OF ILLICIUM PARVIFLORUM MICHX.*

BY P. A. FOOTE.[1]

The phytochemist in Florida has at his door many plants which should be investigated. If he fails to look for them the chances are that some will be brought to him. The writer has five new volatile oils awaiting investigation. These were brought to him by a farmer looking for commercial possibilities. Several years ago our attention was called to the large amount of oil in the leaves of *Illicium parviflorum Michx.* (Fam. *Magnoliaceæ*). This is a shrub 1–2 m. tall and according to Small (1) the habitat is in low woods and swamps in the coastal plain from Florida to Georgia. The appearance of tiny oil cells on the under side of the leaves is very pronounced. When crushed a strong sassafras odor is obtained. This is due to the high safrol content which we found to be higher than in any other oil yielding this compound. A search of the literature indicated that this oil has never been reported on.

EXPERIMENTAL.

The leaves were collected in Gainesville in October 1933. Upon steam distillation, 2.6 Kg. gave 12.1 Gm. of a colorless oil heavier than water. It stood in diffused light for three years, during which time it turned slightly yellow. A determination of the acid and ester values indi-

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