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THE CONSTITUENTS
OF THE
EXPRESSED OIL OF NUTMEG

BY

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CLXII.—*The Constituents of the Expressed Oil of Nutmeg.*

By **Frederick Belding Power** and **Arthur Henry Salway.**

Having undertaken a complete study of the constituents of the nutmeg, the essential oil of which has already been investigated by us (Trans., 1907, **91**, 2037), it was necessary to obtain somewhat more precise information than is at present available respecting the composition of the expressed oil or fat. An examination of the latter appeared the more important in view of the fact that the nutmeg is known to possess narcotic properties, and that the only known constituent to which it has been possible to attribute this action is myristicin, $C_{11}H_{12}O_3$ (3-methoxy-4 : 5-methylenedioxy-1-allylbenzene), which is a component of the essential oil, and therefore also contained in the expressed oil or fat.

The deficiency of knowledge respecting the constituents of the expressed oil of nutmeg, commonly known as "nutmeg butter," is indicated by the following statement recorded in Lewkowitsch's *Chemical Technology and Analysis of Oils, Fats, and Waxes*, Vol. II., p. 718 : "This fat varies considerably in its composition. It contains from 4 to 10 per cent. of an ethereal oil, and consists of about 45 per cent. of a solid fat—chiefly trimyristin—the rest being a liquid fat and free fatty acids." The only further information of importance regarding the composition of this fat appears to be the statement that the liquid portion consists chiefly of olein (compare Koller, *Arch. Pharm.*, 1865, **173**, 286 ; Benedikt, *Analyse der Fette und Wachsarten*, 4te Aufl., 1903, p. 572 ; C. R. Alder Wright, *Fats and Oils*, 2nd ed., 1903, p. 546 ; Hefter, *Technologie der Fette und Oele*, 1907, Bd. II., p. 627). Although a genuine expressed oil of nutmeg is likely to vary considerably in character, it is quite probable that the statements recorded concerning its composition are based, for the most part, on the examination of commercial products, which are often of uncertain origin and subject to adulteration.

EXPERIMENTAL.

For the purpose of a complete examination of the constituents of nutmeg fat, a quantity of it was kindly expressed for us by Messrs. Stafford Allen and Sons, of London, the material employed having been a portion of the same lot of Ceylon nutmegs as that from which the essential oil previously examined had been distilled (Trans., 1907, **91**, 2037).

The crushed nutmegs (23·7 kilograms), after being warmed, were subjected to a pressure of 4000 pounds per square inch, at a temperature ranging between 45° and 75°, for a period of eight hours, and were then allowed to remain under pressure at a gradually decreasing temperature for about twelve hours. The total amount of fat thus obtained was 6·3 kilograms, corresponding to a yield of 26·6 per cent. This fat, at the ordinary temperature, was a soft, brownish-yellow solid, possessing the characteristic odour of nutmeg. A portion of the same lot of nutmegs, when finely ground and extracted in a Soxhlet apparatus with ether, yielded 42·9 per cent. of fat.

The total amount of expressed fat was liquefied by a gentle heat, and subsequently stirred until it solidified, in order to render it perfectly homogeneous. Determinations were then made of the constants of the expressed fat, of that obtained by extraction with ether, and of the expressed fat from which the essential oil had been removed, as also of the total fatty acids. The results were as follows:

	Expressed fat.	Fat extracted by ether.	Expressed fat free from essential oil.	Total fatty acids.
Melting point	48°	50°	49°	49°
Density 50°/50°	0·9399	0·9337	0·9443	0·9012
Acid value...............	11·2	12·9	14·0	218·3
Saponification value..	174·6	180·5	199·6	—
Iodine value............	57·8	45·7	35·7	23·1

An observation by Lewkowitsch (*loc. cit.*, p. 719), that the iodine value of nutmeg fat is not appreciably altered by the removal of the essential oil, cannot be confirmed by the above figures.

Separation of the Essential Oil and Trimyristin.

A quantity (2000 grams) of the expressed fat was heated in a current of steam until the essential oil had been removed as completely as possible. The aqueous distillate, which contained a quantity of oil, had a faintly acid reaction. It was extracted twice with ether, the ethereal liquid being washed with a little water, dried with anhydrous sodium sulphate, and the ether removed. About 250 grams of essential oil were obtained, thus representing 12·5 per cent. of the weight of nutmeg fat employed. The essential oil had the following characters: D^{20}_{20} 0·8794; $\alpha_D + 22°30'$ in a 1-dcm. tube.

The aqueous distillate, which had been extracted with ether, still contained a very small amount of volatile acid, which, after conversion into a barium salt, was found to consist chiefly of a mixture of formic and acetic acids.

The contents of the distillation flask, after being allowed to cool, consisted of a solid cake of fat, together with some water. The fat was removed and dissolved in hot alcohol, when, on cooling, a large amount of a crystalline solid separated. This was purified by several crystallisations from hot alcohol, after which it was quite colourless, and melted at 54—55°:

0·1453 gave 0·3962 CO_2 and 0·1588 H_2O. C = 74·4; H = 12·1.

$C_3H_5(C_{14}H_{27}O_2)_3$ requires C = 74·8; H = 11·9 per cent.

This substance was thus identified as trimyristin.

Hydrolysis of the Fatty Oil.

The alcoholic mother liquors from the trimyristin were united and heated for an hour on a water-bath with an excess of potassium hydroxide. The greater part of the alcohol was then removed, water added, and the alkaline mixture repeatedly extracted with ether.

Unsaponifiable Constituents of the Oil.

The ethereal liquids, obtained by the extraction of the above-mentioned alkaline mixture, were combined, washed, dried, and the ether removed, when a quantity (170 grams) of a thick, yellow liquid was obtained. On dissolving this in warm 70 per cent. alcohol, and allowing the solution to stand, a small amount of solid was deposited, which was removed, and subsequently crystallised from a mixture of ethyl acetate and alcohol. It was thus obtained in colourless, glistening leaflets, melting at 134—135°:

0·1679, when dried at 105°, lost 0·0094 H_2O. H_2O = 5·6.

0·1090 gave 0·3304 CO_2 and 0·1180 H_2O. C = 82·7; H = 12·0.

$C_{20}H_{34}O,H_2O$ requires H_2O = 5·8 per cent.

$C_{20}H_{34}O$ requires C = 82·8; H = 11·7 per cent.

The composition of this substance, together with its characteristic colour reactions, established its identity as a phytosterol.

Isolation of a New Substance, $C_{18}H_{22}O_5$.

The alcoholic solution of unsaponifiable material, from which the phytosterol had been separated as above described, was freed from alcohol, and the residual product fractionally distilled under 15 mm. pressure. After several distillations, the following fractions were collected: 140—170° (27 grams); 170—200° (25 grams); 200—260° (5 grams); 260—270° (16 grams); 270—280° (55 grams).

The lowest boiling fraction was a limpid liquid, and contained a considerable proportion of myristicin, which was identified by means of its bromo-derivative (m. p. 128—129°). The fraction boiling at 270—280°/15 mm. was the largest in amount, and possessed the most constant boiling point. At the ordinary temperature, it was a yellow, transparent, extremely viscid liquid, which showed no tendency to crystallise, even on long standing. Two different preparations of this substance were analysed, with the following results:

I. 0·2523 gave 0·6274 CO_2 and 0·1546 H_2O. C = 67·8; H = 6·8.
0·1145 ,, 0·2854 CO_2 ,, 0·0732 H_2O. C = 68·0; H = 7·1.
0·1380 ,, 0·3452 CO_2 ,, 0·0902 H_2O. C = 68·2; H = 7·3.
II. 0·1902 ,, 0·4736 CO_2 ,, 0·1173 H_2O. C = 67·9; H = 6·9.
0·2006 ,, 0·5015 CO_2 ,, 0·1258 H_2O. C = 68·2; H = 7·0.
Mean C = 68·0; H = 7·0.

$C_{11}H_{14}O_3$ requires C = 68·0; H = 7·2 per cent. M.W. = 194.
$C_{18}H_{22}O_5$,, C = 67·9; H = 6·9 ,, M.W. = 318.
$C_{26}H_{32}O_7$,, C = 68·4; H = 7·0 ,, M.W. = 456.

The molecular weight of the substance was determined by the cryoscopic method in benzene solution:

0·1889 in 21·73 of benzene gave $\Delta t - 0·150°$. M.W. = 290.
0·4205 ,, 21·73 ,, ,, $\Delta t - 0·337°$. M.W. = 287.

From a consideration of these results, it would appear probable that the substance possesses the formula $C_{18}H_{22}O_5$, and this conclusion is supported by a determination of its iodine value:

0·2233 absorbed 0·1707 iodine. I = 76·4.

$C_{18}H_{22}O_5$, with one ethylenic linking, requires I = 79·9 per cent.

As the above-described constituent of nutmeg fat is quite dissimilar in character to any substance of the formula $C_{18}H_{22}O_5$ which has hitherto been recorded, it may be regarded as a new compound.

The *substance*, $C_{18}H_{22}O_5$, is very readily soluble in all the usual organic solvents, except light petroleum, which dissolves it but sparingly, and it is also soluble in 70 per cent. alcohol. It contains neither hydroxyl nor carbonyl groups, since acetic anhydride, hydroxylamine, and semicarbazide have no action on it. The substance contains, however, at least two methoxyl groups, but an accurate quantitative determination of the latter was not possible owing to the continued slow evolution of alkyl iodide, even after several hours' heating with hydriodic acid. This behaviour is probably to be attributed to a dioxymethylene group which is only slowly attacked by hydriodic acid. Attempts were made to prepare a crystalline derivative of the substance by acting on it in the cold with bromine and nitric acid respectively, but only amorphous products were obtained. When oxidised with alkaline permanganate, it yielded only uncrystallisable substances of a resinous nature.

As it was thought possible that the above-described substance, $C_{18}H_{22}O_5$, might possess some definite physiological action, it was kindly tested for us by Dr. H. H. Dale, Director of the Wellcome Physiological Research Laboratories. It was ascertained, however, that when administered to cats, in doses of 0·5 and 1 gram respectively, no obvious effects were produced.

The Fatty Acids.

The alkaline, aqueous solution of potassium salts, resulting from the above-described hydrolysis of the fatty oil, was acidified with sulphuric acid and distilled with steam. No acid was found in the distillate with the exception of a very small quantity of myristic acid. The fatty acids remaining in the distillation flask were then extracted with ether, when a quantity (about 30 grams) of an insoluble, black resin separated. This was collected and extracted with various solvents, but nothing crystalline could be obtained from it.

The above-mentioned ethereal solution was subsequently washed, dried, and the ether removed, when the fatty acids were obtained in the form of a solid cake. These acids, when dissolved in chloroform, were devoid of optical activity. They were distilled under diminished pressure, and the following fractions collected: 205—220°; 220—245°; above 245°/20 mm.; a small amount of undistillable resin remaining in the flask.

Fraction 205—220°/20 mm.—This formed a solid mass, and amounted to 310 grams. After crystallisation from alcohol, a product was obtained, which melted at 53—54°, and was found to consist of myristic acid:

0·1125 gave 0·3027 CO_2 and 0·1257 H_2O. $C = 73·4$; $H = 12·4$.

$C_{14}H_{28}O_2$ requires $C = 73·7$; $H = 12·3$ per cent.

Fraction 220—245°/20 mm.—This fraction amounted to about 100 grams, and became partly solid on cooling. The solid portion was separated by filtration, and, after crystallisation from alcohol, was identified as myristic acid. The liquid portion of this fraction, together with the alcoholic mother liquors from the preceding one, was neutralised with potassium hydroxide, and treated with an alcoholic solution of lead acetate. The precipitated lead salt was washed with water, digested with ether, and the filtered ethereal liquid shaken with dilute hydrochloric acid. The ethereal liquid was then separated from the lead chloride, washed with water, dried, and the ether removed, when about 50 grams of unsaturated acids were obtained. On distilling this product, it was found that the greater portion boiled between 220° and 230° under a pressure of 10 mm.:

0·2030 gave 0·5633 CO_2 and 0·2039 H_2O. $C = 75·7$; $H = 11·2$.
0·2246 absorbed 0·2674 iodine. Iodine value = 119·1.
0·3059 neutralised 9·3 c.c. *N*/10 KOH. Neutralisation value = 170·5.
$C_{18}H_{34}O_2$ requires $C = 76·6$; $H = 12·1$ per cent. Iodine value = 90·1;
Neutralisation value = 199.

The analysis and constants of this product indicated it to be a mixture containing some acid of a higher degree of unsaturation than oleic acid. In order to ascertain more definitely the character of its constituents, a portion (11 grams) was oxidised in alkaline solution with 1000 c.c. of a 1 per cent. solution of potassium permanganate in the cold. The pure white oxidation product was collected and digested with much ether, which extracted a considerable amount of a crystalline solid. This was recrystallised from alcohol, when it was obtained in glistening laminæ, melting at 128—129°:

0·1218 gave 0·3041 CO_2 and 0·1298 H_2O. $C = 68·1$; $H = 11·8$.
0·0999 „ 0·2497 CO_2 „ 0·1044 H_2O. $C = 68·2$; $H = 11·6$.
$C_{18}H_{36}O_4$ requires $C = 68·4$; $H = 11·4$ per cent.

This substance was evidently dihydroxystearic acid, and its formation proved the presence of oleic acid in the original mixture.

In addition to the above-mentioned product of oxidation, a very small quantity of a crystalline acid was isolated, which melted at 200—205°. This was doubtless linusic acid (a hexahydroxystearic acid), which is stated to melt at 203°, and its formation indicated the presence of linolenic acid in the oil. As no sativic acid (tetrahydroxystearic acid) could be isolated from the product of oxidation, it may be concluded that linolic acid is not a constituent of the oil, and that the unsaturated acids of nutmeg fat therefore consist chiefly of oleic acid with a small amount of linolenic acid. The presence of the latter is, furthermore, confirmed by the iodine value of the original mixture of liquid acids.

Fraction above 245°/20 mm.—This fraction was small in amount, and consisted of a thick, glutinous, brown oil. On treating it with cold alcohol, it partly solidified. The solid substance was collected and crystallised several times from ethyl acetate, when it appeared quite homogeneous and melted at 74—75°:

0·0599 gave 0·1717 CO_2 and 0·0712 H_2O. $C = 78·2$; $H = 13·2$.
$C_{26}H_{52}O_2$ requires $C = 78·8$; $H = 13·0$ per cent.

0·1145 neutralised 2·8 c.c. *N*/10 KOH. Neutralisation value = 137.

$C_{26}H_{52}O_2$ requires a neutralisation value of 142.

This substance was undoubtedly cerotic acid.

Summary.

The preceding investigation of a genuine expressed oil of nutmeg has shown its composition to be approximately as follows :

Essential oil	12·5 per cent.
Trimyristin	73·0 ,,
Oleic acid, as glyceride	3·0 ,,
Linolenic acid, as glyceride	0·5 ,,
Formic, acetic, and cerotic acids	(very small amounts
Unsaponifiable constituents	8·5 per cent.
Resinous material	2·0 ,,
	99·5 per cent.

The unsaponifiable constituents consisted of a new compound, $C_{18}H_{22}O_5$ (amounting to about 5 per cent. of the expressed oil), together with some myristicin, $C_{11}H_{12}O_3$, and a very small amount of a phytosterol, $C_{20}H_{34}O$ (m. p. 134—135°). Although the myristicin is a constituent of the essential oil, it was not practicable to effect its complete removal by the preliminary treatment of the fat with steam.

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