CALCULATIONS FOR SPECIFIC OPTICAL ROTATION

Compound	Grams	$CHCl_3$, cc.	Ang. rotn. 100-mm. tube	$[\alpha]^{25}D$
Alepric acid	2.2703	25	7.00	77.12
Ethyl aleprate	2.5562	25	6.80	66.54
Aleprylic acid	2.6712	50	4.85	90.78
Ethyl aleprylate	4.0433	50	6.40	79.14

Aleprestic Acid.—Since this acid was obtained only 70.5% pure we can determine its constants only from the curves made with the other pure homologs. These probable constants are shown in Tables II and III.

Aleprolic Acid.—Fraction 49W, 1, Table I, clearly indicates the presence of this very low homolog of chaulmoogric acid. The boiling point of ethyl aleprolate should be 70° at 10 mm.; being impure it boiled slightly lower.

The homolog between ethyl aleprestate and ethyl aleprolate should boil at 96° at 10 mm. It is probably present but our final fractions were too small to attempt further fractionation to prove its presence.

An optically inactive unsaturated acid with one double bond must be present in fraction 50W, 2 to account for the iodine number found. There may also be present a saturated acid of low molecular weight.

For purposes of comparison the constants of the other known optically active acids and their ethyl esters are included in Tables II and III.

Summary

Four optically active fatty acids hitherto unknown have been discovered in *Hydnocarpus wightiana* oil. They have been named alepric, aleprylic, aleprestic and aleprolic acids.

The characteristics of these new acids and their ethyl esters are given and their relationship to their previously known homologs, hydnocarpic and chaulmoogric acids, is shown.

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[CONTRIBUTION FROM THE INTERNATIONAL LEPROSY CENTER, RIO DE JANEIRO]

Analysis of Chaulmoogra Oils. III. *Hydnocarpus Wightiana* Oil

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Of the various chaulmoogra oils used in the treatment of leprosy, that expressed from the seeds of *Hydnocarpus wightiana* is by far the most generally employed. This is largely due to the fact that an oil of excellent quality is easily obtainable in large quantities at a reasonable price. *H. wightiana* occurs abundantly in southwestern India. The tree grows to a height of 7 to 10 meters. The fruit measures 6 to 12 cm. in diameter. The seed is about 2 cm. long with longitudinal grooves and a knot on the end. The species is one of the most abundant and easily accessible of the *Hydnocarpaceae*. Although *H. wightiana* oil has been so widely used for the past fifteen years in the treatment of leprosy, no accurate qualitative or quantitative analysis has ever been made due to the difficulty in separating the constituents. In 1905 Power and Barrowcliff[1] reported that the total fatty acids of this oil consisted chiefly of hydnocarpic and chaulmoogric acids and that they found evidences of a still lower homolog of the same series having the formula $C_{14}H_{24}O_2$ in the mother liquor but were unable to isolate it. Since the iodine number of the final mother liquor was so large (140.7) they concluded that it indicated the presence of an acid or acids belonging to the linolic or linolenic series. Our analysis shows that acids of neither of these series are present but that the high iodine number (and high rotation, 50.4) that they obtained are due to gorlic acid.[2] No evidence of the presence of palmitic acid was found by them and they make no mention of oleic acid. Since their analysis was made practically nothing has been added to our knowledge of the composition of this important medicinal oil. A single reference has been made to the possible presence of gorlic acid.[3] We have succeeded in analyzing *H. wightiana* oil by the method for chaulmoogra oils given in the first article of this series.[4] Our analysis is shown in Table I. It shows six fatty acids not previously reported in this oil, four of which are new homologs of chaulmoogric acid.

(1) Power and Barrowcliff, *J. Chem. Soc.*, **87**, 884 (1905).

Experimental

The sample of oil was taken from a 300-liter drum of *H. wightiana* oil, cold-pressed from fresh, selected seeds imported for the routine production of leprosy drugs for Brazil from the Ernakulam Trading Co., Ernakulam, South India. The characteristics of the oil were as follows: sp. gr. $^{25}/_{25}$, 0.9549; F. F. A. (as % oleic), 2.7; sapon. no., 201; iodine no. (Hanus), 98.4; sp. rotn.,

(2) Cole and Cardoso, THIS JOURNAL, **60**, 612 (1938).
(3) Anon., *Bull. Imp. Inst.*, **34**, 145 (1936).
(4) Cole and Cardoso, THIS JOURNAL, **60**, 614 (1938).

+55.0°; ref. index (at 25°), 1.4799; unsaponifiable matter, 0.25%.

Method of Analysis.—Since the medicinal properties of chaulmoogra oils depend on the percentage of optically active acids, the analysis is reported in percentage of the various fatty acids present. The sample of oil was saponified and the fatty acids liberated and washed in the usual manner. The solid acids were separated from the liquid acids by crystallization from 80% ethyl alcohol. The two fractions were changed to ethyl esters and then fractionally distilled in a Podbielniak Model B high temperature fractionating apparatus. The details of the separation and distillation were given in the first article of this series, the only change being that the two final crystallizations for the separation of the liquid acids were made with 80% acetone to prevent the formation of ethyl esters.

Qualitative Analysis

The fatty acids of *H. wightiana* oil contain hydnocarpic, chaulmoogric, gorlic, oleic, palmitic, alepric, aleprylic and aleprestic acids besides a very small amount of a low-boiling, optically inactive, unsaturated acid with one double bond and another homolog of chaulmoogric acid containing only six carbon atoms which we have named aleprolic acid. The acids were identified as follows.

Hydnocarpic Acid.—This acid was isolated easily from fraction 2, Table III, by repeated crystallization from 80% ethyl alcohol. It gave the correct optical rotation, iodine number, neutralization equivalent and melting point for pure hydnocarpic acid as well as the characteristic crystalline growth previously described.[5]

Chaulmoogric Acid.—Pure chaulmoogric acid was obtained readily from fraction 4, Table III, by crystallization to constant melting point from 80% ethyl alcohol. It gave the correct optical rotation, iodine number, neutralization equivalent and melting point for pure chaulmoogric acid.[5]

Gorlic Acid.—Ethyl gorlate was isolated by several fractional distillations of fraction 4, Table II. It gave the correct optical rotation, iodine number and boiling point for ethyl gorlate. Changed to acid it also gave the correct constants for gorlic acid.[2]

Oleic Acid.—Oleic acid was not obtained pure but its presence was indicated in the liquid fraction by the distillation curve of the ethyl esters and by the correct iodine numbers for mixtures containing ethyl oleate in fractions 2, 3 and 4, Table II. The elaidic acid test could not be used as gorlic acid gives a similar reaction. Hydrogenation tests were equally unsatisfactory in the presence of hydnocarpic and chaulmoogric acids.

Palmitic Acid.—It is practically impossible to separate ethyl palmitate from hydnocarpate by distillation but the separation can be accomplished easily by cooling a fraction of esters high in palmitate in the icebox. By separating the solid ethyl palmitate and crystallizing it twice from alcohol it was obtained pure (m. p. 24°). Upon changing it to palmitic acid and crystallizing two or three times the correct melting point and neutralization equivalent for palmitic acid was obtained.

Alepric Acid.—This acid is the next lower homolog to hydnocarpic acid, differing from the latter by C_2H_4 and having the formula $C_{14}H_{24}O_2$. It occurs in very small amount (less than 0.5%) in *H. wightiana* oil. No attempt was made to isolate it in the sample here analyzed but it was isolated from a much larger sample (200 liters) and its properties were determined. The method of separation of this homolog and the determination of its properties as well as those of the following homologs of chaulmoogric acid form the subject of another paper.[6]

Aleprylic Acid.—This acid is a homolog of chaulmoogric acid next lower in the series to alepric acid having the formula $C_{12}H_{20}O_2$. In the same sample about ten times as much of this acid can be isolated as of alepric or aleprestic acid. *H. wightiana* oil contains about 3% of aleprylic acid. It was isolated from the large sample mentioned above and its properties were determined.[6]

Aleprestic Acid.—This is the next lower homolog to aleprylic acid having the formula $C_{10}H_{16}O_2$. It occurs in very small amounts in *H. wightiana* oil (less than 0.5% and was not isolated from this sample but was obtained 70.5% pure from the large sample mentioned above.

Aleprolic Acid.—This is the lowest homolog of chaulmoogric acid yet discovered, being the second lower homolog after aleprestic acid having the formula $C_6H_8O_2$. Even from the large sample mentioned above we obtained only a very small amount of this acid, but the boiling point of its ethyl ester (65° at 10 mm.) and its specific rotation indicated its presence and from the latter we were able to determine its purity (42%). From our distillation curves we were unable to say whether or not the homolog between aleprestic and aleprolic acids was present.

In the sample at our disposal we were unable to isolate the optically inactive unsaturated acid with one double bond indicated as present by the iodine number.

Quantitative Analysis

The total fatty acids of *H. wightiana* oil when separated into liquid and solid acids by the method described by us consisted of 84.3% solid acids and 15.7% liquid acids. Although the separation is by no means complete, the breaks in the distillation curves of the ethyl esters made from these two fractions are much more distinct than when the whole esters are used. Complete separation is not necessary as the amounts of the various constituents can be computed by taking advantage

TABLE I

PERCENTAGE COMPOSITION OF THE FATTY ACIDS OF *H. Wightiana* OIL (FROM TABLES II AND III)

Acids	%
Hydnocarpic	48.7
Chaulmoogric	27.0
Gorlic	12.2
Oleic	6.5
Palmitic	1.8
Lower homologs of chaulmoogric acid (alepric, aleprylic, aleprestic, aleprolic and unidentified acids)	3.4
Loss	0.4

(5) Cole and Cardoso, THIS JOURNAL, **59**, 963 (1937).

(6) Cole and Cardoso, *ibid.*, **61**, 2349 (1939).

TABLE II

FRACTIONAL DISTILLATION OF ETHYL ESTERS FROM LIQUID ACIDS OF *H. Wightiana* OIL (15.7% OF TOTAL FATTY ACIDS)

Fraction	B. p., °C. (10 mm.)	Cc.	Sp. rotn. $[\alpha]^{25}D$	Iodine no.	Percentage in liquid fraction: Hydnocarpate	Chaulmoograte	Gorlate	Oleate	Palmitate	Lower homologs
1	120–187	3.3	50.64	86.7	..	..	..	..	0.9	2.4[a]
2	187–203	24.0	46.79	95.4	15.2	..	3.3	4.5	1.0	...
3	203–207	14.0	46.25	121.7	5.0	..	6.1	2.9	...	..
4	207–212	55.7	49.01	142.0	..	13.3	39.3	3.1	...	...
Residue	.....	3.0	...	...	..	..	..	..	...	...
			% in liquid fraction		20.2	13.3	48.7	10.5	1.9	2.4
			% in total fatty acids		3.2	2.1	7.7	1.6	0.3	0.4

[a] Alepric, aleprylic, aleprestic, aleprolic and unidentified acids.

TABLE III

FRACTIONAL DISTILLATION OF ETHYL ESTERS FROM SOLID ACIDS OF *H. Wightiana* OIL (84.3% OF TOTAL FATTY ACIDS)

Fraction	B. p., °C. (10 mm.)	Cc.	Sp. rotn. $[\alpha]^{25}D$	Iodine no.	Percentage in solid fraction: Hydnocarpate	Chaulmoograte	Gorlate	Oleate	Palmitate	Lower homologs
1	117–189	5	53.13	83.3	..	..	...	...	1.4	3.6[a]
2	191–202	55	57.57	91.3	49.7	..	1.6	3.3	0.4	...
3	202–210	5	54.75	93.6	4.2	..	0.3	0.5	...	...
4	210–214	35	52.38	90.3	..	29.6	3.4	2.0	...	...
			% in solid fraction		53.9	29.6	5.3	5.8	1.8	3.6
			% in total fatty acids		45.5	24.9	4.5	4.9	1.5	3.0

[a] Alepric, aleprylic, aleprestic, aleprolic and unidentified acids.

of the boiling points, optical activity and iodine numbers or absence of one or both of the two latter constants as described in part one of this series. The results of these computations are given in Tables II and III and these are summarized in Table I. Fraction 1 of Table II and of Table III were too small to be further divided but we know from distillation of much larger samples that there is about ten times as much aleprylic acid in this first fraction as there is of the homolog above and below it or of the optically inactive, unsaturated acid. We have therefore figured these two fractions on the basis of the specific optical rotation of ethyl aleprylate (79.14) which gives us 0.9% for the amount of saturated ester present in fraction 1, Table II, and 1.4% in fraction 1, Table III. This is admittedly only an approximation.

Summary

The qualitative and quantitative analyses of the total fatty acids of *H. wightiana* oil have been made by the method described in the first article of this series.

This is the first quantitative analysis that has been made of this oil. Six constituents not previously reported have been found, four of which are new homologs of chaulmoogric acid.

This analysis shows *H. wightiana* oil to be quite similar in composition to *Carpotroche braziliensis oil.*

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