tests are indications that the substance is hydrocarbon, and according to its melting point it may be characterized as triacontane which is reported in the literature as having a m. p. of 69° to 70° C. The yield was thirty-five Gm.

Verification of Triacontane ($C_{30}H_{62}$).—That the substance isolated is a hydrocarbon and that it might be triacontane is indicated by the following experimental work:

1. The substance is highly inactive, failing to form an acetate.
2. It is non-saponifiable and gives a negative test for sterol.
3. It is not affected by concentrated sulphuric acid.
4. It does not decolorize a 1% permanganate solution.
5. It was obtained in a manner that Leys prescribes for the isolation of hydrocarbon material.
6. While these 5 points classify it as a hydrocarbon, the m. p. of 69° to 69.5° C. classifies it as triacontane.

SUMMARY.

I. The percentage of total fat (petroleum-ether extractive) in digitalis leaves varies from 1.023% to 1.750%, a value much lower than any previously reported.

II. Organic compounds isolated from the fat and not previously reported in the literature are:

a. Fatty Acids—Saturated
  1. Myristic Acid
  2. Palmitic Acid
  3. Cerotic Acid
  4. Melissic Acid (?)

b. Fatty Acids—Unsaturated
  1. Oleic Acid
  2. Linolic Acid
  3. Linolenic Acid

c. Alcohols—Saturated
  1. Glycerol
  2. Melissyl Alcohol

d. Alcohols—Unsaturated (Sterols)
  1. Sitosterol

e. Hydrocarbons—Saturated
  1. Triacontane.

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IX. THE STANDARDIZATION AND STABILIZATION OF ERGOT PREPARATIONS.*

BY CLARENCE E. POWELL, HANS A. SCHULZE AND EDWARD E. SWANSON.

The stability of the fluidextract of ergot has been a serious difficulty in its pharmaceutical and therapeutic use. Previously, Haskell and Eckler (1), Garcia (2), Prybill and Maurer (3), Wokes (4), Thompson (5), Swanson (6), Smith and Stohlman (7), Rowe and Scoville (8) and Swanson, Powell, Stevens and Stuart (9) have reported rapid deterioration of ergot preparations. The purpose of this investigation is a continuation of previous stability tests (6 and 9) and an attempt to ascertain definitely (*a*) whether or not the hydrogen-ion concentration factor, (*b*) buffer salts or (*c*) reducing agents prevent the deterioration of ergot and its alkaloids.

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* Scientific Section, Toronto meeting, 1932.

Solutions of the alkaloid ergotamine tartrate (0.05 per cent) were prepared in 40 per cent, 60 per cent and 80 per cent alcohol. To produce various hydrogen-ion concentrations, hydrochloric acid and tartaric acid were used. In some of the alkaloidal solutions, the buffer salt, sodium dihydrogen phosphate; or the reducing agents, sodium dihydrogen hypophosphite; or sodium hydrosulphite were used. To some of the buffer or reducing agents of the solutions of the alkaloid, hydrochloric acid or tartaric acid were used to change the hydrogen-ion concentration. A fluidextract of ergot was prepared without an acid menstruum and divided into eighteen parts. As in the alcoholic alkaloidal solutions, these fluidextracts were treated with acids, buffer or reducing agents. All potency tests were made by the Broom and Clark method and Smith's Chemical method.

As shown in Table I, the various solutions of ergotamine tartrate do not retain their original potency at the end of six months' aging. Various percentages of alcohol (40, 60 or 80 per cent) do not stabilize the alkaloid. Forty per cent alcohol is just as efficient as 80 per cent alcohol, as shown in solutions Nos. 1, 2 and 3 in Table I. With hydrogen-ion concentrations (2.1 to 3.6) and the various percentages of alcohol, the alkaloid shows distinctly more activity at the end of six months' aging. This stability appears to be due to the presence of the acids (hydrochloric

TABLE I.—SOLUTIONS OF ERGOTAMINE TARTRATE 0.05% POTENCY AFTER SIX MONTHS' AGING AT ROOM TEMPERATURE.

Solution Number.	Alcohol, Per Cent.	Buffer, 2.5 Per Cent.	Acid.	p_H When Made.	p_H 6 Mo. Later.	Per Cent Activity. Broom and Clark Method.	Per Cent Activity. Smith's Chemical Method.
1	40			6.7	4.2	7	
2	60			5.3	4.6	13	
3	80			4.3	5.13	10	
4	40		HCl	3.0	3.1	32.5	
5	60		HCl	2.4	2.1	25	
6	80		HCl	2.4	2.4	22	
7	40		Tartaric	3.0	3.6	58	40
8	60		Tartaric	3.1	3.5	72	50
9	80		Tartaric	3.4	3.6	47	30
10	40		HCl	1.0	1.2	18	10
11	40		HCl	2.1	2.1	60	60
12	40		HCl	4.9	4.6	−10	−10
13	40		HCl	5.7	4.9	18	25
14	40		HCl	7.1	5.7	8	−10
15	40	$NaH_2PO_4H_2O$		4.7	4.5	15	−10
16	40	$NaH_2PO_4H_2O$	HCl	4.2	4.0	41	20
17	60	$NaH_2PO_4H_2O$		4.4	4.8	4.7	−10
18	60	$NaH_2PO_4H_2O$	HCl	3.3	3.3	63	54.4
19	40	$NaH_2PO_2H_2O$		5.1	3.9	6	−10
20	40	$NaH_2PO_2H_2O$	HCl	3.0	2.9	−10	20
21	60	$NaH_2PO_2H_2O$		5.05	4.2	−10	−10
22	60	$NaH_2PO_2H_2O$	HCl	3.1	3.1	−10	−10
23	40	$Na_2S_2O_4$		8.2	9.0	43	50
24	40	$Na_2S_2O_4$	HCl	3.0	1.8	40	50
25	60	$Na_2S_2O_4$		Above 10	Above 10	34	48.4
26	60	$Na_2S_2O_4$	HCl	3.0	8.3	38	46
27	40	$NaH_2PO_4H_2O$	Tartaric	3.4	3.3	43	27.4
28	40	$NaH_2PO_2H_2O$	Tartaric	2.9	3.0	−10	−10
29	40	$Na_2S_2O_4$	Tartaric	ppt.	2.3	34	45

acid or tartaric acid) rather than the alcohol. Tartaric acid is more efficient than hydrochloric acid. With a low p_H (below 2.0) or a high p_H (above 4.00), the deterioration of the alkaloid is approximately the same as with the various percentages of alcohol. This shows that an acid alcoholic solvent with a p_H of 2 to 4 is more efficient in preventing the deterioration of ergotamine tartrate than an alcoholic solution or an acid alcoholic solvent with a p_H below 2.00 or higher than 4.00.

As shown in solutions Nos. 15, 16, 17, 18 and 27 (Table I), the alkaloid with sodium dihydrogen phosphate and acids (hydrochloric acid or tartaric acid) is distinctly more stable than with the buffer alone. This shows that the stability of the alkaloid is due to the acid rather than the buffer. With or without the acids, sodium dihydrogen hypophosphite does not prevent the loss of activity of the alkaloid as shown in solutions Nos. 19, 20, 21, 22 and 28 (Table I). This shows that the alkaloid with the reducing agent (sodium dihydrogen hypophosphite) with or without acid deteriorates rapidly. Sodium hydrosulphite with or without the acids or regardless of the hydrogen-ion concentration appears to stabilize 34 per cent to 50 per cent of the alkaloid, as shown in solutions Nos. 23, 24, 25, 26 and 29 (Table I). This shows that sodium hydrosulphite partially prevents the deterioration of the alkaloid as reported by Smith and Stohlman (7). However, as shown in Table I solutions Nos. 4, 7, 8, 9 and 11, an acid alcoholic solution with a p_H of 2 to 4 is just as efficient in preventing the deterioration of the alkaloid as sodium hydrosulphite.

As shown in Table II, the fluidextracts of ergot do not deteriorate as rapidly as the solutions of the alkaloid after six months' aging. In this series, the hydrogen-ion concentration appears to prevent a loss in potency. A fluidextract of ergot with a p_H of 3.2, as in No. 3 (Table II), retains its original potency. A low p_H of 1.0 to 1.8 or a high p_H of 6.5 to 7.0 shows only 23 per cent and 55 per cent activity, respectively. Thus, in this series of fluidextracts of ergot the hydrogen-ion con-

TABLE II.—F. E. ERGOT. ORIGINAL ASSAY—110% BY THE BROOM AND CLARK AND 100% BY SMITH'S CHEMICAL METHOD. POTENCY AFTER SIX MONTHS' AGING AT ROOM TEMPERATURE.

F. E. Number.	Buffer, 2.5 Per Cent.	Acid.	p_H When Made.	p_H 6 Mo. Later.	Per Cent Activity. Broom and Clark Method.	Per Cent Activity. Smith's Chemical Method.
1		HCl	1.0	1.8	23	26
2		HCl	2.0	2.1	73	88
3		HCl	3.0	3.2	109	106
4		HCl	4.0	4.0	100	100
5		HCl	5.0	5.0	77	67
6		NaOH	6.0	5.7	64	68
7		NaOH	7.0	6.5	55	50
8			5.6	5.5	81	62
9	$NaH_2PO_4H_2O$		5.3	5.2	82	88
10	$NaH_2PO_4H_2O$	HCl	3.0	3.1	85	88.8
11	$NaH_2PO_2H_2O$		5.6	5.4	91	67
12	$NaH_2PO_2H_2O$	HCl	3.0	3.2	100	88
13	$Na_2S_2O_4$		6.6	6.7	88	100
14	$Na_2S_2O_4$	HCl	3.0	2.9	100	100
15		Tartaric	3.8	4.0	85	100
16	$NaH_2PO_4H_2O$	Tartaric	4.7	4.7	80	100
17	$NaH_2PO_2H_2O$	Tartaric	4.8	5.1	70	80
18	$Na_2S_2O_4$	Tartaric	4.9	5.3	83	100

centration appears to have some part in the stability of its activity. However, as previously reported (9) some fluidextracts of ergot deteriorate rapidly regardless of the hydrogen-ion concentration. This discrepancy cannot be explained at this time.

The addition of sodium dihydrogen phosphate, sodium dihydrogen hypophosphite or sodium hydrosulphite with or without acids, as shown in Table II, Nos. 9 to 18, inclusive, shows no marked loss of potency in six months' aging at room temperature. Sodium hypophosphate shows a greater loss than either sodium dihydrogen phosphate or sodium hydrosulphite. A comparative study of Tables I and II shows that the fluidextract with various hydrogen-ion concentrations, buffer or reducing agents deteriorates less in six months than the solutions of ergotamine tartrate. Apparently, *the fluidextract or the crude ergot drug contains some principle other than the alkaloids (ergotamine or ergotoxine) that aids in its stability.* There is also evidence, as recently reported by Moir (10), (11), that the ergot drug contains an unknown principle which has a much more rapid physiological action than either ergotamine or ergotoxine. A longer period of aging is required for this series of fluidextracts to show the value of the hydrogen-ion concentration, buffer and reducing agents. This series of fluidextracts will be reassayed at the end of 1 and 2 years' aging at room temperature. These results will be reported later.

CONCLUSIONS.

1. Various percentages of alcohol (40, 60 or 80 per cent) fail to prevent the deterioration of ergotamine tartrate.

2. A definite hydrogen-ion concentration appears to partially stabilize alcoholic solutions of ergotamine tartrate.

3. Sodium dihydrogen phosphate with acid (hydrochloric acid or tartaric acid) is more efficient in preventing deterioration of the alkaloid than without acid. The stability appears to be due to the acids rather than the buffer salt.

4. Sodium dihydrogen hypophosphite with or without the acids fails to stabilize the alkaloid.

5. Sodium hydrosulphite regardless of the hydrogen-ion concentration partially stabilizes the alkaloid.

6. The hydrogen-ion concentration still appears to have some influence in the stability of fluidextracts of ergot.

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