Digitonin and in smaller amount gitonin are the principal saponins of digitalis seeds. In recent work Windaus (1) and coworkers have made observations which indicate that still other saponins must be present. Although the latter were not isolated as such their presence was detected by the isolation of characteristic degradation products. When the pure sapogenins, digitogenin or gitogenin, were oxidized with chromic acid only acid substances, digitogenic acid and gitogenic acid were obtained respectively, with no neutral by-products. If, however, a digitogenin was used which had been obtained from crude digitonin, then an appreciable amount of neutral fraction was secured. Most of this consisted of a diketone, \( \text{C}_{26}\text{H}_{38}\text{O}_4 \), which was presumably an oxidation product of a dihydroxy compound, \( \text{C}_{26}\text{H}_{42}\text{O}_4 \), an isomer of gitogenin and in which the hydroxyl groups are not vicinal as in gitogenin. In still much smaller amount a neutral monoketone was obtained which was apparently an oxidation product of the secondary alcoholic group of still another sapogenin, \( \text{C}_{26}\text{H}_{42}\text{O}_3 \), and therefore isomeric with sarsapogenin. The sapogenins themselves were not isolated.

These conclusions have been substantiated in the case of the sapogenin, \( \text{C}_{26}\text{H}_{42}\text{O}_3 \), by the following observations which we have been able to make. In connection with one of our problems we have had occasion to prepare gitogenin by the hydrolysis of the saponin which we had collected in the course of the preparation of the cardiac glucosides from the leaves of *Digitalis purpurea*. Crude gitonin was found to crystallize in characteristic leaflets on concentration of the purified 50 per cent alcoholic extract of
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the leaves. When the crude saponin was hydrolyzed, the result-
ing sapogenin was found to melt too low for gitogenin and the
analytical figures were consistently high in carbon. It was then
found possible to separate the contaminant from gitogenin by
taking advantage of the greater solubility of the former in petrolic
ether. By this means gitogenin was readily obtained in pure
form. The more soluble substance was also readily purified and
on analysis proved to possess the formula C_{36}H_{52}O_{6}. This sub-
stance, which may be conveniently called tigogenin, proved to
be a secondary alcohol yielding on oxidation a ketone which is
probably identical with the ketone, C_{26}H_{40}O_{2}, of Windaus and
Willerding. Tigogenone yielded a monooxime. Tigogenin gave
a monoacetate and a monobenzoate. As in the case of digitogenin
and gitogenin, the remaining two oxygens cannot be characterized
directly and appear to be of oxidic character.

A comparison of sarsapogenin from the saponin of sarsaparilla
root as well as its ketone sarsapogenone with tigogenin and its
derivatives has shown that these sapogenins are isomeric. The
substances which resulted by the reduction of the ketones accord-
ing to the method of Clemmensen also proved to be different.

EXPERIMENTAL.

Tigogenin.—2 kilos of Digitalis purpurea leaves, after prelimi-
nary extraction with water, were extracted twice with 6 liters of 50
per cent alcohol. The alcoholic extracts were precipitated with
basic lead acetate, and the filtrate was freed from the excess of
lead by careful addition of ammonium sulfate. The filtrate from
PbSO_{4} was concentrated under diminished pressure to remove the
alcohol. The shining platelets which separated were collected
with water. This product, which contained considerable colored
impurity, was dissolved in a mixture of 500 cc. of 50 per cent
alcohol and 50 cc. of HCl (1.19). The solution was refluxed for 3
hours and on cooling a dark green product was obtained. This
was collected with water and then dissolved in 100 cc. of alcohol
and 15 cc. of concentrated HCl and the solution was again heated
for 3 hours. The crystals which separated on dilution with water
were repeatedly recrystallized from a small volume of alcohol until
the product was freed from colored impurities. This procedure
yielded 1.3 gm. of a mixture of tigogenin and gitogenin which
melted between 240 and 250°. An additional amount of this mixture of genins was obtained by extraction of the lead sulfate precipitate with 50 per cent alcohol and working up this extract in a manner similar to that outlined above.

A chloroform solution saturated with this mixture at room temperature was precipitated by the addition of 2 volumes of petrol ether (b.p. 40–60°). This precipitate consisted of gitogenin which was still slightly contaminated since it melted at 260–262°.

4.800 mg. substance: 4.280 mg. H₂O, 13.100 mg. CO₂.


The mother liquor was evaporated to dryness and the process was repeated until no more gitogenin could be obtained. The final residue was recrystallized several times from acetone from which it separated in the form of prisms which melted at 203–204°. About 30 to 40 per cent of the mixture of genins was found to be tigogenin.

Tigogenin is soluble in all of the ordinary solvents. It proved to be more soluble in acetone, ether, ligroin (b.p. 80–90°), and petrol ether (b.p. 40–60°) than is gitogenin. This difference in solubility is most marked in the case of petrol ether (b.p. 40–60°).

The cholesterol test gave a light yellow color which turned to a reddish brown when the solution was warmed.

[α]D₉ = −49 (c = 1.023 in pyridine).

For analysis the substance was dried at 100° and 30 mm.


Found. (a) “ 77.77, “ 10.67.
(b) “ 77.53, “ 10.72.

The molecular weight determination was made according to the method of Rast.

30.547 mg. camphor: 3.118 mg. anhydrous substance, δ = 11.75. Mol. wt. calculated, 402.3; found, 382.

Tigogenin Acetate.—A solution of 0.2 gm. of tigogenin and an equal amount of fused sodium acetate in acetic anhydride was
refluxed for 5 hours. After dilution with water the acetate separated in the form of shining plates. After recrystallization from alcohol it melted at 200°–202°.

\[ \alpha_l^\infty = -57 \text{ (c = 1.023 in pyridine).} \]

4.365 mg. substance: 3.912 mg. H₂O, 12.110 mg. CO₂.
4.880 " " 4.450 " " 13.570 " "
Found. (a) " 75.67, " 10.03.
(b) " 75.83, " 10.20.

**Tigogenin Benzoate.**—A benzene solution of 0.1 gm. of tigogenin was refluxed for 2 hours with an excess of benzoyl chloride and pyridine. After concentrating the washed benzene solution, the residue was recrystallized from acetone. The benzoate separated in the form of plates which melted at 224°–225°.

\[ \alpha_l^\infty = -37 \text{ (c = 1.027 in pyridine).} \]

3.965 mg. substance: 3.360 mg. H₂O, 11.410 mg. CO₂.
3.367 " " 2.860 " " 9.690 " "
C₂₄H₄₂O₄. Calculated. C 78.21, H 9.16.
Found. (a) " 78.48, " 9.48.
(b) " 78.49, " 9.53.

**Tigogenone.**—An acetic acid solution of 0.1 gm. of CrO₃ was added to a solution of 0.3 gm. of tigogenin in 10 cc. of acetic acid and the reaction mixture was heated on a steam bath for \( \frac{1}{2} \) hour. The solution was then diluted with 2 volumes of water and the product extracted with ether. The washed ether solution was evaporated to dryness and the residue was recrystallized from acetone. The substance separated in the form of plates which melted at 206°–207° (204°–205° according to Windaus (1)).

\[ \alpha_l^\infty = -35 \text{ (c = 1.000 in pyridine).} \]

5.447 " " 4.960 " " 15.620 " "
Found. (a) " 78.15, " 10.04.
(b) " 78.22, " 10.19.

**Tigogenone Oxime.**—A solution of 0.1 gm. of tigogenone in absolute alcohol was refluxed with an excess of hydroxylamine
hydrochloride and sodium acetate for 3 hours. The alcohol was then removed and the residue was recrystallized from acetone. The oxime separated in the form of needles which melted at 256–258° with decomposition.

3.973 mg. substance: 3.595 mg. H₂O, 10.992 mg. CO₂.
4.212 " " : 3.855 " " 11.655 " "
5.000 " " : 0.142 cc. N (28°, 759 mm.)

Found. (a) " 75.46, " 10.12.
(b) " 75.47, " 10.24.
(c) N 3.22.

Reduction of Tigogenone by Clemmensen's Method.—A solution of 0.1 gm. of tigogenone in 10 cc. of acetic acid was refluxed with 4 gm. of amalgamated zinc and 2 cc. of HCl (1.19) for ½ hour. The solution was diluted with 3 volumes of water and extracted with ether. The residue from this extract was crystallized from acetone. The product was recrystallized from methyl alcohol from which it separated as leaflets which melted at 265–267°. The yield was very poor.

4.050 mg. substance: 4.095 mg. H₂O, 12.065 mg. CO₂.
1.283 " " : 1.252 " " 3.750 " "

Found. (a) " 81.24, " 11.30.
(b) " 80.35, " 10.92.

Sarsapogenone.—0.3 gm. of sarsapogenin, which had been prepared (2) from commercial Honduras sarsaparilla root, was dissolved in 10 cc. of acetic acid. This was oxidized according to the procedure used in the case of tigogenin. The product was finally recrystallized from acetone from which it separated in the form of shining plates which melted at 220–222°.

\[ [\alpha]_D^{58} = -46 \text{ (c = 1.027 in pyridine).} \]

3.956 " " : 3.670 " " 11.345 " "

Found. (a) " 78.27, " 10.38.
(b) " 78.20, " 10.37.
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*Sarsapogenone Oxime.*—The oxime was prepared as in the case of tigogenone. The product was recrystallized from acetone from which it separated in the form of plates which melted at 126–128°.

3.967 mg. substance: 3.590 mg. H₂O, 10.992 mg. CO₂.
5.410 “ “ 0.155 cc. N (27°, 759.5 mm.).

C₃₈H₄₄O₂N. Calculated. C 75.13, H 9.95, N 3.37.
Found. (a) 75.55, 10.12.
(b) 75.56, 10.11.
(c) N 3.26.

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TIGOGENIN, A DIGITALIS SAPOGENIN
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