

Chemical examination of the leaves of Anona muricata / by Thomas Callan and Frank Tutin.

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Publication/Creation

London : Wellcome Chemical Research Laboratories, [1911]

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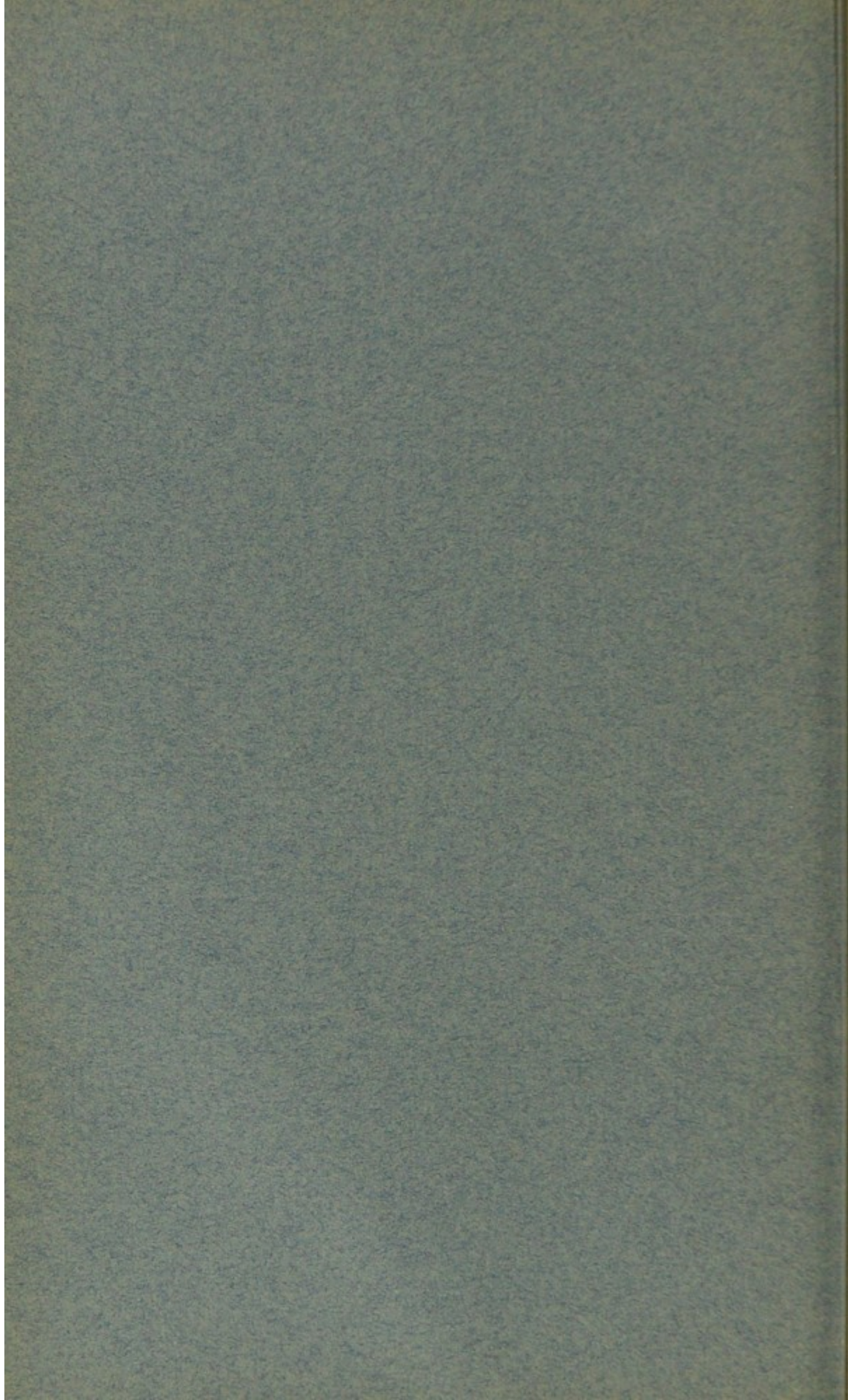
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CHEMICAL EXAMINATION
OF THE LEAVES OF
ANONA MURICATA

BY
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AND
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CHEMICAL EXAMINATION OF THE LEAVES OF ANONA MURICATA.*

BY

THOMAS CALLAN & FRANK TUTIN.

The family Anonaceæ, to which the *Anona muricata*, Linné (popularly known as "soursop") belongs, consists for the most part of tropical trees which possess considerable economic importance. Some of these trees yield edible fruits, whilst other representatives of the family are characterised by their aromatic, bitter, or antiperiodic properties. The leaves of the "soursop" are reputed to possess medicinal properties which render them useful in fever, nervousness, etc., and they are also said to be used as an anthelmintic. The seeds of *Anona muricata* and other closely related species are stated to be employed for poisoning fish and for the extermination of destructive insects (*Pharm. Review*, 1896, 14, 231).

With regard to the origin of the name *Anona*, W. C. Safford, of the United States Bureau of Plant Industry, has recorded the following information,† from which it would appear that the generic name of the plant under examination should be written *Annona*, notwithstanding the fact that *Anona* appears to be generally used by modern botanists:—"The genus *Annona*, which includes the 'custard apple' (*Annona reticulata*) and the soursop (*Annona muricata*) was described by Plumier (1703) under the name *Guanabanus*, which he adopted from *guanabano*, the vernacular name of one of the species on the island of Santo Domingo, published by Ovideo in his account of the fruit trees of the New World (1535)."

"Linnæus was at first inclined to accept as the name of this genus, *Anona*, from the vernacular name 'anon,' or 'hanon,' applied to other species, and used by various early authors; but in his '*Hortus Cliffortianus*' (1737) he rejects both *Guanabanus* and *Anona* as barbarous words, and substitutes for them the classic

* A contribution from the Wellcome Chemical Research Laboratories, London, and reprinted from *The Pharmaceutical Journal*, December 2, 1911.

† *Journal of the Washington Academy of Sciences*, 1911, p. 118.

Latin, *Annona*. This name, signifying 'the year's harvest,' of fruit, wine, etc., he thought particularly applicable, on account of the edible fruit of the *Annona*, which is relished by the natives of the countries where it grows. This was in accordance with the principle of rejecting barbarous names, which he afterwards defended in his '*Philosophie Botanique*' (1788)."

"*Annona* then, and not *Anona*, must be the name used for the genus. It was published in the first edition of the '*Species Plantarum*' (1753), from which modern binomial nomenclature takes its origin, and it is equivalent to Plumier's genus *Guanabanus*, as stated by Linnæus in his '*Genera Plantarum*' (1754). He changes the name to *Annona* and typifies the genus by the species *Annona muricata*, Plumier's "*Guanabanus fructu e viride lutescente molliter aculeato*."

"The name of the family must also preserve its original form, Annonaceæ, as published by Richard in 1808; not Anonaceæ, as published by Dunal in 1817 and by De Candolle in 1818."

EXPERIMENTAL.

The material employed for this investigation consisted of the dried leaves of *Annona muricata*, and was obtained from Dominica, W.I. A small portion (10 grammes) of the material was first tested for an alkaloid, when distinct indications of the presence of such a substance were obtained.

Twenty-five grammes of the ground material were successively extracted in a Soxhlet apparatus with various solvents, when the following amounts of extract, dried at 100°, were obtained.

	Grammes.	Per cent.
Petroleum (b.p. 35-50°) extracted	0·89	= 3·56
Ether "	0·81	= 3·24
Chloroform "	0·10	= 0·40
Ethyl Acetate "	0·50	= 2·00
Alcohol "	1·90	= 7·60
Total	4·20 Gms.,	or 16·8 per cent.

For the purpose of a complete examination, a quantity (14·38 kilograms) of the ground leaves was extracted by continuous percolation with hot alcohol. After the removal of the greater part of the solvent a dark green extract was obtained, which amounted to 2·57 kilograms.

DISTILLATION OF THE EXTRACT WITH STEAM. SEPARATION OF AN ESSENTIAL OIL.

The entire amount of the above-mentioned alcoholic extract was mixed with water, and steam passed through the mixture for several hours. The distillate, which contained some oily

drops in suspension, was thoroughly extracted with ether, the ethereal liquid being dried and the solvent removed, when 1.2 grammes of a greenish-coloured essential oil were obtained. This oil possessed a strong, rather agreeable odour, but the amount obtained was too small to permit of its further examination.

NON-VOLATILE CONSTITUENTS OF THE EXTRACT.

After the distillation of the extract with steam, as above described, there remained in the distillation flask a dark-coloured, aqueous liquid (A), together with a quantity of a soft, dark-green, oily resin (B). These products were separated by filtration, and the resin repeatedly washed with hot water until nothing further was removed, the washings being added to the main bulk of the aqueous liquid.

EXAMINATION OF THE AQUEOUS LIQUID (A).

The aqueous liquid (A) was extracted many times with ether, the combined ethereal liquids being evaporated to dryness. About 3 grammes of a dark-coloured, resinous product were thus obtained from which nothing definite could be isolated. The aqueous liquid was then similarly extracted with chloroform, and with amyl alcohol, but only small amounts of amorphous material were removed.

The original aqueous liquid, after extraction with amyl alcohol, was evaporated to a low bulk under diminished pressure, and kept for some days, when a quantity (47 grammes) of potassium chloride separated. The filtrate from this salt was diluted with alcohol, when a further 21 grammes of the same compound were obtained. The final filtrate from the potassium chloride was deprived of alcohol, diluted with water, and treated with a slight excess of a solution of basic lead acetate, when a very copious, yellow precipitate separated. This was collected, and washed with water, after which it was suspended in water and decomposed by means of hydrogen sulphide. The filtrate from the lead sulphide was dark in colour, and gave reactions which indicated it to contain a considerable amount of tannin, and also some alkaloid. It was concentrated under diminished pressure, rendered alkaline with sodium carbonate and then extracted repeatedly with ether. This removed a small amount of amorphous material, the greater part of which was evidently of an alkaloidal nature. The solution of this base in dilute hydrochloric acid gave precipitates with the usual alkaloidal reagents, and also with gold chloride and picric acid. The aurichloride and picrate obtained, however, were amorphous, and resinified on being slightly warmed.

The original filtrate from the basic lead acetate precipitate was deprived of lead by means of hydrogen sulphide, and the filtered liquid concentrated under diminished pressure to a small bulk. This concentrated liquid yielded a further amount of potassium chloride, but it contained no alkaloid. On treatment with phenylhydrazine acetate it yielded a small amount of *d*-phenylglucosazone (melting-point 205-206°), and on heating with acetic anhydride it gave a compound which crystallised from slightly diluted alcohol in glistening leaflets, melting at 115-116°.

0.1017 gave 0.1833 CO₂ and 0.0542 H₂O. C = 49.1; H = 5.9.

C₁₀H₂₂O₁₁ requires C = 49.2; H = 5.6 per cent.

The substance was therefore a penta-acetyl derivative of dextrose, and since, when mixed with β-penta-acetyldextrose, it melted at 102°, it was evidently the α-compound. The sugar present in the aqueous liquid was therefore dextrose, and no indication of the presence of any other definite compound could be obtained. No glucoside appeared to be present.

EXAMINATION OF THE RESIN (B).

The resin (B) was of a very soft, oily nature, and amounted to about 1,080 grammes. It was mixed with purified sawdust, and the thoroughly dried mixture extracted successively in a large Soxhlet apparatus with light petroleum (b.-p. 35-50°), ether, chloroform, ethyl acetate, and alcohol.

PETROLEUM EXTRACT OF THE RESIN.

The petroleum extract of the resin formed a very dark green, oily mass, and amounted to 812 grammes. It was dissolved in alcohol, and hydrolysed by boiling for some hours with an alcoholic solution of 250 grammes of potassium hydroxide. After the removal of the greater part of the solvent, the liquid was diluted with water, and the resulting mixture extracted many times with ether. The combined ethereal extracts were dried and the solvent removed, when a large amount of a viscid, yellow, oily product was obtained.

Isolation of Myricyl Alcohol, C₃₀H₆₂O.

The entire amount of the unsaponifiable matter was dissolved in 2 litres of alcohol, and the solution kept for ten days. The solid which had separated was then collected, and recrystallised several times from ethyl acetate, when a quantity (4.9 grammes) of a substance was obtained in small leaflets, melting at 84.85°.

0.1466 gave 0.4378 CO₂ and 0.1888 H₂O. C = 81.5; H = 14.3.

C₃₀H₆₂O requires C = 82.2; H = 14.1.

The substance thus appears to be myricyl alcohol.

Isolation of Sitosterol, C₂₇H₄₆O.

The original, alcoholic mother liquor from the myricyl alcohol was concentrated, when a further small amount of the same substance separated. The filtrate from the latter was then diluted with water, and kept for some time, when a large amount of dark orange-coloured oil, together with some crystalline material, separated. The solid was collected and fractionally crystallised from alcohol, when it was resolved into myricyl alcohol and a substance which formed glistening plates, melting at 133°. This substance gave the colour reactions of the phytosterols.

0.3014, on heating at 100°, lost 0.0156 H₂O. H₂O = 5.1.

0.1443* gave 0.4426 CO₂ and 0.1610 H₂O. C = 83.6; H = 12.4.

C₂₇H₄₆O, H₂O requires H₂O = 4.5 per cent.

C₂₇H₄₆O requires C = 83.9; H = 11.9 per cent.

A determination of the optical rotatory power gave the following result:—

0.2556,* made up to 20 C.c. with chloroform, gave $\alpha_D - 0^\circ 46'$ in a 2-dcm. tube; whence $[\alpha]_D - 30.0^\circ$.

The properties of this phytosterol are thus seen to agree with those of sitosterol. On heating with acetic anhydride it yielded sitosteryl acetate, which formed lustrous leaflets, melting at 126-127°.

The original, dilute alcoholic mother liquors from the crude sitosterol, which contained a large amount of oil, yielded, on further dilution, only an additional quantity of the same phytosterol, together with a little myricyl alcohol.

Examination of the Fatty Acids.

The alkaline liquid which had been deprived of unsaponifiable matter by extraction with ether, as above described, was acidified, and again extracted with ether. The ethereal liquid was observed to contain some solid material in suspension. This was collected, when it was found to contain a considerable amount of copper, together with some organic matter, but no definite organic compound could be separated from it. The clear, ethereal solution was evaporated somewhat, and a large volume of light petroleum added. This caused the precipitation of a quantity of very dark green resinous material, which consisted largely of chlorophyll, and from which nothing definite was obtained. The solvent was then removed from the petroleum-ether solution, and the residual fatty acids esterified with methyl alcohol in the presence of dry hydrogen chloride. The resulting esters, after being freed from traces of free acids, were

* Anhydrous substance.

distilled under diminished pressure, when the greater part of the material passed over as a light yellow oil, but a small portion of it, which distilled at a higher temperature, solidified on cooling.

The liquid esters were hydrolysed, and the resulting acids isolated and converted into their lead salts. On digesting the latter with ether only a portion dissolved. The acids were then regenerated from both the soluble and insoluble lead salts.

The unsaturated acids, obtained from the soluble lead salts, were distilled under diminished pressure, after which an analysis and a determination of the iodine value yielded the following results:—

0.1322 gave 0.3738 CO_2 and 0.1442 H_2O . C = 77.1; H = 12.1.

0.2442 absorbed 0.3230 iodine. Iodine value = 132.2.

$\text{C}_{18}\text{H}_{34}\text{O}_2$ requires C = 76.6; H = 12.1 per cent.; iodine value = 90.1.

$\text{C}_{18}\text{H}_{32}\text{O}_2$ requires C = 77.1; H = 11.4 per cent.; iodine value = 181.4.

It would thus appear that the unsaturated acids consisted of a mixture of oleic and linolic acids.

The saturated acids, regenerated from the insoluble lead salts, were crystallised from ethyl acetate, when they melted at 54-56°.

0.1616 gave 0.4572 CO_2 and 0.1874 H_2O . C = 76.1; H = 12.9.

$\text{C}_{18}\text{H}_{36}\text{O}_2$ requires C = 76.1; H = 12.7 per cent.

This result indicates that the saturated acids consisted chiefly of stearic acid, but the low melting-point shows that other acids must also have been present.

The previously-mentioned fraction of esters of high boiling-point, which solidified on cooling, was hydrolysed, and the resulting acid crystallised several times from glacial acetic acid. Small, glistening leaflets were then obtained, which melted at 74°.

0.1042 gave 0.2964 CO_2 and 0.1248 H_2O . C = 77.6; H = 13.3.

0.1022 neutralised 0.01633 KOH. Neutralisation value 159.8.

$\text{C}_{24}\text{H}_{48}\text{O}_2$ requires C = 78.2; H = 13.0 per cent.; neutralisation value = 152.2.

The acid obtained from the solid methyl ester is thus seen to consist of a fatty acid of high molecular weight, or a mixture of such compounds. It agrees most nearly in its properties and composition with lignoceric acid, $\text{C}_{24}\text{H}_{48}\text{O}_2$.

ETHER EXTRACT OF THE RESIN.

The ether extract of the resin (B) formed a very dark green, soft mass, and amounted to 221 grammes. It was digested with

about 300 C.c. of ether, and a small amount (about 3 grammes) of a dark green, sparingly soluble solid removed by filtration from the cooled mixture.

The filtrate from the above-mentioned solid, which contained the greater part of the ether extract of the resin, was thoroughly examined, and found to consist chiefly of a dark green, neutral product, together with chlorophyll. The neutral material was hydrolysed by heating with an alcoholic solution of potassium hydroxide, when it yielded some unsaponifiable matter containing myricyl alcohol and sitosterol, together with a quantity of acids. The latter were converted into their methyl esters, but these were undistillable, and nothing definite could be obtained from them.

Isolation of a New Dihydric Alcohol, Anonol, $C_{23}H_{36}O_2(OH)_2$.

The above-mentioned sparingly soluble material, which was separated from the ether extract of the resin, was washed with ether, and then extracted in a Soxhlet apparatus with ethyl acetate for one day. This treatment removed the greater part of the chlorophyll. The partially purified product was then extracted for many days with boiling alcohol, when an almost colourless substance was slowly removed. This product, which was nearly insoluble in cold alcohol, was purified by crystallisation from dilute pyridine, with the employment of animal charcoal. Very small, colourless leaflets were then obtained, which decomposed and melted at 294-298°.

0.1172 gave 0.3132 CO_2 and 0.1900 H_2O . C = 72.9; H = 10.3.

$C_{23}H_{36}O_2(OH)_2$ requires C = 73.0; H = 10.1 per cent.

This compound does not agree in its composition and properties with any substance previously described, and it is therefore proposed to designate it *anonol*, with consideration of the generic name of the plant from which it was obtained. Anonol is isomeric with grindelol, a dihydric alcohol isolated by Dr. Power and one of us from *Grindelia* (*Proc. Amer. Pharm. Assoc.*, 1907, 55, 342; compare also *Journ. Amer. Chem. Soc.*, 1910, 33, 90). Anonol yields colour reactions similar to those given by the dihydric alcohol, ipurganol, and it evidently belongs to the same series of compounds.

Diacetylanonol, $C_{23}H_{36}O_2(O\cdot CO\cdot CH_3)_2$.—A quantity of anonol was heated with acetic anhydride in the presence of pyridine, and the resulting product crystallised from alcohol. Long colourless, flattened needles were then obtained, which melted sharply at 166°.

0.1023 gave 0.2662 CO_2 and 0.0825 H_2O . C = 71.0; H = 8.9.

$C_{23}H_{36}O_2(O\cdot CO\cdot CH_3)_2$ requires C = 70.8; H = 8.8 per cent.

This substance was therefore diacetylanonol.

Dibenzoylanonol, $C_{23}H_{36}O_2(O\cdot CO\cdot C_6H_5)_2$.—A quantity of anonol was dissolved in pyridine and benzoyl chloride added. The mixture was then heated to boiling, cooled, and treated with water, when the precipitated solid was collected. This was dissolved in chloroform, and the solution diluted with alcohol, when small, colourless needles were obtained, which melted at 197° - 198° .

0.1148 gave 0.3197 CO_2 and 0.0804 H_2O . C = 75.9; H = 7.8.

$C_{23}H_{36}O_2(O\cdot CO\cdot C_6H_5)_2$ requires C = 75.8; H = 7.8 per cent.

This compound is thus seen to be dibenzoylanonol.

CHLOROFORM, ETHYL ACETATE, AND ALCOHOL EXTRACTS OF THE RESIN.

These products consisted of black resins, and amounted to 6.1, 6.4, and 32.0 grammes respectively. They were carefully examined, but nothing definite could be isolated from any of them, and they gave no indication of containing any glucoside.

SUMMARY.

The results of this investigation may be summarised as follows:—

The material employed consisted of the dried leaves of *Anona muricata*, Linné, which had been obtained from Dominica, W.I. An alcoholic extract of this material, when distilled with steam, yielded a small amount of an essential oil, which possessed a strong, somewhat agreeable odour.

The portion of the alcoholic extract which was soluble in water contained a large amount of potassium chloride, together with dextrose, tannin, amorphous products, and a small amount of an alkaloidal substance, which could not be crystallised.

The portion of the extract which was insoluble in water was a dark green resin, consisting largely of fatty matter. From this resin the following definite substances were isolated:—Myricyl alcohol (m.-p., 84° - 85°); sitosterol, $C_{27}H_{46}O$ (m.-p., 133°); a mixture of fatty acids, consisting largely of oleic, linolic and stearic acids, together with a higher fatty acid, possibly lignoceric acid; and a new, dihydric alcohol, *anonol*, $C_{23}H_{36}O_2(OH)_2$ (m.-p., 294° - 298°), which yields a *diacetyl derivative*, $C_{23}H_{36}O_2(O\cdot CO\cdot CH_3)_2$, melting at 166° , and a *dibenzoyl derivative*, $C_{23}H_{36}O_2(O\cdot CO\cdot C_6H_5)_2$, melting at 197° - 198° .

