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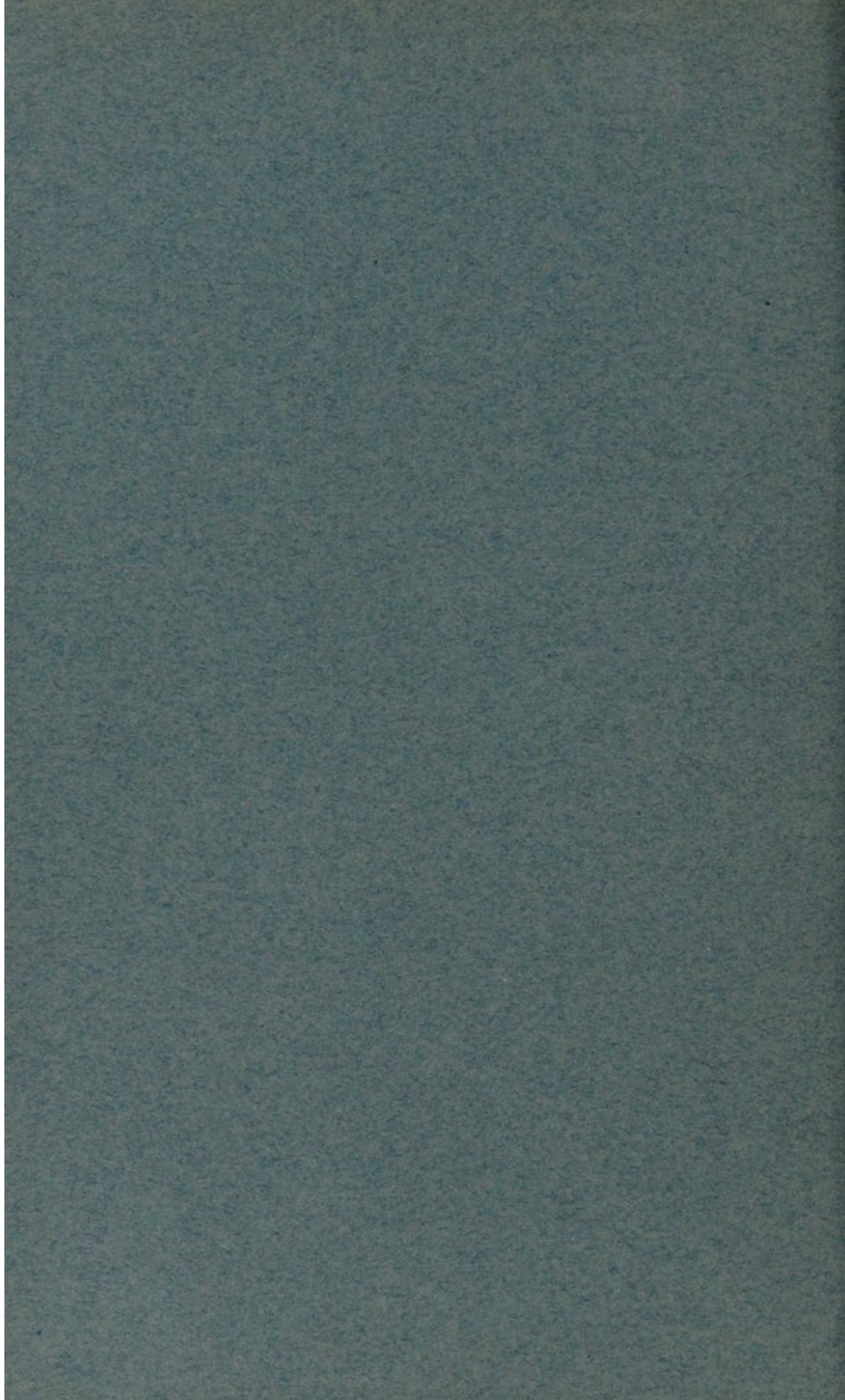
THE CONSTITUENTS
OF
COLOCYNTH

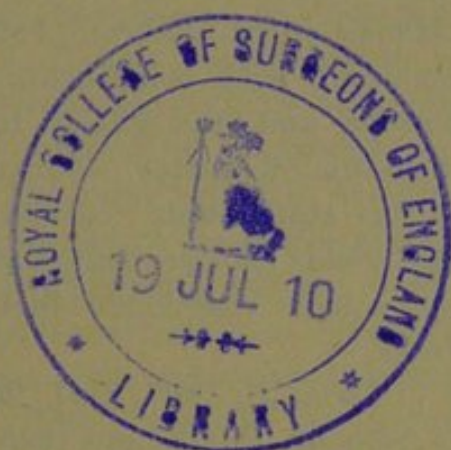
BY
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XII.—*The Constituents of Colocynth.*

By FREDERICK BELDING POWER and CHARLES WATSON MOORE.

UNDER the title of "*Colocynth*" the various national Pharmacopœias recognise the dried, peeled fruit, or the dried pulp of the fruit, of *Citrullus Colocynthis*, Schrader. Although this fruit has been used medicinally for a very long period, and has been the subject of several investigations, no complete chemical examination has hitherto been made of it, and the various products described in the literature as having been obtained therefrom were either amorphous or of an indefinite nature. It was recorded, for example, many years ago by Walz (*N. Jahrb. Pharm.*, 1858, 9, 16, 225; 1861, 16, 10) that colocynth contains a bitter glucoside, designated "*colocynthin*," which, although usually forming a yellow, amorphous mass, could be obtained in a crystalline state by the slow evaporation of its alcoholic solution.

This so-called colocynthin, to which the formula $C_{56}H_{84}O_{23}$ was assigned, was stated to yield, on heating with dilute acids, dextrose and "colocynthein," the latter having been described as an amorphous resin. The same investigator noted the occurrence of a tasteless, crystalline substance, designated "colocynthitin," which was found to be insoluble in water and cold absolute alcohol, but soluble in boiling alcohol and ether, although its characters do not appear to have been further determined. Henke (*Arch. Pharm.*, 1883, 221, 200) could obtain a product corresponding with colocynthin only in the form of a yellow, amorphous powder, and was unable to confirm the statement respecting its glucosidic character. Johannson (*Zeitsch. anal. Chem.*, 1885, 24, 154) has stated that "colocynthin, when heated with dilute sulphuric acid, yields colocynthein, elaterin, and bryonin," and he recorded some colour reactions which were supposed to differentiate these products.

Naylor and Chappel (*Pharm. J.*, 1907, [iv], 25, 117), in a paper entitled: "On *Cucumis trigonus*, Roxb., and Colocynthin," have compared a product obtained by them from the fruit of the above-mentioned species of *Cucumis*, indigenous to India, with the so-called "colocynthin" obtained from colocynth by Henke's method and by a modification of the latter. It is stated that whilst the product obtained from either the Indian fruit or from colocynth by Henke's process was amorphous, "that resulting from the modified process was most largely deposited on spontaneous evaporation of its solvent in pale yellow needles." They were thus led to conclude, in the first place, that "colocynthin prepared from *Citrullus Colocynthis* may be obtained in a crystalline state, despite the failure of Henke and of Wagner to induce it to assume a crystalline form"; secondly, that notwithstanding the doubts cast by Henke upon its decomposition by acids into colocynthein and a sugar, their results on the contrary confirm those of Johannson (*loc. cit.*), that colocynthin is capable of hydrolysis, and that it yields, amongst other products, colocynthein and elaterin, to which they may add—and a sugar, dextrose. The same authors furthermore state that "colocynth contains a white, crystalline body, agreeing in its general characters with the colocynthetin (*colocynthitin*) of Walz." There is, however, no evidence that any of the products prepared and examined by Naylor and Chappel were pure or homogeneous substances, and their comparison of them was chiefly restricted to certain colour reactions which are by no means characteristic of the substances they are supposed to identify. On the other hand, it may quite safely be assumed that the products referred to were very indefinite mixtures.

The present investigation has shown that colocynth contains a considerable amount of α -elaterin (*Trans.*, 1909, 95, 1989), which

is present in the free state, together with other compounds which have not previously been isolated. A complete summary of the results now obtained, with the deductions from them, is given at the end of this paper.

EXPERIMENTAL.

The material employed in this investigation was Turkish colocynth, consisting of the dried, peeled fruit of *Citrullus Colocynthis*, Schrader. The original weight of this material was 105 kilograms. After separating as completely as possible the seeds from the pulp, the latter was found to weigh 25.6 kilograms, or 24.4 per cent. of the whole. The seeds amounted to 79.3 kilograms, thus representing 75.5 per cent. of the weight of the entire peeled fruit.

A small portion (10 grams) of the above-mentioned pulp was subjected to the test for an alkaloid, when reactions were obtained indicating the presence of an appreciable amount of such a substance.

A further portion (20 grams) of the ground pulp was extracted successively in a Soxhlet apparatus with various solvents, when the following amounts of extract, dried at 100°, were obtained.

Petroleum (b. p. 35—50°)	extracted	0.33 gram	=	1.65 per cent.
Ether	"	1.75 "	=	8.75 "
Chloroform	"	1.06 "	=	5.30 "
Ethyl acetate	"	0.61 "	=	3.05 "
Alcohol	"	0.92 "	=	4.60 "
Total		4.67 grams	= 23.35 per cent.	

For the purpose of a complete examination, 24.6 kilograms of the ground colocynth pulp were completely extracted with hot alcohol. After the removal of the greater portion of the alcohol, a viscid, dark-coloured extract was obtained, amounting to 6.63 kilograms.

Distillation of the Extract with Steam.

A quantity (2 kilograms) of the above-mentioned extract, representing 7.42 kilograms of the pulp, was mixed with water, and steam passed through the mixture for several hours. The distillate, which amounted to 4 litres, contained some drops of oil floating on the surface. It was extracted with ether, the ethereal liquid being washed, dried, and the solvent removed, when a small quantity of an essential oil was obtained. This was a pale yellow liquid, which possessed a characteristic odour, and, after some time, deposited a small amount of a crystalline substance. The amount of this oil was, however, too small to permit of its further investigation.

Non-volatile Constituents of the Extract.

After the distillation of the extract with steam, as described above, there remained in the distillation flask a dark-coloured, aqueous liquid (A) and a quantity of a brown resin (B). The latter was collected and repeatedly washed with water until nothing further was removed, the washings being added to the above-mentioned aqueous liquid.

*Examination of the Aqueous Liquid (A).**Isolation of a New Dihydric Alcohol, Citrullol, $C_{22}H_{36}O_2(OH)_2$.*

The aqueous liquid (A), which amounted to 6.5 litres, was repeatedly extracted with ether, and the ethereal extracts united, after which a quantity of a colourless, sparingly soluble substance which accompanied them was separated by filtration.

This substance was almost insoluble in all the ordinary solvents, and appears to have been contained in the aqueous liquid in a colloidal form. It was, however, readily soluble in hot pyridine, from which it crystallised in glistening plates, melting and decomposing at 285—290°. The quantity so obtained was 0.9 gram:

0.1253 gave 0.3310 CO_2 and 0.1192 H_2O . $C = 72.0$; $H = 10.6$.

$C_{22}H_{38}O_4$ requires $C = 72.1$; $H = 10.4$ per cent.

This substance, when dissolved in chloroform with a little acetic anhydride, gave on the addition of a few drops of concentrated sulphuric acid a series of colour reactions similar to those produced by ipuranol, $C_{23}H_{38}O_2(OH)_2$ (Trans., 1909, 95, 249), and it appears, in fact, to be a lower homologue of the latter. As it does not agree in its properties with any substance of the above formula which has hitherto been described, it is proposed to designate it *citrullol*, with reference to the generic name of the plant from which it has been obtained.

It was ascertained that citrullol exhibits no physiological activity when administered to a dog in doses of 0.05 gram.

Diacetylcitrullol, $C_{22}H_{36}O_4(CO \cdot CH_3)_2$.—This was obtained by heating citrullol with acetic anhydride, from which it separated in glistening needles, melting at 167°:

0.1330 gave 0.3378 CO_2 and 0.1098 H_2O . $C = 69.3$; $H = 9.2$.

$C_{26}H_{42}O_6$ requires $C = 69.3$; $H = 9.3$ per cent.

The ethereal liquid from which the citrullol had been separated by filtration, as above described, was subsequently evaporated, but it yielded only a resinous product from which nothing definite could be isolated.

Isolation of an Alkaloidal Principle.

The aqueous liquid, which had previously been extracted with ether, was treated with a solution of basic lead acetate. This produced a voluminous, yellow precipitate, which was collected, washed, and then suspended in water and decomposed by hydrogen sulphide. On filtering the mixture a liquid was obtained which, after acidifying with hydrochloric acid, responded to the ordinary alkaloid reagents. It was rendered alkaline by means of ammonia, and extracted many times with chloroform. The chloroform extracts were united and repeatedly shaken with dilute (10 per cent.) hydrochloric acid. The acid liquids were at once brought into a solution of ammonia, and the precipitated base extracted by means of chloroform. On the evaporation of the solvent there was obtained a small amount (about 5 grams) of a light brown product, which was resinous in character, very weakly basic, and possessed an extremely bitter taste. It dissolved sparingly in dilute acids, and was precipitated from its solutions by the usual alkaloid reagents, including tannin. Neither the free base nor its salts could be obtained in a crystalline condition. On warming the base with alkali hydroxides it dissolved, and, on prolonged boiling, ammonia was evolved. When heated with 20 per cent. hydrochloric acid it yielded ammonia and pyridine, the latter having been identified by its odour, and by the formation of its platinochloride.

The basic principle was not glucosidic, as no sugar was formed on boiling its acid solutions. It represents one of the physiologically active constituents of colocynth, as doses of 0.1 gram administered to dogs produced very drastic purgation.

The filtrate from the above-mentioned basic lead acetate precipitate was treated with hydrogen sulphide for the removal of the excess of lead, and the filtered liquid concentrated under diminished pressure to a small volume. It was then treated with a large volume of strong alcohol, which effected the precipitation of a quantity of inorganic salts, consisting chiefly of the chloride, sulphate, and nitrate of potassium, together with a little sugar. The latter yielded *d*-phenylglucosazone, melting at 208—210°. The clear alcoholic liquid was decanted from the precipitated material, mixed with purified sawdust, and the thoroughly dried mixture extracted in a Soxhlet apparatus with chloroform. This removed a small quantity of a brown syrup, which, on hydrolysis, yielded a sugar which readily reduced Fehling's solution, and from which *d*-phenylglucosazone, melting at 208—210°, was prepared. It is therefore evident that the aqueous liquid contained a very small amount of a glucosidic substance, but this could

not be obtained in a form which would permit of its being more definitely characterised.

Examination of the Resin (B).

Isolation of α -Elaterin.

This resin was a brown solid, which softened below 100° , and amounted to 675 grams. It was digested with about 2 litres of strong alcohol, in which it only partly dissolved. The undissolved portion was collected, washed first with alcohol, and then with ether, when it was obtained in small, colourless crystals, melting and decomposing at $227-230^{\circ}$. On recrystallising this product from alcohol, it formed small, glistening, hexagonal prisms, melting and decomposing at 232° . The amount of crystalline substance thus obtained was 80 grams, corresponding with about 1.08 per cent. of the weight of colocynth pulp employed :

0.1446 gave 0.3655 CO_2 and 0.1060 H_2O . C = 68.9 ; H = 8.1.

$\text{C}_{20}\text{H}_{28}\text{O}_5$ requires C = 68.9 ; H = 8.0 per cent.

$\text{C}_{24}\text{H}_{34}\text{O}_6$,, C = 68.9 ; H = 8.0 ,, ,,

$\text{C}_{28}\text{H}_{38}\text{O}_7$,, C = 69.1 ; H = 7.8 ,, ,,

This substance agrees in crystalline form, melting point, and solubility, and in all its chemical properties with α -elaterin, as previously described by us (Trans., 1909, 95, 1989). Its empirical formula cannot yet be considered definitely established.

A determination of its specific rotatory power gave the following result :

0.3121, made up to 20 c.c. with chloroform, gave $\alpha_D - 2^{\circ}9'$ in a 2-dcm. tube, whence $[\alpha]_D - 68.9^{\circ}$.

The alcoholic solution of the resin (B), from which the α -elaterin had been separated by filtration as above described, together with the alcoholic and ethereal washings from the latter, was mixed with purified sawdust, the thoroughly dried mixture being then successively extracted in a Soxhlet apparatus with light petroleum (b. p. $35-50^{\circ}$), ether, chloroform, ethyl acetate, and alcohol.

Petroleum Extract of the Resin (B).

Isolation of Hentriacontane, $\text{C}_{31}\text{H}_{64}$, and a Phytosterol, $\text{C}_{27}\text{H}_{46}\text{O}$.

This extract was a dark green, waxy solid, and amounted to 34 grams. It was dissolved in ether, the ethereal solution being successively shaken with dilute aqueous sodium carbonate and sodium hydroxide, which, however, removed nothing. The ether was accordingly evaporated, and the residue hydrolysed by boiling with an

alcoholic solution of potassium hydroxide, after which the alcohol was removed, water added, and the alkaline solution of potassium salts extracted with ether. The ethereal liquid was washed, dried, and the solvent removed, when a small quantity of a crystalline product was obtained. This was dissolved in 250 c.c. of absolute alcohol, and the solution kept for some hours, when a small quantity of an almost colourless substance separated. This was collected and washed with cold alcohol, after which it was distilled under diminished pressure. The distillate, which rapidly solidified, was crystallised from ethyl acetate, when small, glistening, colourless leaflets, melting at 68° , were obtained:

0.1344 gave 0.4176 CO_2 and 0.1824 H_2O . $\text{C} = 84.7$; $\text{H} = 15.0$.

$\text{C}_{31}\text{H}_{64}$ requires $\text{C} = 85.3$; $\text{H} = 14.7$ per cent.

The substance was thus identified as hentriacontane.

The alcoholic solution from which the hentriacontane had been removed by filtration was concentrated to a small volume and diluted with water, when a quantity of a crystalline substance separated. This was collected and washed with a little ethyl acetate, after which it was distilled under diminished pressure. The distillate was crystallised from a mixture of dilute alcohol and ethyl acetate, when it formed colourless, glistening leaflets, melting at 160 — 162° . The amount of substance so obtained was 1.3 grams:

0.2205, heated at 115° , lost 0.0104 H_2O . $\text{H}_2\text{O} = 4.7$.

0.1493 gave 0.4560 CO_2 and 0.1590 H_2O . $\text{C} = 83.3$; $\text{H} = 11.8$.

$\text{C}_{27}\text{H}_{46}\text{O}, \text{H}_2\text{O}$ requires $\text{H}_2\text{O} = 4.5$ per cent.

$\text{C}_{27}\text{H}_{46}\text{O}$ requires $\text{C} = 83.9$; $\text{H} = 11.9$ per cent.

This substance thus agrees in composition with a phytosterol, and it yielded the colour reactions of this class of compounds. It was found to be optically inactive, and in this respect appears to differ from any of the phytosterols which have hitherto been recorded. The acetyl derivative, when crystallised from acetic anhydride, separated in glistening plates, melting at 175 — 177° .

Examination of the Fatty Acids.

The aqueous, alkaline solution of potassium salts, from which the hentriacontane and phytosterol had been removed by extraction with ether, was acidified and again extracted with ether. The ethereal solution was washed, dried, and the solvent removed, when a quantity (12 grams) of fatty acids was obtained which, when distilled under diminished pressure, passed over between 220° and $250^{\circ}/15$ mm. Ten grams of the mixed acids were converted into their lead salts, and the latter digested with ether, when the greater portion dissolved. Both the soluble and insoluble portions were decomposed by hydro-

chloric acid, and the regenerated fatty acids purified by distillation under diminished pressure. The soluble portion of the lead salts yielded 8 grams of liquid acids, whilst the insoluble portion gave 1.5 grams of solid acids.

The Liquid Acids.—These acids, when distilled under diminished pressure, passed over between 225° and $235^{\circ}/15$ mm. An analysis and a determination of the iodine value gave the following results:

0.1406 gave 0.3964 CO_2 and 0.1460 H_2O . $\text{C} = 76.9$; $\text{H} = 11.5$.

0.5625 absorbed 0.8346 iodine. Iodine value = 148.4.

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

$\text{C}_{18}\text{H}_{32}\text{O}_2$ „ $\text{C} = 77.1$; $\text{H} = 11.4$ „ „ Iodine value = 181.4.

In order to obtain more definite information respecting the nature of the above mixture, a quantity of it was oxidised according to the method described by Lewkowitsch (*Chemical Technology and Analysis of Oils, Fats, and Waxes*, 1904, Vol. I., p. 360). This resulted in the formation of dihydroxystearic acid (m. p. $125-127^{\circ}$) and tetrahydroxystearic acid (m. p. $157-160^{\circ}$), the latter in predominating amount.

It may thus be concluded that the liquid acids consisted chiefly of a mixture of oleic and linolic acids, the latter predominating.

The Solid Acids.—These acids melted at $56-58^{\circ}$, and, on analysis, gave the following result:

0.1430 gave 0.3955 CO_2 and 0.1636 H_2O . $\text{C} = 75.4$; $\text{H} = 12.7$.

$\text{C}_{16}\text{H}_{32}\text{O}_2$ requires $\text{C} = 75.0$; $\text{H} = 12.5$ per cent.

$\text{C}_{18}\text{H}_{36}\text{O}_2$ „ $\text{C} = 76.1$; $\text{H} = 12.7$ „ „

By repeated crystallisation from acetic acid a small amount of an acid melting at $68-69^{\circ}$ was obtained, from which a silver salt was prepared and analysed:

0.2118 gave 0.0576 Ag. $\text{Ag} = 27.2$.

$\text{C}_{18}\text{H}_{35}\text{O}_2\text{Ag}$ requires $\text{Ag} = 27.6$ per cent.

From the above results it is evident that the solid acids consisted of a mixture of palmitic and stearic acids.

Ether and Chloroform Extracts of the Resin (B).

These extracts amounted to 169 and 180 grams respectively. They were light-coloured resins, and, with the exception of about 10 grams of α -elaterin and a little of the previously-mentioned citrullol, nothing definite could be isolated from them. When heated with a solution of sulphuric acid in dilute alcohol they yielded no sugar, and therefore contained nothing glucosidic.

Both of the above-mentioned extracts were found to possess a very marked cathartic action, which was doubtless due in part to

the presence of small quantities of the previously described alkaloidal principle, as about 3 grams of the latter were obtained from them. The activity of the extracts was, however, not appreciably diminished by the complete removal of the alkaloidal principle, as they then produced drastic purgation when administered to dogs in doses of 0.1 gram.

Ethyl Acetate and Alcohol Extracts of the Resin (B).

These extracts were brown resins, amounting to 85 and 100 grams respectively, and nothing definite could be isolated from them. They were not glucosidic, and possessed no purgative action.

Examination of Colocynth Seeds.

The material required for the proceeding investigation of the pulp of colocynth fruit having rendered available a large quantity of the seeds, it appeared desirable to examine the latter with respect to their more important constituents.

A small portion (10 grams) of the crushed seed was tested for the presence of an alkaloid by treatment with Prollius's fluid, when distinct reactions were obtained with the usual reagents. These reactions were probably due to the presence of a very small amount of the same alkaloidal principle as that contained in the pulp of the fruit.

Separation of an Enzyme.

A quantity (2 kilograms) of the crushed seed was extracted by percolation with cold light petroleum for the removal of the fatty oil, after which the material was mixed with cold water and the mixture kept for several hours. The aqueous liquid was then expressed and filtered, and to it a quantity of strong alcohol was added. A voluminous, light-coloured precipitate was thus produced, which was collected, washed with a little alcohol, and dried in a desiccator. The product so obtained amounted to 10 grams, and, although containing a large proportion of inorganic material, it readily hydrolysed β -glucosides.

The Fatty Oil.

The amount of fatty oil contained in the seed, as determined by the extraction of 50 grams of the ground material in a Soxhlet apparatus with light petroleum (b. p. 35—50°), was 12.72 per cent.

The oil obtained was a clear pale yellow liquid, which was devoid of optical activity. A determination of its constants gave the following results: specific gravity, 20°/20° = 0.9273; acid value, 2.6; saponification value, 186.7; iodine value, 126.6.

Hydrolysis of the Fatty Oil. Isolation of a Phytosterol, C₂₀H₃₄O.

A quantity (150 grams) of the oil was hydrolysed by boiling with alcoholic potassium hydroxide, the alcohol removed, water added, and the alkaline solution of potassium salts extracted with ether. The ethereal liquid was washed, dried, and the solvent removed, when a small quantity of a crystalline substance was obtained. This was distilled under diminished pressure, after which it was crystallised from a mixture of dilute alcohol and ethyl acetate, when it separated in colourless, glistening plates, melting at 158—160°. The amount of substance so obtained was 0.3 gram:

0.1700 gave 0.5154 CO₂ and 0.1724 H₂O. C = 82.7; H = 11.3.

C₂₀H₃₄O requires C = 82.8; H = 11.7 per cent.

This substance was evidently a phytosterol, and it yielded the colour reactions of this class of compounds. A determination of its specific rotatory power gave the following result:

0.2473, made up to 20 c.c. with chloroform, gave $\alpha_D + 0^\circ 12'$ in a 2-dcm. tube, whence $[\alpha]_D + 8.1^\circ$.

The acetyl derivative, when crystallised from acetic anhydride, separated in glistening plates, melting at 167—170°.

The Fatty Acids.

The alkaline solution of potassium salts, which had been extracted with ether as above described, was acidified and again extracted with ether, the ethereal solution being washed, dried, and the solvent removed. The fatty acids thus obtained amounted to 87 per cent. of the weight of the oil. When distilled under diminished pressure, they passed over between 240° and 245°/15 mm. as a viscous liquid, which solidified on cooling to a soft, nearly colourless mass. A determination of the constants of the total acids gave the following results:

Melting point (complete fusion), 29.5—32°; specific gravity, 50°/50° = 0.8910; neutralisation value, 195.6; iodine value 131.1.

These constants, both for the fatty oil and the total acids obtained therefrom, are in fairly close agreement with those recently recorded by Grimaldi and Prussia (*Chem. Zeit.*, 1909, 33, 1239). The last-mentioned investigators had, however, extracted the colocynth seeds by means of carbon tetrachloride, and describe the oil as having a reddish-yellow colour with a slight green fluorescence.

Summary.

The results of the preceding investigation may be summarised as follows:

The material employed consisted of the dried, peeled fruit of *Citrullus Colocynthis*, Schrader. The pulp of the fruit, deprived of its seeds, represented 24.4 per cent. of the whole.

On extracting the pulp with alcohol, and subjecting the resulting extract to distillation with steam, a very small amount of a pale yellow essential oil was obtained. From the portion of the extract which was soluble in water, the following substances were isolated: (i) A new dihydric alcohol, $C_{22}H_{36}O_2(OH)_2$ (m. p. 285—290°), designated as *citrullol*, which is apparently a lower homologue of ipuranol, and yields a *diacetyl* derivative melting at 167°. (ii) An amorphous, alkaloidal principle, which is a very weak base, and from which no crystalline derivative could be prepared; it possesses an extremely bitter taste, and represents one of the purgative principles of the fruit. The aqueous liquid from which the above-mentioned substances were isolated contained, furthermore, a quantity of inorganic salts, a little sugar, and a very small amount of an amorphous, glucosidic substance.

The portion of the alcoholic extract which was insoluble in water consisted chiefly of resinous material, from which, however, a quantity of α -elaterin (m. p. 232°; $[\alpha]_D - 68.9^\circ$) was isolated (compare Trans., 1909, 95, 1989). After the separation of the latter substance, the resin was extracted with various solvents, when it yielded a small amount of hentriacontane, $C_{31}H_{64}$ (m. p. 68°); a phytosterol, $C_{27}H_{46}O$ (m. p. 160—162°, optically inactive); a mixture of fatty acids, and a further quantity of α -elaterin, together with a little of the above-described alkaloidal principle. None of the extracts from the resin were glucosidic. The ether and chloroform extracts possessed marked purgative properties, even after the complete removal of the active alkaloidal principle.

The seeds of the colocynth, which represented 75.5 per cent. of the entire peeled fruit, were found to contain traces of an alkaloidal principle, a small amount of an enzyme which hydrolyses β -glucosides, and a quantity of fatty oil corresponding to 12.72 per cent. of the weight of the seed. The constants of the fatty oil, and of the total fatty acids obtained therefrom, were determined, and from the oil a small amount of a phytosterol, $C_{20}H_{34}O$, was isolated, which melted at 158—160°, and had $[\alpha]_D + 8.1^\circ$.

The results of the present research have established the fact that the so-called "colocynthin" and "colocynthitin," as well as the other products obtained from colocynth by previous investigators to which specific names have been attached, consisted of mixtures of a very indefinite character, and that the amount of glucosidic substance contained in the fruit is extremely small. On the other hand, it has now been ascertained that the purgative action of colocynth is due to

at least two principles, one of which is alkaloidal, although a very weak base, and apparently incapable of forming any crystalline salts, whilst the other source of activity is represented by some non-basic principle or principles contained in both the ether and chloroform extracts of the resin. All the attempts to obtain the last-mentioned active principle in a more definite form were, however, unsuccessful. No evidence could be obtained of the presence in colocynth of β -elaterin, which constitutes the physiologically active constituent of the fruit of *Ecballium Elaterium*.

In conclusion, the authors desire to express their best thanks to Dr. H. H. Dale, Director of the Wellcome Physiological Research Laboratories, for having kindly conducted the numerous physiological tests involved in this investigation.

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