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THE CONSTITUENTS  
OF  
RHUBARB

BY  
FRANK TUTIN  
AND  
HUBERT W. B. CLEWER

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## XCIX.—*The Constituents of Rhubarb.*

By FRANK TUTIN and HUBERT WILLIAM BENTLEY CLEWER.

PERHAPS no drug recognised by any of the national Pharmacopœias has more frequently engaged the attention of chemists than rhubarb. Notwithstanding this fact, it appeared to the present authors that our knowledge respecting the constituents of this drug was by no means complete, and a thorough investigation of the subject was therefore undertaken.

Amongst the earliest communications on the subject were those by Geiger (*Annalen*, 1823, **8**, 47; 1824, **9**, 91, 304), who described



a product called "rhabarberin." This was shown by Schlossberger and Döpping (*Annalen*, 1844, **50**, 214) to be identical with chrysophanic acid, which had, in the meantime, been described by Rochleder and Heldt, but it would appear probable that it was a mixture of this compound and emodin monomethyl ether. De la Rue and Müller (*Journ. Chem. Soc.*, 1857, **10**, 298) examined a deposit from "*Extractum Rhei*," from which they obtained "chrysophane" and a new compound, designated as emodin. Hesse (*Pharm. J.*, 1895, [iv], I, 352; and *Annalen*, 1899, **309**, 32) recorded the occurrence in rhubarb of rhein and "rhabarberon" (an isomeride of emodin), but was unable to isolate pure chrysophanic acid, this being always associated with a methylated constituent, which was assumed to be a methyl ether of chrysophanic acid. The next communication of importance on Chinese rhubarb was by Tschirch and Heuberger (*Arch. Pharm.*, 1902, **204**, 596), who failed to obtain the "rhabarberon" of Hesse, but isolated gallic acid, a substance giving the reactions of a cholesterol, impure chrysophanic acid, emodin, rhein, and two amorphous, glucosidic products, namely, rheotannoglucoside and rheoanthraglucoside. The former of these products, on hydrolysis, gave a levorotatory sugar and small amounts of gallic and cinnamic acids, together with amorphous products, whilst the latter "glucoside" yielded a dextrorotatory sugar, small amounts of the acids mentioned, a mixture of anthraquinone derivatives, and amorphous material. Eyken (*Pharm. Weekblad*, 1904, **41**, 177) isolated impure chrysophanic acid, emodin, "isoemodin," and rhein, together with "anthraglucosides," and Tschirch and Eyken (*Schweiz. Woch. Pharm.*, 1904, Nos. 40 and 41) stated that "isoemodin" is probably identical with Hesse's "rhabarberon." Gilson (*Compt. rend.*, 1903, **136**, 385) claimed to have isolated two crystalline glucosides, "glucogalline" and "tétrarine." The former of these was stated to yield dextrose and gallic acid, whilst the latter gave the same sugar, gallic and cinnamic acids, and "rhéosmine." Quite recently, Oesterle and Johann (*Arch. Pharm.*, 1910, **248**, 476) showed in an indirect way that the methylated substance with which the chrysophanic acid from rhubarb is invariably associated was emodin monomethyl ether, identical with that associated with chrysophanic acid in *Rumex Ecklonianus*, Meissner (Tutin and Clewer, *Trans.*, 1910, **97**, 1).

In addition to the compounds mentioned in the foregoing review of the literature, most of the above-mentioned investigators also describe, under various names, a number of amorphous products, which were obviously of indefinite composition. Mention is several times made, however, of the presence in rhubarb of "glucose" and of a neutral fat.



The results of the present investigation are summarised at the end of this paper, but a few of them may be discussed here.

The present authors have isolated emodin monomethyl ether from rhubarb,\* thus confirming Oesterle and Johann's statement, and have found that the "rhabarberon" of Hesse and the "isoemodin" of Tschirch and Eyken were really only somewhat impure aloemodin. A new anthraquinone derivative,  $C_{17}H_{10}O_6$ , which it is proposed to designate *rheinolic acid*, has also been isolated. The opinion of Tschirch and Heuberger (*loc. cit.*) that rhubarb contains two glucosides, "rheotannoglucoside" and "rheoanthraglucoside," cannot be accepted. A mixture of the glucosides of rhein, emodin, aloemodin, emodin monomethyl ether, and chrysophanic acid occurs in rhubarb, and when free from resin this mixture crystallises well, but it is entirely devoid of purgative action. The mother liquors from the anthraquinone glucosides yielded, however, a quantity of a non-glucosidic resin, which was strongly purgative. The "rheoanthraglucoside" of Tschirch and Heuberger, which was amorphous, was evidently a mixture of the non-glucosidic resin and the glucosides of the anthraquinone derivatives. Only a relatively small amount of a product which can properly be called a tannin is present in rhubarb, free gallic acid, which is present in very large amount, being the chief astringent constituent of the drug. No glucoside of gallic acid is present, but this acid, together with cinnamic acid, occurs to a small extent as an ester, although the latter acid, like the former, is chiefly present in the free state. The sugar yielded by the various glucosidic products was in every case dextrose. It is evident, therefore, that the lævorotatory sugar obtained by Tschirch and Heuberger from their "rheotannoglucoside" must have contained considerable lævulose, which had been occluded in the indefinite mixture which was regarded by them as a glucoside.

The only anthraquinone derivatives present in rhubarb which possess a purgative action are aloemodin and chrysophanic acid, but neither of these is nearly so active as the resin.

Finally, it may be of interest to recall the present state of our knowledge regarding the mutual relationship of the anthraquinone derivatives occurring in rhubarb: Chrysophanic acid\* is a dihydroxymethylanthraquinone, but the relative positions of the groups is not known with certainty. Emodin is a hydroxychrysophanic acid, whilst emodin monomethyl ether is the corresponding methoxychrysophanic acid. Aloe-emodin is the primary alcohol

\* The name "chrysophanic acid" is misleading, as the substance contains no carboxyl group. Chrysophanol would be a much more appropriate designation for the compound in question (compare *Arch. Pharm.*, 1911, 249, 222).



(hydroxymethyldihydroxyanthraquinone) corresponding with chrysophanic acid, whilst rhein is the corresponding carboxylic acid, and may be formed by the oxidation of aloë-emodin.

### EXPERIMENTAL.

The material employed in the present investigation consisted of the best quality of sun-dried "Shensi" rhubarb. As a preliminary experiment, 20 grams of the ground rhizome were extracted successively in a Soxhlet apparatus with various solvents, the following amounts of extract, dried at 110°, being obtained:

Petroleum (b. p. 35—50°) extracted	0.35 per cent.
Ether	4.25 " "
Chloroform	0.85 " "
Ethyl acetate	16.95 " "
Alcohol	21.85 " "

Total ..... = 44.25 per cent.

A quantity (20.84 kilograms) of the ground rhizome was then completely extracted by continuous percolation with hot alcohol, and the resulting extract concentrated under diminished pressure, when 10.8 kilograms of a viscid extract containing small lumps of granular solid were obtained. Five kilograms of this extract were then mixed with water, and steam passed through the mixture until volatile products ceased to be removed.

#### *Examination of the Steam Distillate.*

The yellow distillate was extracted with ether, and the ethereal liquid shaken successively with aqueous ammonium carbonate,\* sodium carbonate, and potassium hydroxide. The ammonium carbonate extract yielded, on acidification, 0.2 gram of a liquid acid, which was identified by the analysis of its silver salt as a hexoic acid.

The sodium carbonate extract yielded a little palmitic acid (m. p. 62°), and the potassium hydroxide extract gave a small amount of a product crystallising in golden-coloured plates, melting at 190°, which was found to be pure chrysophanic acid.

The ethereal liquid which had been extracted with alkalis yielded about 0.5 gram of an essential oil, which possessed in a high degree the characteristic odour of the drug.

\* The ammonium carbonate solution referred to throughout this work was prepared by dissolving Kahlbaum's "ammonium carbonate" in water, and then saturating the solution with carbon dioxide.



*Non-volatile Constituents of the Extract.*

After the steam distillation, the mixture remaining in the flask consisted of a viscid, resinous product, and a dark-coloured, aqueous liquid. The mixture was diluted and allowed to cool, when the resin was separated. The latter was then thoroughly washed several times with hot water, the concentrated washings being added to the original aqueous liquid. There were thus obtained a clear, dark-coloured, aqueous liquid (A), amounting to about 40 litres, and a dark greenish-yellow resin (B), which weighed 414 grams.

*Examination of the Aqueous Liquid (A).*

The aqueous liquid (A) deposited a brown resinous product on keeping, but this dissolved when the mixture was shaken with ether. The entire aqueous liquid was thoroughly extracted ten times with a large volume of ether, the ethereal liquid being washed and concentrated. To this concentrated liquid was added the ether-soluble portion of the amyl-alcoholic extract, obtained as subsequently described. The concentrated ethereal solution of the entire ether-soluble constituents of the aqueous liquid deposited on keeping a quantity of a semi-crystalline, yellow powder, which was collected. The filtrate was evaporated, and the residue heated with ethyl acetate, when a quantity of a yellow powder remained undissolved. A considerable volume of petroleum (b. p. 35—50°) was then added to the filtered ethyl acetate solution, after which the liquid was decanted from the precipitated tarry product, and evaporated to a small bulk. This treatment with petroleum was twice repeated in a similar manner, when further small precipitates of the yellow powder were obtained, which were added to the similar products mentioned above.

*Isolation of Cinnamic Acid.*

The product which remained on evaporating the final petroleum solution obtained as above described, was dissolved in ether, and extracted successively with 10 per cent. aqueous ammonium carbonate, sodium carbonate, and potassium hydroxide.

The ammonium carbonate extract, after acidification, deposited 0.5 gram of cinnamic acid (m. p. 131—132°), (Found, C=72.9; H=5.6. Calc., C=73.0; H=5.4 per cent.), a compound which has not previously been recorded as occurring in rhubarb in the free state. The original acid, aqueous filtrates from the cinnamic acid yielded nothing but a further small quantity of the same compound.

The sodium carbonate and potassium hydroxide extracts of the petroleum soluble products yielded only small quantities of aloe-



emodin (m. p.  $216^{\circ}$ ) and chrysophanic acid (m. p.  $189^{\circ}$ ) respectively, the isolation of which in larger amount will subsequently be described.

The material remaining dissolved in the ether after extraction with potassium hydroxide consisted of a small amount of fatty matter, which was added to the petroleum extract of the resin (B), subsequently to be described.

*Isolation of Rhein,  $C_{14}H_5O_2(OH)_2 \cdot CO_2H$ .*

The several fractions of yellow powder obtained from the ethereal extract of the aqueous liquid were united, and heated with amyl alcohol, the mixture cooled, and then filtered. The material undissolved by this treatment (3 grams) was crystallised three times from pyridine, when glistening, orange-coloured needles were obtained. These crystals fell to a powder when heated at  $130^{\circ}$ , after which they melted at  $318^{\circ}$ :

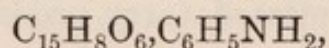
0.1962,\* on heating at  $130^{\circ}$ , lost 0.0421 of pyridine.  $C_5H_5N = 21.5$ .

0.0889 † gave 0.2055  $CO_2$  and 0.0230  $H_2O$ .  $C = 63.0$ ;  $H = 2.9$ .

$C_{15}H_8O_6, C_5H_5N$  requires  $C_5H_5N = 21.8$  per cent.

$C_{15}H_8O_6$  requires  $C = 63.4$ ;  $H = 2.8$  per cent.

The substance was, therefore, rhein (a dihydroxyanthraquinone carboxylic acid), which is thus seen to separate from pyridine in combination with the latter. It appears to be owing to this salt-formation that rhein, which is nearly insoluble in most solvents, dissolves readily in organic bases; the *aniline* salt,



crystallised in orange-red needles.

*Diacetylrhein,  $C_{14}H_5O_4Ac_2 \cdot CO_2H$ .*—The statements in the literature regarding acetylrhein are rather discrepant. Thus, Hesse (*Annalen*, 1899, **309**, 32) stated that rhein yielded a monoacetyl derivative (m. p.  $262-263^{\circ}$ ) and a diacetyl derivative (m. p.  $236^{\circ}$ ). Subsequently Tschirch and Heuberger (*loc. cit.*) obtained only the diacetyl compound, melting at  $236^{\circ}$ , whilst Oesterle (*Schweiz. Woch. Pharm.*, 1903, **40**, 600) states that this compound melts at  $247-248^{\circ}$ . Later, Robinson and Simonsen (*Trans.*, 1909, **95**, 1090) prepared diacetylrhein, agreeing in its general properties with this compound as described by Hesse, by Tschirch and Heuberger, and by Oesterle, but they stated that they were able to obtain only anomalous results by its analysis. The present authors, however, have found that pure diacetylrhein, melting at  $258^{\circ}$ , may readily be obtained by heating rhein for one hour with a large excess of acetic anhydride to which a little camphorsulphonic acid (or

\* Air-dried substance.

† Dried at  $130^{\circ}$ .



pyridine) had been added. After concentration, diacetylrhein separated in rosettes of pale yellow needles, melting at  $258^{\circ}$ :

0.1152 gave 0.2601  $\text{CO}_2$  and 0.0364  $\text{H}_2\text{O}$ .  $\text{C}=61.6$ ;  $\text{H}=3.5$ .

$\text{C}_{19}\text{H}_{12}\text{O}_8$  requires  $\text{C}=62.0$ ;  $\text{H}=3.3$  per cent.

Diacetylrhein is readily removed from its solution in immiscible solvents by means of aqueous sodium carbonate, on account of its containing a carboxyl group. The diacetylrhein prepared by the present authors, however, exhibited a remarkable behaviour on heating with xylene. When subjected to this treatment it first entirely dissolved, but then suddenly separated completely from the boiling liquid. The reprecipitated compound was now practically insoluble in all solvents except alkalis, but melted at the same temperature as the original preparation ( $258^{\circ}$ ), and, on analysis, appeared to possess the same composition. (Found,  $\text{C}=62.1$ ;  $\text{H}=3.4$  per cent.).

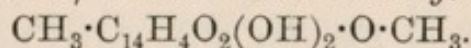
*Dibenzoylrhein*,  $\text{C}_{14}\text{H}_5\text{O}_4\text{Bz}_2\cdot\text{CO}_2\text{H}$ .—No benzoyl derivative of rhein has heretofore been described. Rhein was therefore benzoylated by the Schotten-Baumann method, when the *potassium* salt of *dibenzoylrhein* was obtained as a sparingly soluble compound. This was dissolved in glacial acetic acid, when, on cooling, *dibenzoylrhein* separated. After recrystallisation, this compound formed yellowish-brown prisms, melting at  $262^{\circ}$ :

0.0936 gave 0.2415  $\text{CO}_2$  and 0.0284  $\text{H}_2\text{O}$ .  $\text{C}=70.4$ ;  $\text{H}=3.4$ .

$\text{C}_{29}\text{H}_{16}\text{O}_8$  requires  $\text{C}=70.7$ ;  $\text{H}=3.3$  per cent.

Dibenzoylrhein is removed from its solution in chloroform by aqueous alkalis.

#### *Isolation of Emodin Monomethyl Ether,*



The pyridine mother liquors from which the rhein had been separated, as above described, were evaporated, and the residue was dissolved in the original amyl alcohol solution from which the crude rhein had been separated. The solution was then concentrated somewhat, when, on cooling, about 2 grams of emodin monomethyl ether (m. p.  $195^{\circ}$ . Found,  $\text{C}=67.3$ ;  $\text{H}=4.3$ . Calc.,  $\text{C}=67.6$ ;  $\text{H}=4.2$  per cent.) were obtained. It was found to be identical with the product obtained by the present authors from *Rumex Ecklonianus*, Meissner (*loc. cit.*), and the synthetical ether prepared from emodin by Jowett and Potter (Trans., 1903, 77, 1330). Its identity was further confirmed by the formation of its diacetyl derivative, which melted at  $186^{\circ}$ , and by its conversion into emodin by means of concentrated sulphuric acid.

Emodin monomethyl ether has not previously been obtained from



rhubarb, but, after it had been thus isolated by the present authors, it was shown by Oesterle and Johann (*loc. cit.*) to be the methylated compound which is associated with chrysophanic acid in this drug.

*Dibenzoylmodin Monomethyl Ether*,  $\text{CH}_3 \cdot \text{C}_{14}\text{H}_4\text{O}_4\text{Bz}_2 \cdot \text{O} \cdot \text{CH}_3$ , was prepared by the Schotten-Baumann reaction. It crystallised readily from a mixture of glacial acetic acid and alcohol in long, silky, pale yellow needles, melting at  $228^\circ$ :

0.1000 gave 0.2680  $\text{CO}_2$  and 0.0366  $\text{H}_2\text{O}$ .  $\text{C}=73.1$ ;  $\text{H}=4.1$ .

$\text{C}_{30}\text{H}_{20}\text{O}_7$  requires  $\text{C}=73.2$ ;  $\text{H}=4.1$  per cent.

It was known that the large amount of product remaining dissolved in the original amyl alcohol solution from which the emodin monomethyl ether had been separated, as above described, consisted, at least, for the most part, of a mixture of anthraquinone derivatives. Previous experience had shown that the best way to effect a separation of these would be to extract them fractionally by shaking their solutions in ether or chloroform with successive portions of various aqueous alkalis. In the present instance, however, owing to the large amount of material to be dealt with and its sparing solubility in the solvents mentioned, it was necessary, in the first place, to carry out the extraction with the alkalis with the employment of the amyl alcohol solution. This rendered the preliminary separation by no means exact, as the salts of the anthraquinone derivatives are appreciably soluble in amyl alcohol.

The amyl-alcoholic solution was therefore extracted successively with aqueous solutions of ammonium carbonate, sodium carbonate, and potassium hydroxide, each extract being acidified as soon as it was separated.

#### *Isolation of Emodin*, $\text{CH}_3 \cdot \text{C}_{14}\text{H}_4\text{O}_2(\text{OH})_3$ .

The ammonium carbonate extract yielded a nearly black, amorphous powder, from which nothing definite could be isolated. The sodium carbonate extract, however, gave, on acidification, a yellow powder, which, after being crystallised three times from pyridine, yielded 19 grams of a product crystallising in deep orange-coloured needles. On exposure to the air, or on heating, this compound readily lost pyridine, after which it melted at  $252^\circ$ , and was identified as emodin. (Found,  $\text{C}=66.5$ ;  $\text{H}=3.9$ . Calc.,  $\text{C}=66.7$ ;  $\text{H}=3.7$  per cent.) Its identity was further confirmed by its conversion into triacetylmodin, which formed slender, pale yellow prisms, melting at  $192^\circ$ .

*Tribenzoylmodin*,  $\text{CH}_3 \cdot \text{C}_{14}\text{H}_4\text{O}_5\text{Bz}_3$ .—Emodin was benzoylated by Oesterle (*Arch. Pharm.*, 1899, 237, 703) and by Tschirch and Heuberger (*loc. cit.*), but these investigators obtained only a



dibenzoyl derivative (m. p.  $225^{\circ}$ ). The product of the benzylation of emodin, as obtained by the present authors, consisted, however, entirely of *tribenzoylemodin* (m. p.  $186^{\circ}$ ).

Emodin was benzyolated by the Schotten-Baumann method, and the product crystallised from glacial acetic acid. Small, nodular masses, consisting of minute, pale yellow needles, were thus obtained, which melted at  $186^{\circ}$ :

0.1034 gave 0.2804  $\text{CO}_2$  and 0.0366  $\text{H}_2\text{O}$ .  $\text{C}=74.0$ ;  $\text{H}=3.9$ .

$\text{C}_{36}\text{H}_{22}\text{O}_8$  requires  $\text{C}=74.2$ ;  $\text{H}=3.8$  per cent.

*Isolation of Rheinolic Acid,  $\text{C}_{16}\text{H}_9\text{O}_4 \cdot \text{CO}_2\text{H}$ .*

The pyridine mother liquors from the emodin were concentrated, and the solution then poured into a quantity of ether. This caused a product to be precipitated, which, on examination, proved to be rhein, together with some amorphous material. The ethereal filtrate was then extracted with an aqueous solution of ammonium carbonate, when, on acidifying the alkaline liquid, a reddish-coloured powder was precipitated. This product was collected, and crystallised several times from pyridine, when dark red, lustrous needles were obtained, which, on drying at  $130^{\circ}$ , lost pyridine, and then melted at  $295-297^{\circ}$ , previously changing slightly at  $290^{\circ}$ :

0.1086 gave 0.2613  $\text{CO}_2$  and 0.0329  $\text{H}_2\text{O}$ .  $\text{C}=65.6$ ;  $\text{H}=3.4$ .

0.0748 „ 0.1797  $\text{CO}_2$  „ 0.0244  $\text{H}_2\text{O}$ .  $\text{C}=65.5$ ;  $\text{H}=3.6$ .

$\text{C}_{17}\text{H}_{10}\text{O}_6$  requires  $\text{C}=65.8$ ;  $\text{H}=3.2$  per cent.

This substance is therefore seen to be a new compound, possessing the formula  $\text{C}_{17}\text{H}_{10}\text{O}_6$ , and it is proposed to designate it as *rheinolic acid*, with consideration of the fact that it is a carboxylic acid, and also contains at least one hydroxyl group. Rheinolic acid is rather more soluble in the usual solvents than is rhein, and it is also of a much more pronounced red colour than the latter. Its homogeneity was confirmed by converting it into its acetyl derivative, which, after several recrystallisations, was hydrolysed, when rheinolic acid was regenerated, possessing the same properties as before its acetylation. *Acetylrheinolic acid* crystallises in rosettes of small, orange-coloured needles, which melt at  $236^{\circ}$ . It quickly dissolves in cold aqueous sodium carbonate, thus indicating the presence of a carboxyl group.

Rheinolic acid is evidently an anthraquinone derivative, as it dissolves in both alkalis and concentrated sulphuric acid with an intense red colour, but differs from rhein, inasmuch as it is not reprecipitated by the addition of water to its dilute solution in the latter solvent. Rheinolic acid is probably related structurally to rhein, but since it differs from the latter by the increment of the



elements  $C_2H_2$ , it probably contains a bridged ring. Further quantities of rheinolic acid were subsequently isolated from the tarry product precipitated by the addition of petroleum to the ethereal extract of the aqueous liquid (p. 957), and also from the ethereal extract of the resins (p. 965), but the total amount obtained did not greatly exceed 0.3 gram.

There were some indications that the mother liquors from the emodin, from which the rheinolic acid had been isolated, contained yet another substance in small amount, but it could not be isolated.

*Isolation of Aloe-emodin,  $C_{14}H_5O_2(OH)_2 \cdot CH_2 \cdot OH$ .*

On acidifying the potassium hydroxide extract of the amyl-alcoholic solution, obtained as above described, a yellow product was precipitated. This was dissolved in chloroform, when, on keeping, a quantity (1.5 grams) of a substance separated. This separated from ethyl acetate in long, highly lustrous needles of a light brownish-orange colour, which melted at  $216^\circ$ , and proved to be aloe-emodin. (Found,  $C=66.4$ ;  $H=4.0$ . Calc.,  $C=66.7$ ;  $H=3.7$  per cent.) Its identity was further confirmed by the preparation of its triacetyl derivative, which crystallised well in pale yellow needles, but decomposed somewhat indefinitely from  $165^\circ$  to  $175^\circ$  (Found,  $C=63.3$ ;  $H=4.1$ . Calc.,  $C=63.6$ ;  $H=4.0$  per cent.), and its tribenzoyl derivative melting at  $232^\circ$  (compare Robinson and Simonsen, *loc. cit.*). Aloe-emodin is removed from its solution in chloroform or ether somewhat slowly by fairly concentrated sodium carbonate solution, but is much more quickly extracted by the alkali hydroxides.

Aloe-emodin has not previously been recorded as a constituent of rhubarb, but no doubt can be entertained that the "rhabarberon" of Hesse and the "isoemodin" of Tschirch and Eyken, both of which melted at  $212^\circ$ , were, in reality, aloe-emodin in a state of approximate purity. Hesse, however, in one communication (*J. pr. Chem.*, 1908, [ii], 77, 383) describes both "rhabarberon" and aloe-emodin, and evidently regarded them as distinct substances.

*Isolation of Chrysophanic Acid,  $CH_3 \cdot C_{14}H_5O_2(OH)_2$ .*

The chloroform solution from which the aloe-emodin had separated, as above described, was extracted with several successive portions of 0.5 per cent. aqueous potassium hydroxide. This treatment removed further quantities of aloe-emodin, and when this compound ceased to be extracted the strength of the alkali employed was increased to 5 per cent. The deep purple-red, alkaline extracts then obtained yielded, on acidification, a quantity (6 grams) of a



yellow powder, which was found to consist of a mixture of emodin monomethyl ether (about one part) and chrysophanic acid (about four parts). As no pure substance could be isolated from this product by crystallisation, it was heated at  $160^{\circ}$  with concentrated sulphuric acid in order to demethylate the emodin monomethyl ether. The product was then dissolved in chloroform and extracted with aqueous sodium carbonate, which removed emodin, after which it was shaken with aqueous potassium hydroxide, which dissolved the chrysophanic acid.

The product obtained on acidifying the last-mentioned alkaline extract was crystallised from ethyl acetate, when chrysophanic acid was obtained in deep golden-coloured spangles, melting at  $191^{\circ}$ . (Found, C=70.9; H=4.0. Calc., C=70.9; H=3.9 per cent.) It yielded diacetylchrysophanic acid, which formed slender, pale yellow prisms, melting at  $204^{\circ}$ .

*Dibenzoylchrysophanic Acid*,  $\text{CH}_3 \cdot \text{C}_{14}\text{H}_5\text{O}_4\text{Bz}_2$ .—Chrysophanic acid was benzoylated by the Schotten-Baumann method, and the resulting product crystallised from a mixture of glacial acetic acid and alcohol. *Dibenzoylchrysophanic acid* was then obtained in very pale yellow needles, melting at  $204^{\circ}$ :

0.1119 gave 0.3084  $\text{CO}_2$  and 0.0400  $\text{H}_2\text{O}$ . C=75.2; H=4.0.

$\text{C}_{29}\text{H}_{18}\text{O}_6$  requires C=75.3; H=3.9 per cent.

#### *Isolation of Gallic Acid.*

The tarry product which was precipitated by the first addition of petroleum to the ethereal extract of the aqueous liquid (p. 950) was heated with a large volume of ether, when only partial solution was effected. The undissolved portion was therefore dissolved in alcohol, the solution poured into the ethereal liquid, and the mixture washed several times with water. This caused the separation of a quantity of brown, tarry matter, which yielded nothing crystalline. The aqueous-alcoholic washings which had been separated from the ethereal solution and from the tar were evaporated to a low bulk under diminished pressure, and extracted many times with ether. The ethereal liquid thus obtained was extracted successively with aqueous solutions of ammonium carbonate, sodium carbonate, and potassium hydroxide. The last two extracts yielded only small quantities of emodin and aloë-emodin respectively, but on acidifying the ammonium carbonate extract and again extracting with ether, gallic acid, crystallising from water in colourless needles, was obtained. This, after being dried at  $130^{\circ}$ , melted and decomposed at  $253^{\circ}$ . (Found, C=49.3; H=3.8. Calc., C=49.4; H=3.5 per cent.) Its identity was confirmed by its conversion into trimethyl-



gallic acid, which melted at  $165^{\circ}$ . The melting point of gallic acid is usually recorded as about  $220^{\circ}$ , but the present authors were unable to cause any specimen of gallic acid to fuse at so low a temperature unless it were partly decomposed by prolonged heating above  $200^{\circ}$ .

Gallic acid has once previously been stated to occur in rhubarb (Tschirch and Heuberger, *loc. cit.*), but no experimental evidence was recorded.

The original ethereal liquid from which the gallic acid had been removed by washing with water was extracted with various alkalis, and very fully examined. It yielded only small quantities of gallic and cinnamic acids, rhein, rheinolic acid, emodin, aloe-emodin, emodin monomethyl ether, chrysophanic acid, and an amorphous, tarry product. The total amount of gallic acid isolated from the ethereal extract of the aqueous liquid was about 20 grams, but a much larger quantity was subsequently obtained.

*Isolation of a Mixture of Glucosides of the Anthraquinone Derivatives.*

The original aqueous liquid (A), which had been extracted with ether, as previously described, was deprived of this solvent, and extracted in portions with amyl alcohol. Each portion was extracted twenty-five times, and, owing to the large volume of liquid, this necessitated nearly 1000 operations. Each amyl-alcoholic extract of the aqueous liquid, after being washed with water, was evaporated to a low bulk under diminished pressure. The first extract obtained from each portion of aqueous liquid, on evaporation, yielded a quantity of brown, tarry matter, but all the subsequent extracts, when sufficiently concentrated, deposited a brown, granular solid. The entire amount of the latter was dried on porous earthenware, after which it was digested with ethyl alcohol, in which it was only sparingly soluble, even on boiling. The product, which was at first amorphous, gradually assumed a crystalline form, and when this change was complete the mixture was filtered and the solid washed with alcohol. In this way a quantity (130 grams) of a bright yellow, crystalline solid was obtained. The filtrate from the latter was dark reddish-brown, and contained only tarry matter similar to that yielded by the first extractions with amyl alcohol.

The yellow, crystalline solid was insoluble, or practically so, in xylene, ether, chloroform, or ethyl acetate, sparingly soluble in alcohol, and very sparingly so in water, but it dissolved much more readily in glacial acetic acid, pyridine, or solutions of the alkali



hydroxides. With the latter, or with dilute pyridine, it yielded a deep purple-red colour. It separated in an amorphous state from all solvents other than ethyl alcohol.

A quantity (10 grams) of the yellow, crystalline product was dissolved in glacial acetic acid, and the solution poured into 9 litres of boiling water. Such an amount of sulphuric acid was then added to the solution as would represent one per cent. of the total liquid, after which the mixture was boiled for twenty minutes. A yellow precipitate formed in the boiling mixture after a few moments, and rapidly increased in amount. This was collected, and the aqueous filtrate extracted with chloroform, after which the solid precipitate was digested with the chloroform solution so obtained. The material undissolved by this treatment was found to be rhein (0.8 gram), whilst the chloroform solution, on systematic examination, yielded emodin (2.0 grams), aloe-emodin (0.3 gram), emodin monomethyl ether (1.0 gram), and chrysophanic acid (1.4 grams). The aqueous liquid from which the above-mentioned anthraquinone derivatives had been separated was colourless. It was deprived of sulphuric acid by means of barium hydroxide, and evaporated to a low bulk. A quantity of a syrup was thus obtained, which was found to contain dextrose. It was converted into the osazone, and the latter carefully examined for rhamnosazone (compare, Perkin, Trans., 1910, **97**, 1777), when it was found to consist entirely of *d*-phenylglucosazone (m. p. 213°). These results prove that the yellow, crystalline product was a mixture of the glucosides of rhein, emodin, aloe-emodin, emodin monomethyl ether, and chrysophanic acid, and it probably also contained a small percentage of the glucoside of rheinolic acid.

With the endeavour to isolate an individual glucoside from this mixture, a quantity of the material was fractionally crystallised many times from alcohol. A product was eventually obtained which formed highly lustrous, bright yellow leaflets, which melted constantly at 235°, and appeared quite homogeneous. Although some separation had been effected, it was, however, still a mixture, for, on hydrolysis, in addition to dextrose, chrysophanic acid and emodin monomethyl ether were obtained. It is not surprising that the glucosides of these two substances should be inseparable, since the substances themselves cannot be separated by crystallisation. This inseparable mixture of the glucosides of emodin monomethyl ether and chrysophanic acid contained one molecule of alcohol of crystallisation:

0.1548, on heating at 130°, lost 0.0154 EtOH. EtOH=9.9.

0.0853 \* gave 0.1848 CO<sub>2</sub> and 0.0399 H<sub>2</sub>O. C=59.1; H=5.2.

\* Anhydrous substance.



$C_{21}H_{20}O_9$ , EtOH requires EtOH = 9.9 per cent.

$C_{22}H_{22}O_{10}$ , EtOH „ EtOH = 9.3 „ „

$C_{21}H_{20}O_9$  requires C = 60.6; H = 4.8 per cent.

$C_{22}H_{22}O_{10}$  „ C = 59.2; H = 4.9 „ „

A further attempt to separate the original mixture of glucosides was made by the recrystallisation of the sodium derivative from very dilute alcoholic sodium hydroxide, but only a partial separation, similar to that just described, could be effected. Various other methods were also tried, but all were equally unsuccessful.

As a final attempt to isolate an individual glucoside, a portion of the original mixture was acetylated, when an acetyl derivative was obtained, which crystallised in pale yellow needles. This acetyl derivative was crystallised many times from glacial acetic acid and from ethyl acetate, after which it melted somewhat indefinitely at about  $190^{\circ}$ , but, on hydrolysis with dilute acid, it was found that no appreciable separation had been effected.

The dark reddish-brown, tarry product contained in the first amyl-alcoholic extracts and in the original amyl-alcoholic filtrates from the crude mixture of glucosides was deprived of solvent as completely as possible by evaporation under diminished pressure, and the residue dissolved in alcohol. An equal volume of chloroform was then added to the warm solution, whereupon a large amount of a dark-coloured, resinous product was precipitated. This material is subsequently referred to as the product (a). The liquid decanted from this precipitated resin was evaporated to a low bulk, and then largely diluted with chloroform, with which it was heated for some time. This caused the separation of a large amount of a yellow, granular solid. The latter, which is subsequently referred to as the product (b), was collected, washed with chloroform, and dried. The chloroform filtrate from the product (b) was evaporated to a low bulk, and then largely diluted with ether. The small precipitate produced by this treatment yielded nothing definite, and the ethereal filtrate was added to the original ethereal extract of the aqueous liquid (A)

#### *Examination of the Product (a).*

The product (a), which amounted to about 1000 grams, was heated with water, when it entirely dissolved, but the greater part of the material separated again on cooling as a brown resin. The dark-coloured aqueous liquid which had been decanted from the brown resin was treated with basic lead acetate solution, which removed some amorphous colouring matter. The filtrate from the lead precipitate was then examined for glucosides soluble in water,



but was found to contain only a little sugar. The resin, which was sparingly soluble in cold water, represented, as stated in the introductory part of this paper, the chief purgative principle of the rhubarb, but nothing definite could be directly isolated from it. A quantity (30 grams) of this material was dissolved in boiling water, a solution of potassium hydroxide added, and the mixture boiled for one minute. The liquid was then poured into hydrochloric acid, and extracted with ether. The greater part of the material was undissolved by the ether, and formed a pitch-like mass, but on systematically examining the ethereal liquid, small amounts of cinnamic and gallic acids, emodin, and aloë-emodin were obtained. These compounds had evidently been present in the resin in the form of esters, or some analogous compound, since a control experiment showed that the glucosides of the anthraquinone derivatives were not decomposed by the treatment with alkali to which the resin had been subjected, and, moreover, cinnamic acid could not yield a glucoside, since it contains no hydroxyl group. Several previous investigators have stated that rhubarb contained a "glucoside" which gave gallic and cinnamic acids on hydrolysis, but it is evident that the relatively small proportions of these acids which do not occur in the free state in rhubarb are combined as esters.

*Isolation of a New Compound,  $C_{14}H_9(OH)_3$ .*

A further portion of the above-described resin was dissolved in hot water, and such an amount of sulphuric acid added as to represent 3 per cent. of the total liquid, which was then heated on a water-bath for one hour. The mixture was then cooled, and the aqueous liquid decanted from the pitch-like mass which had separated, and extracted with ether. The ethereal liquid was then extracted with aqueous ammonium carbonate, sodium carbonate, and potassium hydroxide. The products dissolved by the first-mentioned alkali were gallic and cinnamic acids, and rhein, whilst the potassium hydroxide extract yielded only aloë-emodin, emodin monomethyl ether, and chrysophanic acid. The sodium carbonate extract, however, was found to contain a new substance, together with a large proportion of emodin. The product obtained on acidifying the sodium carbonate extract was redissolved in ether, and extracted with successive portions of dilute sodium carbonate solution until all the emodin had been removed. The strength of the alkali was then increased, when, on acidifying the alkaline extracts, the new substance was obtained. This compound was crystallised from dilute alcohol, when it formed long, flattened needles of a pale brown colour, which melted at  $256^\circ$ :



0.1012 gave 0.2719  $\text{CO}_2$  and 0.0485  $\text{H}_2\text{O}$ .  $\text{C}=73.3$ ;  $\text{H}=5.3$ .

0.1040 „ 0.2801  $\text{CO}_2$  „ 0.0501  $\text{H}_2\text{O}$ .  $\text{C}=73.5$ ;  $\text{H}=5.4$ .

$\text{C}_{14}\text{H}_{12}\text{O}_3$  requires  $\text{C}=73.7$ ;  $\text{H}=5.3$  per cent.

This *compound* is evidently new, since it does not agree in its properties with any substance of the above formula which has previously been described. It is sparingly soluble in water, but very readily so in alcohol. It yields no colour with ferric chloride, nor, at first, with potassium hydroxide solution, but when dissolved in the latter the mixture gradually becomes yellowish-brown. Concentrated sulphuric acid dissolves the new compound with a yellow colour.

As shown below, this new compound contains three hydroxyl groups, and it is probably a *trihydroxydihydroanthracene*, since, when a small quantity of its acetyl derivative was oxidised by means of chromic acid, and the product hydrolysed, a preparation was obtained which yielded colours with potassium hydroxide and with sulphuric acid similar to those afforded by some anthraquinone derivatives. The amount of material available, however, did not admit of the nature of the substance being conclusively proved.

A small quantity of the trihydroxy-compound was acetylated by means of acetic anhydride, when a *triacetyl* derivative was obtained, which crystallised from ethyl acetate in colourless needles, melting at  $113^\circ$ :

0.0975 gave 0.2422  $\text{CO}_2$  and 0.0468  $\text{H}_2\text{O}$ .  $\text{C}=67.7$ ;  $\text{H}=5.4$ .

$\text{C}_{14}\text{H}_9\text{O}_3(\text{CO}\cdot\text{CH}_3)_3$  requires  $\text{C}=67.8$ ;  $\text{H}=5.1$  per cent.

The formation of this triacetyl derivative proves the presence of three hydroxyl groups in the substance from which it was prepared.

The original acid aqueous liquid, from which the above-described compound and the mixture of anthraquinone derivatives had been removed by means of ether after the hydrolysis, was examined, but nothing definite could be isolated from it. It contained no sugar, thus proving that the resin which had been hydrolysed contained nothing of a glucosidic nature.

#### *Examination of the Product (b).*

The product (b), which amounted to about 318 grams, was dissolved in 600 c.c. of amyl alcohol, and 3 litres of ether were added. This caused the precipitation of a brown resin, from which the liquid was decanted. The latter was then evaporated, and the precipitation with ether repeated, after which the same operations were performed for a third time. The precipitated resin so obtained was similar in character to that yielded by the product (a). The ethereal liquid which had been decanted from the resin, when



evaporated, gave a product which, on crystallisation from water, yielded a large amount of gallic acid. The aqueous filtrate from the latter was saturated with ammonium sulphate, when a quantity (about 50 grams) of a tarry product was precipitated. The aqueous liquid decanted from this tar was extracted with ether, when it yielded a trace of anthraquinone derivative, together with gallic acid. The total amount of gallic acid obtained from the product (b) was about 190 grams.

The tarry product which had been precipitated by the addition of ammonium sulphate was moderately soluble in water, and was the only product obtained which exhibited the properties of a tannin. It was freed from the last traces of gallic acid by being precipitated a second time with ammonium sulphate. A quantity of this tannin was then heated with dilute sulphuric acid, when it was converted, for the most part, into a resinous product. The latter was moderately soluble in water, but differed from the original tannin inasmuch as it did not precipitate gelatin. The treatment of the tannin with sulphuric acid also led to the formation of small amounts of gallic and cinnamic acids, a mixture of anthraquinone derivatives, and a dextrorotatory sugar which yielded *d*-phenyl-glucosazone (m. p. 211°).

A portion of the original aqueous liquid (A), which had been extracted with ether and with amyl alcohol, was treated with a solution of basic lead acetate, when a comparatively small, reddish-coloured precipitate was produced. This, when decomposed by hydrogen sulphide, yielded a dark brown liquid, which gave a blackish-green colour with ferric chloride, but contained no tannin, and nothing could be directly isolated from it.

A portion of the product obtained on decomposing the lead precipitate was dried, and examined for acids, such as malic acid, by esterification with ethyl alcohol, but with a negative result. Another portion of the material was heated with dilute aqueous sulphuric acid, after which the mixture was extracted with ether. During this operation a small amount of sparingly soluble matter separated in the lower part of the ethereal layer. The ethereal liquid contained only traces of gallic acid and anthraquinone derivatives, but the sparingly soluble solid crystallised from pyridine in brown, flattened needles, which did not melt at 340°. A further small quantity of this substance was subsequently isolated from the ethereal extract of the resin (B), but the total amount obtained was not sufficient for analysis. It gave an acetyl derivative, which crystallised from acetic anhydride in pale brown needles, melting at 335°.



*Isolation of Dextrose.*

The filtrate from the basic lead acetate precipitate was deprived of lead, and concentrated, when it formed a viscid, yellow syrup. This was kept for several weeks, when it gradually deposited a considerable quantity of crystals, which were identified as dextrose.

A quantity of the sugar was heated with acetic anhydride and a little camphorsulphonic acid, after which the mixture was shaken with water and then extracted with ether. The ethereal solution, after being washed with aqueous sodium carbonate, was evaporated, when Tanret's " $\alpha$ -penta-acetyldextrose" \* was obtained. This product, after recrystallisation from 95 per cent. alcohol, formed colourless needles, melting at 127—128°. This method of preparation of this acetyldextrose is more expeditious, and gives much better yields than that recommended by Tanret (*Compt. rend.*, 1895, 120, 194). The syrup from which the dextrose had been isolated was lævorotatory, as was also the original syrup before the separation of the dextrose. It gave no indication of containing anything other than lævulose.

*Examination of the Resin (B).*

The resin (B) amounted to 414 grams. It was mixed with prepared sawdust, and extracted successively in a large Soxhlet apparatus with petroleum (b. p. 35—50°), ether, chloroform, ethyl acetate, and alcohol. In order to ensure as complete a separation of the products as possible, the different extracts were then submitted to extraction in the reverse order, as follows: The alcohol extract was again mixed with sawdust, and extracted with ethyl acetate; this new ethyl acetate extract, together with the original one, was then mixed with sawdust, and extracted with chloroform; and so on, until all but the petroleum extract had been treated a second time. Each extract was finally removed from the sawdust by a suitable solvent. This second extraction effected a very considerable change in the amounts of some of the extracts.

*Examination of the Petroleum Extract.*

The petroleum extract of the resin was a dark greenish-brown, viscid liquid, and amounted to 72 grams. It was treated with ether, in which all but a small amount of emodin monomethyl ether dissolved. On extracting the ethereal liquid with aqueous ammonium carbonate, a small amount of rhein was removed, after

\* It has more recently been shown (Koenigs and Knorr, *Ber.*, 1901, 34, 957) that this compound is more correctly designated as the  $\beta$ -derivative.



which the ethereal solution was shaken with several successive portions of potassium carbonate solution. The material precipitated on acidifying the potassium carbonate extracts, after being freed from a little resinous matter and an amorphous product which caused the formation of emulsions, was heated with absolute alcohol containing some sulphuric acid, in order to esterify the acids which it contained. The mixture was then poured into water, the esters extracted with ether, and freed from a small amount of emodin by means of caustic alkali. These esters of the free fatty acids, which amounted to 17 grams, were distilled under diminished pressure, and examined, together with a similar product obtained from the combined acids.

The original ethereal liquid which had been extracted with potassium carbonate, as above described, was shaken with aqueous potassium hydroxide. This removed about 4 grams of a mixture consisting of aloe-emodin, emodin monomethyl ether, and chrysophanic acid. The ethereal solution of the neutral products was then evaporated, and the residual fatty matter heated with an excess of alcoholic potassium hydroxide.

#### *Isolation of Verosterol, $C_{27}H_{46}O$ .*

The liquid obtained by the above saponification was poured into water and extracted with ether, when an oily product was obtained which deposited a quantity of flattened needles. As this solid did not appear homogeneous, and could not be purified by distillation under diminished pressure or by recrystallisation, it was heated with acetic anhydride. The product, after being freed from a small quantity of a hydrocarbon (m. p.  $64^{\circ}$ ), yielded verosteryl acetate, melting at  $118^{\circ}$ :

0.0602 gave 0.1791  $CO_2$  and 0.0622  $H_2O$ .  $C=81.1$ ;  $H=11.5$ .

$C_{27}H_{45} \cdot O \cdot CO \cdot CH_3$  requires  $C=81.3$ ;  $H=11.2$  per cent.

On hydrolysis this acetate yielded verosterol (Power and Rogerson, Trans., 1910, **97**, 1951), which was identified by analysis and by determination of its rotatory power. The original filtrate from the crude verosterol contained, besides a further amount of this substance, only an uncrystallisable oily liquid of high boiling point.

#### *Identification of the Fatty Acids.*

The alkaline aqueous liquid which had been extracted with ether, as above described, was acidified, and the liberated acids, none of which were volatile in steam, extracted with ether and converted into their ethyl esters. The product was distilled under diminished pressure, when it amounted to 11 grams. For the



examination of the fatty acids, these esters, together with the similar product previously obtained from the free acids, were hydrolysed, and the resulting acids converted into their barium salts. The resulting salts were digested with a mixture of benzene (95 parts) and 94 per cent. alcohol (5 parts), according to Vongerichten's method (*Ber.*, 1909, **42**, 1638). After cooling the mixture, the undissolved salt was collected, and the acid regenerated. The product so obtained was crystallised from ethyl acetate several times, when it melted at 54—57°, and was found to be a mixture of palmitic and stearic acids. (Found, C=74.7; H=12.5 per cent. Acid value, 211.2.) Palmitic and stearic acids have acid values of 218.8 and 197.2 respectively.

The barium salts remaining dissolved in the mixture of benzene and alcohol were treated with hydrochloric acid, and the resulting unsaturated fatty acids (16.2 grams) distilled under diminished pressure. This product had an iodine value of 134.8, and when oxidised according to the method described by Lewkowitsch (*Chemical Technology and Analysis of Oils, Fats, and Waxes*, 1904, Vol. I, 360) it yielded about equal quantities of di- and tetra-hydroxystearic acids, and a very small amount of linusic acid. The unsaturated fatty acids therefore consisted of about equal quantities of oleic and linolic acids, together with a small amount of linolenic acid.

#### *Examination of the Ether, Chloroform, Ethyl Acetate, and Alcohol Extracts.*

The ethereal extract amounted to 217 grams. It was very fully examined by fractionally extracting with various alkalis, in a manner analogous to that previously described in connexion with the ethereal extract of the aqueous liquid (p. 953). It yielded rhein, rheinolic acid, emodin, aloe-emodin, emodin monomethyl ether, and chrysophanic acid, together with a small amount of the sparingly soluble substance melting above 340° (p. 962), and a little free verosterol.

The chloroform extract of the resin amounted to 4.6 grams. A portion of it (1.2 grams) was extremely sparingly soluble in chloroform, and was found to consist of a mixture of the glucosides of emodin monomethyl ether and chrysophanic acid. The more readily soluble portion yielded chiefly rhein and emodin, together with small amounts of the other anthraquinone derivatives.

The ethyl acetate extract of the resin was a dark-coloured powder, and amounted to 72.5 grams. It consisted to a considerable extent of a mixture of the glucosides of rhein, emodin, aloe-emodin, emodin



monomethyl ether, and chrysophanic acid, similar to that previously described (p. 957), together with a black, amorphous powder.

The alcoholic extract of the resin was a hard, black solid, and amounted to 33 grams. Nothing crystalline could be separated from it, but on hydrolysis with acid it yielded small amounts of emodin monomethyl ether and chrysophanic acid.

### *Physiological Tests.*

The physiological action of many of the products obtained from rhubarb was investigated, the results in nearly all cases being controlled by experiments on several individuals. The doses administered were in all cases 0.1 gram.

Of the anthraquinone derivatives, rhein, emodin, and emodin monomethyl ether were found to be devoid of purgative action, the first two compounds being quickly excreted in the urine. Aloe-emodin and chrysophanic acid, however, were distinctly purgative, although not very active.

The crystalline mixture of glucosides of the anthraquinone derivatives had a bitter, astringent taste, but was quite devoid of purgative action.

The non-glucosidic resin obtained from the product (a) of the amyl alcohol extract of the aqueous liquid had a prompt purgative action, 0.1 gram causing a much more pronounced effect than the same weight of aloe-emodin or of chrysophanic acid, although it represented a much smaller amount of the drug.

The tannin from the product (b), and the alcohol extract of the resin (B), appeared to be quite devoid of physiological action.

### *Summary.*

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

The material employed consisted of the best quality of sun-dried "Shensi" rhubarb.

An alcoholic extract of the drug, when distilled with steam, yielded small amounts of palmitic and chrysophanic acids, together with a hexoic acid and some essential oil.

The portion of the extract which was soluble in water yielded cinnamic and gallic acids, rhein, emodin, aloe-emodin, emodin monomethyl ether, chrysophanic acid, and a new anthraquinone derivative,  $C_{17}H_{10}O_6$  (m. p. 295—297°), which it is proposed to designate *rheinolic acid*. It yielded, furthermore, a crystalline mixture of glucosides of rhein, emodin, aloe-emodin, emodin monomethyl ether, and chrysophanic acid; dextrose; lævulose; tannin;



and an amorphous, non-glucosidic resin, which represents the chief purgative constituent of the drug. This resin, on hydrolysis, gave small amounts of gallic and cinnamic acids, rhein, emodin, aloemodin, emodin monomethyl ether, and chrysophanic acid, together with a new compound,  $C_{14}H_{12}O_3$  (m. p.  $256^\circ$ ), which is probably a *trihydroxydihydroanthracene*, and a large amount of resinous material.

The portion of the extract undissolved by water yielded a trace of a hydrocarbon (m. p.  $64^\circ$ ); a phytosterol (verosterol),  $C_{27}H_{46}O$ ; a mixture of fatty acids, consisting of palmitic, stearic, oleic, linolic, and linolenic acids, both free and combined; rhein; rheinolic acid; emodin; aloemodin; emodin monomethyl ether; chrysophanic acid; and a trace of a substance which did not fuse at  $340^\circ$ , but which yielded an acetyl derivative, melting at  $335^\circ$ . It also gave some amorphous products, and a further quantity of the crystalline mixture of glucosides of the anthraquinone derivatives.

Of the anthraquinone derivatives, only aloemodin and chrysophanic acid had any purgative action, the mixture of glucosides being quite inert. The chief purgative principle is the above-mentioned non-glucosidic resin.

The percentages of the more important products obtained in the course of the present investigation may be indicated as follows, although the figures represent only approximately the amounts of the various substances actually present in rhubarb:

Essential oil, 0.005; verosterol, 0.1; mixture of fatty acids, 0.31; cinnamic acid (free), 0.01; gallic acid (free), 2.2; rhein, 0.12; rheinolic acid, 0.003; emodin, 0.78; aloemodin, 0.16; emodin monomethyl ether, 0.22; chrysophanic acid, 0.49; non-glucosidic resin, 10.4; tannin, 0.52; crystalline mixture of glucosides of the anthraquinone derivatives, 2.0.

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