

*Products from Some Plants of Hong Kong.*

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[Reprint Order No. 5258.]

From the leaves of the following have been isolated : *Eriobotrya japonica*, a mixture of triterpene acids, including ursolic acid, and a little oleanolic acid; *Rhododendron simsii*, ursolic acid and the flavanone matteucinol; *Allamanda cathartica* and *Rhododendron pulchrum*, ursolic acid (the latter plant does not contain matteucinol); *Psidium guajava*,  $\beta$ -sitosterol.

THE species *Eriobotrya japonica*, Lindl. (loquat), a member of the Rosaceae and one of the common medicinal plants of Hong Kong, is cultivated in the Colony. A decoction of the leaves, and the fruits, are prescribed by herbalists for cough and for nausea. Previous workers have shown that vitamin B<sub>1</sub> and vitamin C are present in the leaves and that ceryl alcohol and ceryl palmitate, and amygdalin, are present in the seeds. In addition to the ursolic acid and oleanolic acid which we have isolated from the leaves of the locally grown species, there occurs another acidic triterpenoid substance which is probably a mixture and is under investigation.

*Rhododendron simsii*, Planch. (synonyms : *R. Calleryi*, Planch.; *R. balfouria*, Leveille; *R. indicum*, var. *Simsii*, Maxim.), is indigenous to the Colony; *Rhododendron pulchrum*,

Sweet (synonym: *R. phoeniceum*, var. *Smithii*, Wils.) is not. *R. simsii* is reputed to be of medicinal interest. Neither species appears previously to have been investigated, though ursolic acid has been reported in the leaves of *R. hymenanthes* (Kuwada and Matsukawa, *J. Pharm. Soc. Japan*, 1933, **53**, 1065), *R. fauriae* (Kuwaguchi, Kim, and Kim, *ibid.*, 1942, **62**, 4), and *R. linearifolium* (Kariyone and Hashimoto, *ibid.*, 1949, **69**, 313). With our isolation of ursolic acid from the two local *Rhododendrons* the list has been extended to five species and it seems possible that the characteristic triterpene acid of this genus is ursolic acid. Ursolic acid also occurs in other members of the Ericaceae. The isolation of (–)-matteucinol (5:7-dihydroxy-6:8-dimethylflavanone; S. Fujise, *Sci. Papers Inst. Phys. Chem. Res., Tokyo*, 1929, **11**, 111) which occurs with ursolic acid in the ethereal extract of the leaves of *R. simsii* is interesting since this flavanone has been reported only once previously (from the fern, *Matteucia orientalis*, Munesada, *J. Pharm. Soc. Japan*, 1924, **505**, 185). The leaves of *R. fauriae* (Kuwaguchi *et al.*, *loc. cit.*) contain rhododendrin, the glucoside of rhododendrol, in addition to ursolic acid, and quercetin has been reported from four species of *Rhododendron*, but matteucinol seems to be the first flavanone reported from this genus.

Leaves of *Allamanda cathartica*, Linn. (Apocynaceae), commonly cultivated in the Colony and yielding vitamin C, contain ursolic acid as the only triterpenoid substance.

*Psidium guajava*, L. (Myrtaceae), is used in the Colony and elsewhere as a medicinal plant; the leaves are used for throat and chest complaints. Carotene and vitamins B<sub>1</sub>, B<sub>2</sub>, B<sub>6</sub>, and C, and niacin, have been isolated from it. Soliman and Farid (*J.*, 1952, **134**) isolated a wax, a phytosterol, and a triterpenoid substance from the leaves. We showed (*J.*, 1954, **1403**) that the leaves contained a mixture of triterpene acids (ursolic, oleanolic, cratogenic, and guaijavolic). We record here the isolation from the petroleum extract of the leaves β-sitosterol which is presumably the phytosterol isolated by Soliman and Farid (*loc. cit.*).

#### EXPERIMENTAL

M. p.s are corrected. Analyses are by Dr. Zimmermann, Melbourne. Ursolic acid and oleanolic acid and their derivatives and β-sitosteryl acetate were characterised by mixed m. p. with authentic specimens.

*Eriobotrya japonica*.—After the dried ground leaves (1 kg.) had been defatted by extraction with light petroleum (b. p. 60–80°) (1 l.) for 4 days at room temperature, they were extracted with ether (2 × 3 l.). The mixed dark green ethereal extracts were shaken with 8% sodium hydroxide solution (2 l.). The green precipitate of crude sodium salts which separated at the interface of the liquids was collected, washed, and then dissolved in hot methanol (charcoal). The solution was acidified; the crude amorphous triterpenoid material which separated on cooling yielded, after 4 crystallisations from ethanol, colourless needles of ursolic acid (5.5 g.), m. p. 289–290°,  $[\alpha]_D^{20} + 64^\circ$  (*c.* 0.71 in 1:1 MeOH–CHCl<sub>3</sub>) (Found: C, 79.2; H, 10.9%; *M*, 457. Calc. for C<sub>30</sub>H<sub>48</sub>O<sub>3</sub>: C, 78.9; H, 10.6%; *M*, 456). It formed ursolic acid acetate, m. p. 292–294° (Found: C, 76.9; H, 9.9. Calc. for C<sub>32</sub>H<sub>50</sub>O<sub>4</sub>: C, 77.1; H, 10.1%), methyl ursolate, m. p. 168–169° (Found: C, 79.5; H, 10.7; OMe, 6.5. Calc. for C<sub>31</sub>H<sub>50</sub>O<sub>3</sub>: C, 79.1; H, 10.7; OMe, 6.6%), methyl ursolate acetate, m. p. 245–246° (Found: C, 77.8; H, 10.2; OMe, 6.3. Calc. for C<sub>33</sub>H<sub>52</sub>O<sub>4</sub>: C, 77.2; H, 10.2; OMe, 6.1%). Methyl ursolate yielded methyl ursonate (prisms from ethanol), m. p. 191–192°, by oxidation with chromic acid (Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2555). Ursolic acid gave a red → violet → blue → green colour in the Liebermann–Burchardt test. After removal of 4 crops (ursolic acid) from the ethanolic mother-liquors, the fifth crop on recrystallisation from ethanol yielded colourless needles of oleanolic acid (0.1 g.), m. p. 310–312°. Oleanolic acid was identified by conversion into methyl oleanolate, m. p. 198–200° (Found: C, 78.6; H, 10.7. Calc. for C<sub>31</sub>H<sub>50</sub>O<sub>3</sub>: C, 79.1; H, 10.7%; the supply of oleanolic acid was insufficient for another analysis), and methyl oleanolate acetate, m. p. 220–222°. Oleanolic acid gave a red → violet → blue → green colour in the Liebermann–Burchardt test.

*Rhododendron simsii*.—Leaves (1 kg.) were extracted with ether (4 l.) and the extract was shaken twice with an equal volume of sodium hydroxide solution (3%). The precipitated sodium salt which formed at the interface was collected, dried, and then dissolved in hot methanol (charcoal). The solution was acidified with concentrated hydrochloric acid. The crude acid separated first as a gel which on recrystallisation from methanol and then ethanol

gave colourless needles of ursolic acid (6 g.), m. p. 289—290° (ursolic acid acetate, m. p. 293—295°; methyl ursolate, m. p. 170°; and methyl ursolate acetate, m. p. 245—246°).

The alkaline extract was filtered through glass wool and the filtrate was immediately acidified. The greenish-yellow precipitate was collected, washed, and recrystallised from methanol (charcoal). Cream-coloured needles separated. Further crystallisation from acetone, methanol, or benzene yielded colourless needles of (–)-matteucinol (4 g.), m. p. 175.5—176°,  $[\alpha]_D^{18} - 30^\circ$  (*c*, 0.91 in COMe<sub>2</sub>) (Found: C, 68.9; H, 5.9; OMe, 9.7%; *M*, 312. Calc. for C<sub>18</sub>H<sub>18</sub>O<sub>5</sub>: C, 68.8; H, 5.9; OMe, 9.9%; *M*, 314). Matteucinol was soluble in organic solvents and sodium hydroxide solution, and also in warm sodium carbonate solution; it gave a dark olive-green colour with ferric chloride solution in ethanol and a bright red colour with magnesium and hydrochloric acid in ethanol. Matteucinol was identified by the following experiments. (–)-Matteucinol (0.62 g.) was dissolved in aqueous-ethanolic 0.12*N*-potassium hydroxide (50 ml.). This solution had  $[\alpha]_D^{18} - 36^\circ$ , then after 2 hr. at room temperature had  $[\alpha]_D^{18} - 30^\circ$ . When the solution had stood overnight, racemisation was completed by warming for 3 hr. on a steam-bath. The solution was acidified and the precipitate collected and recrystallised several times from methanol. Needles of (±)-matteucinol, m. p. 172.5—173°, were obtained. (±)-Matteucinol was methylated with diazomethane in ether; the product, (±)-7-methoxymatteucinol, which separated from methanol as very pale yellow needles, m. p. 102.5° (Found: C, 69.6; H, 6.0; OMe, 18.7, 18.4%; *M*, 319, 362. Calc. for C<sub>19</sub>H<sub>20</sub>O<sub>5</sub>: C, 69.5; H, 6.2; 2OMe, 18.9%; *M*, 328), was insoluble in dilute sodium hydroxide solution, and gave only a pale colour with ferric chloride solution. (–)-Matteucinol (0.25 g.) was dissolved with fused sodium acetate (0.5 g.) in acetic anhydride (5 ml.). The solution was boiled under reflux for 3½ hr. and poured into water. The precipitate was collected and worked up in the usual manner. The product was crystallised 4 times from ethanol and then 3 times from methanol. Colourless needles of (+)-5:7-diacetylmatteucinol, m. p. 169—169.5°, were obtained (Found: C, 66.7; H, 5.6; Ac, 22.0. Calc. for C<sub>22</sub>H<sub>22</sub>O<sub>7</sub>: C, 66.3; H, 5.7; 2Ac, 21.6%); this derivative gave no colour with ferric chloride solution and was insoluble in sodium hydroxide solution.

*Rhododendron pulchrum*.—Leaves (1 kg.) were extracted with ether (4 l.), and the extract was shaken twice with an equal volume of sodium hydroxide solution (3%). The slight precipitate at the interface was discarded. The alkaline extract was acidified, and the green precipitate of crude ursolic acid was collected, dried, and crystallised from ethanol (charcoal) as needles (1.5 g.), m. p. 289—290°. The acid was converted into the three derivatives described above. No second constituent was obtained from the alkaline extract.

*Allamanda cathartica*.—The fresh leaves (500 g.) were chopped finely and extracted twice with ether (2 l.). The green ethereal extracts were mixed and worked up by the method stated for *Eriobotrya japonica*. The crude amorphous triterpenoid material (0.7 g.) separated from ethanol as a gel which, after further treatment with that solvent, gave colourless needles of ursolic acid, m. p. 289—291° (identified as ursolic acid acetate, m. p. 293—295°; methyl ursolate, m. p. 168—169°; methyl ursolate acetate, 245—246°). The ethanolic mother-liquors were mixed and concentrated. Several crops of ursolic acid were taken but there was no evidence of the presence of a second constituent.

*Psidium guajava*.—The powdered leaves (3 kg.) were extracted with light petroleum (b. p. 60—80°) (10 l.). The extract was concentrated to a dark green gelatinous residue which was diluted with methanol and filtered. The filtrate was concentrated under reduced pressure and distilled with steam. The residue from steam-distillation was boiled under reflux with ethanolic potassium hydroxide for 10 hr., cooled, and extracted with ether. The ethereal solution was dried and distilled, and to the brown residue was added methanol. The rosettes which separated were collected and crystallised from ethanol. The product (0.5 g.), β-sitosterol, separated from ethanol in scintillating plates, m. p. 138—139°,  $[\alpha]_D^{21} - 35^\circ$  (*c*, 0.2 in chloroform), and gave a red → violet → blue → green colour in the Liebermann–Burchardt reaction. After its reaction with acetic anhydride and pyridine, β-sitosteryl acetate, m. p. 121—122° (Found: C, 81.9; H, 11.3; Ac, 9.8. Calc. for C<sub>31</sub>H<sub>52</sub>O<sub>2</sub>: C, 81.6; H, 11.4; 1Ac, 9.4%), was obtained by working up the product in the usual manner. Crystallisation from methanol of the product obtained from the treatment of β-sitosterol with benzoyl chloride in pyridine yielded β-sitosteryl benzoate, m. p. 144—145°.

The authors thank Professor J. E. Driver for his interest, Mr. H. C. Tang (Government Herbarium, Hong Kong) for identification of plant material, and Professor Th. Bersin (Hausmann Research Laboratory, St. Gallen) for the sample of authentic β-sitosteryl acetate.