Triterpene Acids

Shortly after the announcement in Great Britain[1] that *Centella asiatica* contained a glucose derivative which was active in the treatment of leprosy, we commenced an examination of the plant, with the object of studying the chemical constitution and therapeutic properties of the active material. In this note the results of analyses carried out on dried plant tissue of Ceylonese origin are reported. We are deeply indebted to Dr. J. L. Simonsen, director of the Colonial Products Research Council, for his help in making supplies of this material available to us, and for his interest in these investigations.

No sugar derivative of the type of asiaticoside could be detected, but three triterpene acids were isolated in a pure, though amorphous, condition. It seemed that these were very likely related to the amorphous aglycone of asiaticoside, which was described[2] as giving a red colour with sulphuric acid, a reaction known to be general for triterpene derivatives[3].

The major component of our triterpene mixture, for which we propose the name 'centoic acid', was separated as the sparingly soluble potassium salt (long needles), and purified through the brucine salt, which formed plates from alcohol, $[\alpha]_D = -39°$ (pyridine). The free acid, an amorphous powder, $[\alpha]_D = +44°$ (alcohol), gave analytical data which show it to be a monobasic acid, $C_{30}H_{48}O_6$. It appears to be a normal pentacyclic triterpene acid, closely analogous, apart from its higher hydroxyl content, with oleanolic acid. It gave sapotalene on dehydrogenation with selenium. Although resistant to hydrogenation, it contains a double bond, since with tetranitromethane a yellow colour was obtained with some difficulty[4]. Among its derivatives, the following have been obtained analytically pure, although none of them could be crystallized: a methyl ester, $[\alpha]_D = +36°$ (alcohol), which was stable to hot dilute alkalis and acids; a methyl ester triacetate, $[\alpha]_D = +7°$ (alcohol), which contained one free hydroxyl group (Zerewitinoff); a periodate fission product, $C_{30}H_{46}O_6$, $[\alpha]_D = +92°$ (alcohol), requiring for its formation 1 mole of the oxidant; and a bromolactone. Centoic acid, therefore, contains a tertiary carboxyl and four hydroxyl groups, two of which are present in a cyclic 1 : 2-glycol system.

The other two triterpene acids of dried *Centella* tissue have also been shown to contain a tertiary carboxyl group, an inert double bond, and a 1 : 2-glycol system. That present in the larger quantity, for which the name 'centellic acid' is proposed, was separated by taking advantage of the high solubility of its potassium salt. The brucine salt formed pellet-like needle aggregates, $[\alpha]_D = -44°$ (pyridine), from which the free acid was regenerated as an amorphous powder, $[\alpha]_D = +36°$ (alcohol). Analytical and titration results showed it to be a monobasic acid $C_{30}H_{48}O_6$. As well as the molecular features mentioned above, it probably contains two more hydroxyl groups; but the evidence on this point is not yet clear-cut. The third acid was found present only in minor amounts. Unlike the others, it was precipitated from dilute alcohol by lead acetate. After further purification through the potassium salt (long needles), it was obtained as an amorphous powder, $C_{30}H_{48}O_5$, $[\alpha]_D = +38°$ (alcohol).

It was clearly a question of importance to find whether any of the above acids were identical with the aglycone of asiaticoside, and a short time ago we got into touch with Dr. E. Lederer, who is carrying out an investigation of asiaticoside in Paris. We have compared results on our substances, and Dr. Lederer very kindly provided us with samples of asiaticoside and of the crystalline methyl ester of its aglycone, asiatic acid; we wish to take this opportunity of thanking him for his courtesy. He and his colleagues[5] have shown asiatic acid to be a triterpene acid with properties closely analogous to those of our own acids, and with the molecular formula $C_{30}H_{48}O_5$. A direct comparison has been made with our $C_{30}H_{48}O_5$ acid, and has shown that they are not identical, but isomeric compounds.

We intend to keep in touch with Dr. Lederer, and to extend our investigations on these triterpene acids.

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[1] *Nature*, **155**, 601 (1945).
[2] Bontems, J. E., *Bull. Sci. pharmacol.*, **49**, 186 (1941).
[3] "Klein's Handbuch der Pflanzenanalyse", **3** (2), 1103 (Vienna, 1932).
[4] Prelog, V., *Coll. Czechoslov.*, **2**, 414 (1930).
[5] Boiteau, P., Buzas, A., Lederer, E., and Polonsky, J., see preceding communication.

Centelloside

Specimens of *Centella asiatica* grown in Madagascar have been found to contain asiaticoside[1], which is said to have value in the treatment of leprosy[2]. Lederer, Boiteau and their colleagues[3] have shown that asiaticoside is a rhamnose–glucose derivative of a triterpene acid, asiatic acid ($C_{30}H_{48}O_5$). Elsewhere[4] it has been suggested that there may be an 'oxidized form' of asiaticoside present in the fresh plant, which is more readily soluble in water.

Work carried out in this Laboratory[5] has shown that dried *Centella asiatica* tissue from Ceylon contains no asiaticoside or similar compound, but that there are present two triterpene acids $C_{30}H_{48}O_6$, closely related to asiatic acid, and traces of a third isomeric with it. It seemed likely that these sugar-free triterpenes might originate as a result of enzyme action on one or more sugar derivative present in the fresh plant, and evidence is now presented which supports that view.

When alcoholic extracts of fresh Ceylonese plant tissue were analysed, free triterpene acids were found only in amounts too small to permit identification. In one fraction of the extracts, however, combined triterpene was present in considerable quantity. This fraction was purified extensively, until only small traces of free sugar were present (as shown by paper chromatography), but no crystalline material could be obtained from it. We think, nevertheless, that it consists substantially of a single substance, which contains a triterpene acid in combination with a sugar system. Its chemical properties resemble closely those of asiaticoside, and accordingly we suggest for it the name 'centelloside'.

Centelloside forms a pale yellow neutral gum, extremely soluble in water, much less soluble in anhydrous alcohol. It reduces Fehling's solution on warming. Dilute acids liberate from it reducing sugars and a triterpene acid, which was identified as centellic acid[5] by conversion to the crystalline brucine salt. The sugar solution left after removal of centellic acid from the hydrolysate was investigated