OPERCULIN I AND II, NEW ETHER-SOLUBLE RESIN GLYCOSIDES ("JALAPIN") WITH FATTY ACID ESTER GROUPS FROM RHIZOMA JALAPAE BRAZILIENSIS (ROOTS OF IPOMOEA OPERCULATA)

Masateru Ono, Kenji Kubo, Kazumoto Miyahara* and Toshio Kawasaki
Faculty of Pharmaceutical Sciences, Setsunan University,
45-1, Nagaotoge-cho, Hirakata, Osaka 573-01, Japan

Two new resin glycosides, operculin I and II, were isolated from the ether-soluble fraction ("jalapin") [W. Mayer, Justus Libigs Ann. Chem., 83, 121 (1852)] of Rhizoma Jalapae Braziliensis, the root of Ipomoea operculata (Convolvulaceae), and their structures have been determined. Both compounds provided on alkaline hydrolysis one identical jalapinolic acid 11-O-glycoside, named operculinic acid A, which forms an intramolecular macrocyclic ester in the parent compounds similarly to the case of analogs isolated from "jalapin" of all the Convolvulaceae plants so far examined. It is noted, however, that operculin I and II have two moles of a fatty acid, n-dodecanoic and n-decanoic acids, respectively, combined at their sugar moiety in place of several organic acids. According to Mosher's method, the absolute configuration at C_{11} of methyl jalapinolate, which was regarded by Horeau's method as R, was shown to be S.

KEYWORDS — resin glycoside; operculin I; operculin II; operculinic acid A; Rhizoma Jalapae Braziliensis; Ipomoea operculata; convolvulaceae; intramolecular macrocyclic ester; n-decanoic acid ester; n-dodecanoic acid ester

Rhizoma Jalapae Braziliensis (Brazilian Jalap), the root of Ipomoea operculata (Gomes) Martin (Operculina macrocarpa L.) (Convolvulaceae) and its ethanol extractive, Resina Operculina (Brazilian resin), is a drastic laxative. It is used as a substitute for Mexican jalap (Vera Curz Jalap), the root of I. purga Hayne, and for Resina Jalapae (Mexican resin) in Europe. Graf, et al. reported that, on alkaline hydrolysis, the ether-soluble resin glycoside, "jalapin"[1,2] from Brazilian jalap furnished acetic, tiglic, n-valeric, trimethylacetic, 2-methylbutyric, iso-valeric and propionic acids as component organic acids, while a "convolvulin" (ether-insoluble fraction[1,2]) afforded, in addition to those from the above "jalapin", 4-oxodecanoic acid and exogonic acid (3,6:6,9-diepoxydecanoic acid) which are characteristic of Brazilian resin.[3] Wagner and Kazmaier[4] isolated as a major glycosidic acid from the "convolvulin" of Brazilian resin, operculinic acid (rhamnoconvolvulinic acid[5]) which was assigned the structure 3,12-dihydroxypalmitic acid 12-O-α-D-glucopyranosyl(1→4)-[α-L-rhamnopyranosyl(1→6)]-α-D-glucopyranosyl(1→3)-α-L-rhamnopyranosyl(1→2)-[β-D-glucopyranosyl(1→3)]-β-D-glucopyranoside.[4]

In the course of our studies on resin glycosides in Convolvulaceae plants, the "jalapin" from Rhizoma Jalapae Braziliensis was examined and two new resin glycosides named operculin I (**1**) and II (**2**) were isolated.

The MeOH extractive of the powdered crude drug[6] was partitioned between ether and H_2O. Column

chromatographies of the ether-soluble fraction on MCI gel CHP 20P and Sephadex LH-20 afforded a "jalapin" (1.03%). Silica gel chromatography of the "jalapin" followed by preparative HPLC (Merck, hibar RP-8, 97% MeOH) furnished **1** (0.14%), colorless needles, mp 103-111°C (dec), $[\alpha]_D$ -24.0° (MeOH), $C_{70}H_{124}O_{25}$, IR (KBr): 3400 (br), 1725 cm^{-1}, and **2** (0.03%), colorless needles, mp 120-128°C (dec), $[\alpha]_D$-23.5° (MeOH), $C_{66}H_{116}O_{25}$, IR (KBr): 3400 (br), 1725 cm^{-1}.[7]

Prior to studying the structures of **1** and **2**, the component organic and glycosidic acids of the "jalapin" were examined. In contrast to another report,[3] only n-decanoic and n-dodecanoic acids were produced in the organic acid fraction of the alkaline hydrolysate (GC-MS in the form of methyl ester). The glycosidic acid fraction was methylated with CH_2N_2, and the mixture gave, along with three minor compounds, a methyl ester of glycosidic acid (**3'**), mp 172-173°C (dec), $[\alpha]_D$ -72.5° (MeOH), $C_{47}H_{84}O_{24}$, IR (KBr): 3350 (br), 1725 cm^{-1}, a negative ion FAB-MS m/z: 1031 $[M-H]^-$, which gave a new glycosidic acid named operculinic acid A (**3**), white powder, mp 180-183°C (dec), $[\alpha]_D$ -63.6° (MeOH), $C_{46}H_{82}O_{24}$, IR (KBr): 3400 (br), 1705 cm^{-1}, negative ion FAB-MS m/z: 1017 $[M-H]^-$, by alkaline hydrolysis.

On acid hydrolysis, **3'** afforded an aglycone and L-rhamnose ($[\alpha]_D$ +10.4° (H_2O)), D-fucose ($[\alpha]_D$ +74.1°, (H_2O)), and D-glucose ($[\alpha]_D$ +46.8°, (H_2O)). The aglycone was transformed to methyl ester, mp 44-45°C, $[\alpha]_D$ +1.1° (c=3.0, $CHCl_3$), which was identified with an authentic methyl jalapinolate[8] (^{1}H-NMR, GC-MS).

Previously the absolute configuration at C_{11} of methyl (+)-jalapinolate was determined to be R[8,9] by Horeau's method,[10] but Kitagawa, et al.[11] have recently revised it to S by direct comparison with synthetic (via Sharpless epoxidation) R and S compounds. We had been trying to verify our result,[8] and now application of the Mosher's method[12] lead to the same configuration (S) as reported by Kitagawa.[11] That is, there was a downfield shift by 0.038 ppm of the 16-H_3 signal of R-(+)-α-methoxy-α-trifluoromethylphenylacetic acid (MTPA) ester (**4**), oil, $[\alpha]_D$ +32.9° ($CHCl_3$), compared with that of S-(-)-MTPA ester (**5**), oil, $[\alpha]_D$ -31.5° ($CHCl_3$). (Fig. 1)

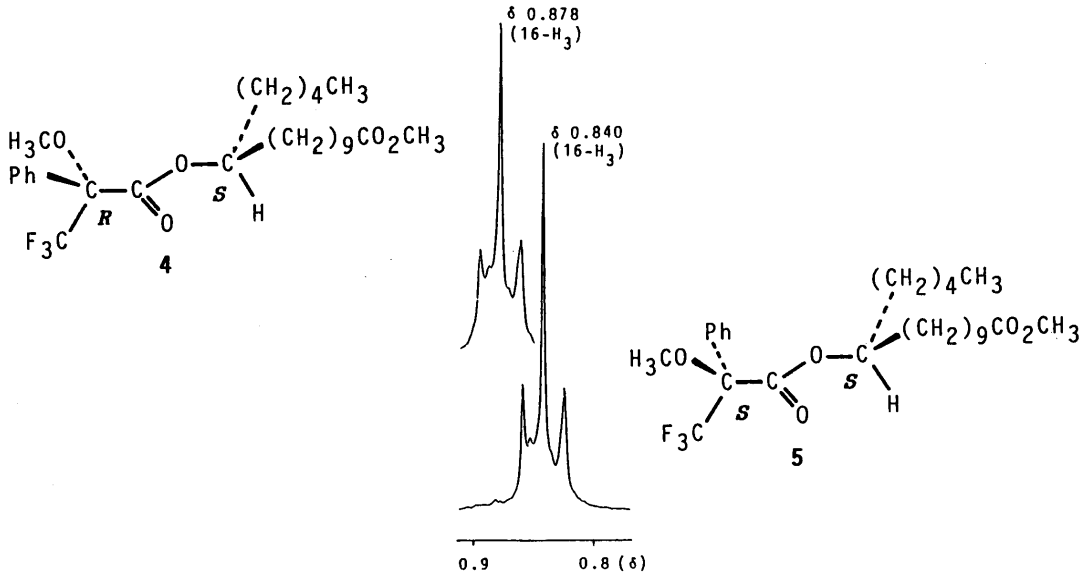

Fig. 1. ^{1}H-NMR Spectra of **4** (Upper) and **5** (in $CDCl_3$, 400 MHz)

In the ^{1}H-NMR spectrum[13], **3'** showed the ester methyl (δ 3.62, s) and 2-CH_2 (δ 2.33, t) signals due to the jalapinolic acid moiety, and five doublet signals at δ 4.77 (J=7.9 Hz), 6.20 (1.5), 5.86 (1.8), 6.17 (1.5) and 5.20 (7.7) that were assignable respectively to the anomeric protons of β-fucopyranose (fuc), α-rhamnopyranose (rha), α-rha', α-rha" and β-glucopyranose (glc) units. The C-H COSY spectrum of **3'** exhibited carbon signals of C_2 of fuc (δ 75.3), C_4 of rha (δ 82.3), and C_3

and C_4 of rha' (δ 82.2, 78.6). These are respectively subject to glycosylation (downfield) shift by 3.3, 8.5, 10.6 and 4.8 ppm in comparison with those of methyl pyranosides cited in the literature.[14] Cross peaks[15] observed between 1-H of glc and 3-H of rha', and 1-H of rha' and 4-H of rha in the NOESY spectrum of **3'**, taking into account the fact that **3'** is a methyl jalapinolate monodesmoside, led us to conclude that the structures of **3'** and **3** are as shown in Fig. 2.

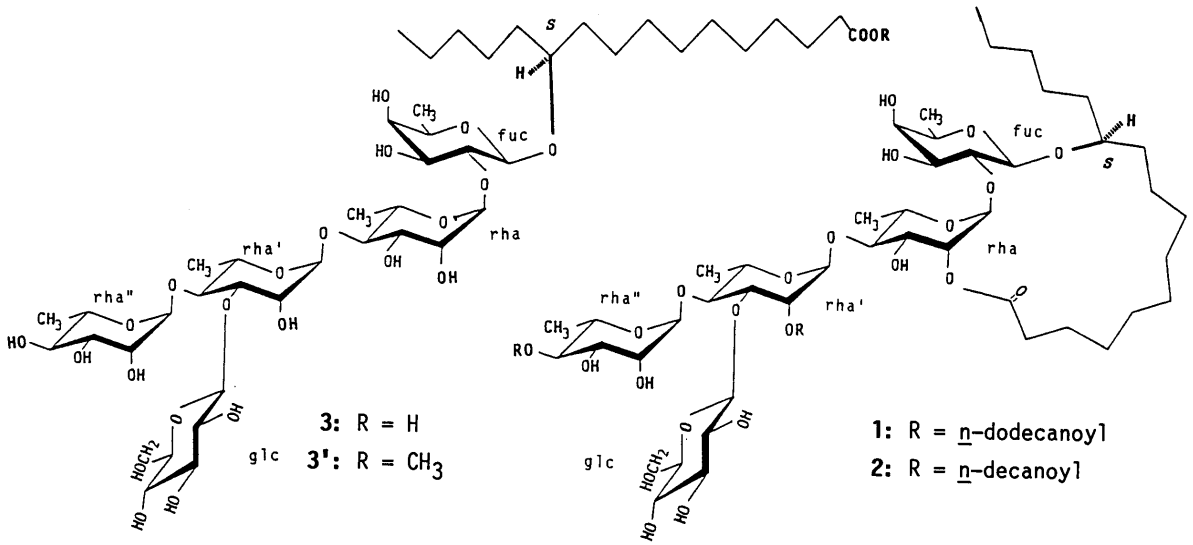

Fig. 2.

Operculin I (**1**), gave a glycosidic acid, mp 179–182°C, which was identified by saponification (3% KOH, 95°C, 1 h) as operculinic acid A (**3**) (^{1}H-NMR), and n-dodecanoic acid (GC-MS). **1** showed three carbonyl carbon signals (δ 173.1, 173.5, 173.6) and three methine protons, 2-H of rha (δ 5.90), 2-H of rha' (δ 6.29) and 4-H of rha" (δ 5.78), deshielded by 1.25, 1.15 and 1.58 ppm from those of **3'**. This indicated that **1** consists of one mol of **3** and two mol of n-dodecanoic acid, and that the carboxy groups of these acids link with one of 2-OH of rha, 2-OH of rha' and 4-OH of rha", respectively. This suggestion was supported by the $[M-H]^-$ ion peak at m/z 1363 in the negative ion FAB-MS spectrum. Further, the spectrum exhibited fragment peaks at m/z 1181 (**a**, R=n-dodecanoyl), 1035 (**b**, R=n-dodecanoyl), 853 (**c**), 545 (**d**) and 417 (**e**) (Fig. 3), indicating that two n-dodecanoic acids are located at 2-OH of rha' and 4-OH of rha" and that the jalapinolic acid of **3** is intramolecularly linked with 2-OH of rha to form a macrocyclic ester ring as shown in Fig. 2.

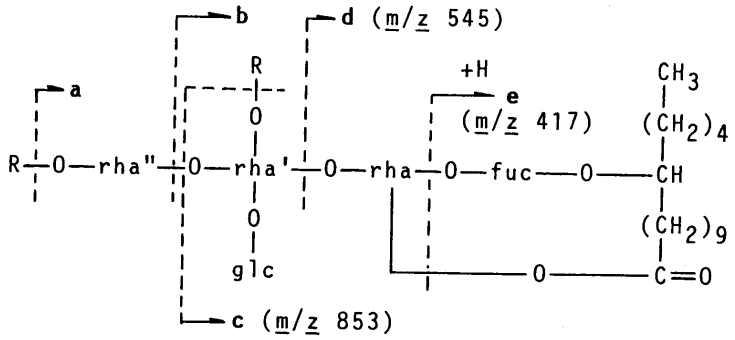

Fig. 3. (**1**: R = n-dodecanoyl, **2**: R = n-decanoyl)

Operculin II (**2**) showed a $[M-H]^-$ ion peak at m/z 1307 which is 56 mass units less than that of **1** in the negative ion FAB-MS spectrum and three carbonyl carbon signals with the same chemical

shifts as those of **1** at δ 173.1, 173.5 and 173.6 in the ^{13}C-NMR spectrum. On alkaline hydrolysis, **2** produced operculinic acid A (^{1}H-NMR) and n-decanoic acid (GC-MS) suggesting that the structure of **2** is the same as that of **1** except for organic acid groups. The ^{1}H-NMR spectrum of **2** was quite similar to that of **1** and, in particular, the chemical shifts of the signals due to 2-H of rha, 2-H of rha' and 4-H of rha" were identical to those of **1**. The negative ion FAB-MS spectrum of **2** presented fragment peaks at m/z 1153 (**a**, R=n-decanoyl), 1007 (**b**, R=n-decanoyl), along with the peaks **c**, **d** and **e**. (Fig. 3) Accordingly, the structure of **2** was defined as shown in Fig. 2.

The so-called resin glycosides have been classified by Mayer[1,2] into two groups, ether-soluble ("jalapin") and -insoluble ("convolvulin"). Not only operculin I and II, but without exception all the resin glycosides so far characterized, orizabins,[8] muricatins[16] and merremosides,[9,11] belong to the "jalapin" group and have a macrocyclic ester ring. Thus, this structure seems to be characteristic of "jalapin". It is worthy of note that the operculin I and II isolated in this work are the first glycosides in the "jalapin" group having two moles of fatty acid, n-dodecanoic or n-decanoic acids, linked to the sugar moiety in place of several organic acids such as isobutyric, 2-methylbutyric, tiglic and nilic acids commonly found in the ether-soluble resin glycosides.

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REFERENCES AND NOTES

1) W. Mayer, Justus Liebigs Ann. Chem., 83, 121, (1852).
2) There has been a confusion in nomenclature. That is, ether-soluble and -insoluble fractions are called in the Great Britain, contrary to in the continent, "convolvulin" and "jalapin", respectively. In this paper the names are used according to the report by Shellard (E. J. Shellard, Planta Med., 9, 102 (1961)).
3) E. Graf, E. Dahlke and H. W. Voigtlander, Arch. Pharm. Ber. Dtsch. Pharm. Ges., 298, 81 (1965).
4) H. Wagner and P. Kazmaier, Phytochemistry, 16, 711 (1977).
5) E. Votocek and V. Prelog, Coll. Trav. Chim. Tchecoslovaquie, 1, 55 (1929).
6) The material was purchased from Paul Mugenburg GmbH & Co. Hannover, FRG, and was microscopically identified as Rhizoma Jalapae Braziliensis by Dr. H. Lorenz of the company, to whom the authors' thanks are due.
7) All melting points were determined on a YANACO MP-3 apparatus and are uncorrected. Specific rotations were measured on a JASCO DIP-140 polarimeter. GC- (SE-30, EI mode) and FAB-MS (Xe, triethanolamine) spectra were recorded on a JEOL JMS DX-300/JMA 3500 spectrometer.
8) N. Noda, M. Ono, K. Miyahara, T. Kawasaki and M. Okabe, Tetrahedron, 43, 3889 (1987).
9) I. Kitagawa, H. Shibuya, Y. Yokokawa, N. I. Baek, K. Ohasi, M. Yoshikawa, A. Nitta and H. Wiriadinata, Chem. Pharm. Bull., 36, 1618 (1988).
10) A. Horeau and H. B. Kagan, Tetrahedron, 20, 2431 (1964).
11) I. Kitagawa, N. I. BaeK, K. Kawashima, K. Ohashi, Y. Yokokawa, H. Shibuya and M. Yoshikawa, Symposium Papers, The 30th Symposium on the Chemistry of Natural Products, Fukuoka, Oct. 1988, p. 252).
12) J. A. Dale and H. S. Mosher, J. Am. Chem. Soc., 95, 512 (1973).
13) NMR spectra were recorded on a JEOL JNM GX-400 instrument in py-d_5 solution, except **4** and **5**. All the ^{1}H- and ^{13}C-signals due to the sugar moieties of **1** - **3'** were assigned and confirmed by COSY, C-H COSY and NOESY techniques. The J values of anomeric and methine proton signals due to their sugar moieties indicated that the conformations of rha, rha', rha", fuc and glc are $^{1}C_4$, $^{1}C_4$, $^{1}C_4$, $^{4}C_1$ and $^{4}C_1$ respectively.
14) R. Kasai, M. Okihara, J. Asakawa and O. Tanaka, Tetrahedron Lett., 1977, 175; S. Yahara, R. Kasai and O. Tanaka, Chem. Pharm. Bull., 25, 2041 (1977).
15) Cross peaks due to 1-H of rha (δ 6.20) and 1-H of rha" (δ 6.17) were also observed in the NOESY spectrum, but their NOE relations could not be defined because their counterparts, 2-H of fuc and 4-H of rha', appeared at the same chemical shift (δ 4.47).
16) N. Noda, H. Kobayashi, K. Miyahara and T. Kawasaki, Chem. Pharm. Bull., 36, 627 (1988); N. Noda, M. Nishi, K. Miyahara and T. Kawasaki, ibid., 36, 1707 (1988).

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