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EXCISANIN A AND B, NEW DITERPENOIDS FROM *RABDOSIA EXCISA*

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Chemical investigation of the bitter principles from *Rabdosia Excisa* has led to the isolation and characterization of two new diterpenoids having an *ent*-kaurene skeleton, excisanin A and B, and their structures were established by spectroscopic and chemical data.

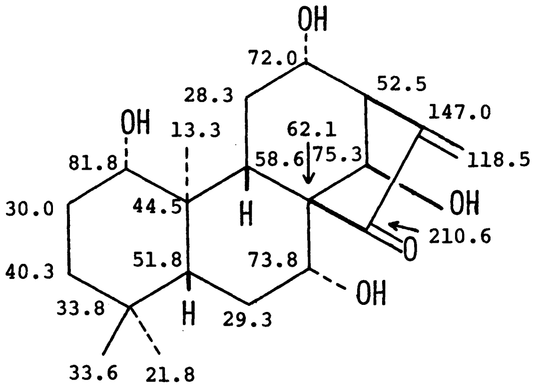
We wish to report the isolation and structural elucidation of excisanin A (1) and B (2), new *ent*-kaurenoids from the leaves of *Rabdosia Excisa* (Maxim.) Hara (collected at Anshan district of China in July of 1979) together with kamebakaurin[1] (3), kamebacetal B[2] (4), and kamebanin[3] (5). Excisanin A and B show a prominent cytotoxic effect against Ehrlich carsinoma cells *in vitro*[4] and have a significant anti-neoplastic effect on some of transplantable animal tumors, such as ECA, S_{180}, P_{388}, etc.[4,5] and appear to be the first 12-oxygenated *ent*-kaurenoid from *Rabdosia* plants.

Excisanin A [1 ; $C_{20}H_{30}O_5$(M^+ 350)[6]; mp. 262-264 °C ; $[\alpha]_D^{20}$ -27.7 (c=1.01, C_5H_5N) ; λ_{max} (EtOH) 234 nm (ε 5560) ; ν_{max} (KBr) 1713 and 1645 cm^{-1}; ^1H nmr (C_5D_5N) δ 5.38 and 6.31 (each 1H, s) ; ^{13}C nmr ($CDCl_3$ + CH_3OH) δ 118.5 (t) and 147.0 (s)(exomethylene), and δ 210.6 (s, ketone)] gave a dihydro compound [9 ; $C_{20}H_{32}O_5$; mp. >308 °C] by catalytic hydrogenation on PtO_2, which showed a negative cd effect [$\Delta\varepsilon_{307}$ -0.37] in methanol. These spectroscopic data suggest that excisanin A has an *ent*-15-oxo-16-kaurene skeleton which is typical of *Rabdosia* diterpenoids.[7]

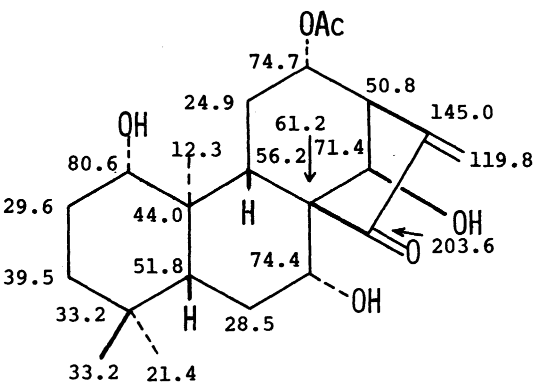
Excisanin A (1) has four secondary hydroxyl groups : ir 3430-3380 cm^{-1}; ^{1}H nmr δ 3.48 (1H, dd, 6 and 10 Hz), 4.41 (1H, t, 4 Hz), 4.87 (1H, dd, 8 and 11 Hz), and 5.99 (1H, s) ; ^{13}C nmr δ 81.8, 75.3, 73.8, and 72.0 (each doublet). This was confirmed by conversion of (1) to a tetraacetate [6 ; mp. 206-208 °C] by acetylation (acetic anhydride-pyridine). On the other hand, (1) gave the 7,14-monoacetonide [7 ; $C_{23}H_{34}O_5$; mp. 244-246 °C] on treatment with acetone and anhydrous copper (II) sulfate. Oxidation of (1) with Beckmann mixture afforded a trione [8 ; $C_{20}H_{26}O_5$; mp. 247-250 °C ; ^{1}H nmr ($CDCl_3$) δ 4.87 (s, 14α-H), 4.46 (dd, 7 and 10 Hz, 7β-H)]. These results revealed that two hydroxyl groups are placed at 14β (δ 5.99, 14α-H) and 7α (δ 4.87, 7β-H) in (1). In fact, NOE (10 %) on 14α-H was observed upon irradiation at the signal (δ 1.91, s) of the 10-CH_3.[3]

EI-MS peaks of excisanin A (1) at m/z 192 ($C_{11}H_{12}O_3$) and 174 ($C_{11}H_{10}O_2$), which were formed by cleavage of the B-ring,[8] showed the existence of one hydroxyl group in the A-ring and two hydroxyl groups in the C-ring. The location of the hydroxyl group other than C-14β in the C-ring was elucidated to be at C-12α by the abnormally low chemical shifts of 10-CH_3 and 14α-H, and further the following decoupling experiments. On irradiation at δ 4.41 (12β-H), the doublet at δ 3.67 (d, 4 Hz, 13α-H) changed into a singlet and the signal pattern at δ 2.07-2.27 (m, 11β-H) was deformed. On irradiation at δ 3.67, the triplet at δ 4.41 collapsed to a doublet (4 Hz). On the other hand, on irradiation at δ 2.17, the triplet at δ 4.41 collapsed to a doublet (4 Hz) and the doublet at δ 3.98 (d, 16 Hz, 11α-H) changed into a singlet. These results suggested that the dihedral angles of 12β-H and 11α-H, and 11α-H and 9β-H are *ca.* 90°, respectively. Thus, the C-ring of (1) seems to be a deformed chair form. The location of the hydroxyl group in the A-ring to be at 1α position of (1) was shown by the coupling pattern of the signal at δ 3.48 (1β-H) and the unusually low chemical shift of 11α-H.[3] Consequently, the structure of excisanin A is represented as (1).

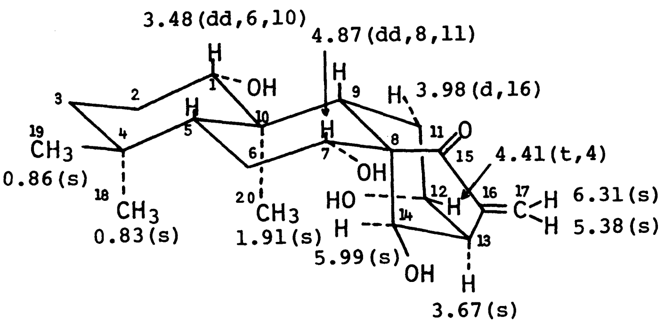
Excisanin B [2 ; $C_{22}H_{32}O_6$ (M^+ 392); mp. 240-243 °C ; $[\alpha]_D^{20}$ -13.9 (c=1.00, C_5H_5N) ; λ_{max} (EtOH) 230 nm (ε 7900) ; ν_{max} (KBr) 3400, 1740, 1726, 1713, and 1646 cm^{-1}] is 12-acetylexcisanin A. The ^{1}H nmr spectrum (C_5D_5N) is very similar to that of (1) except for the presence of signal due to an acetyl group (δ 2.07) and down-field shift of 12β-H signal, from δ 4.41 in (1) to δ 5.26 in (2).



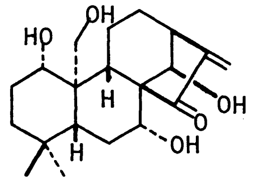
(1) Excisanin A, ^{13}C nmr data in $CDCl_3+CH_3OH$ solution (δ/ppm)[9]



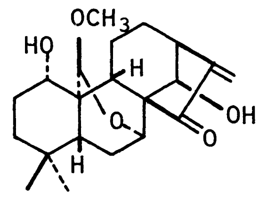
(2) Excisanin B, ^{13}C nmr data in $CDCl_3+CH_3OH$ solution (δ/ppm)[9]



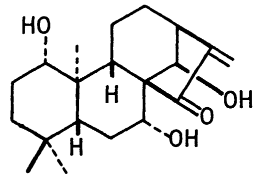
(1a) Excisanin A, ^1H nmr data in C_5D_5N solution; δ values multiplicity and *J* values (in Hz) in parentheses



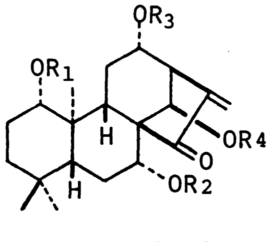
(3)

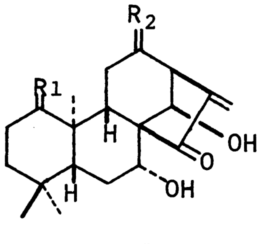


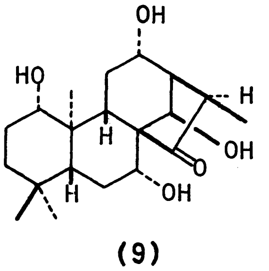
(4)



(5)







(6) $R_1=R_2=R_3=R_4=Ac$

(8) $R_1=R_2=O$

(9)

(7) $R_1=R_3=H$, $\begin{matrix}R_2\\R_4\end{matrix} = \gt C \lt \begin{matrix}CH_3\\CH_3\end{matrix}$

(11) $R_1=O$, $R_2=\lt\begin{matrix}OAc\\H\end{matrix}$

(10) $R_1=H$, $R_3=Ac$, $\begin{matrix}R_2\\R_4\end{matrix} = \gt C \lt \begin{matrix}CH_3\\CH_3\end{matrix}$

The ^{13}C nmr of (2), comparing with that of (1), differs only in number of methyl and carbonyl carbons due to acetyl group. Acetylation (acetic anhydride-pyridine) of (2) gave a tetraacetate [mp. 206-208 °C], which was identical with (6) derived from (1). On the other hand, saponification of (2) with 1 N NaOH afforded (1). Excisanin B (2) gave rise to an acetonide [10 ; mp. 272-274 °C] and the 1-oxo compound [11 ; mp. 230-233 °C] on treatment with acetone-anhydrous copper (II) sulfate and Beckmann mixture, respectively. In addition, an NOE (18 %) was observed for the singlet at δ 5.62 (14α-H) on irradiation at δ 1.54 (10-CH_3) in (2).

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REFERENCES AND FOOTNOTES

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5. The results will be published elsewhere.
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9. The assignments are based on a combination of PND, off-resonance decoupling and comparison with data of kamebanin.[3]

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