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Received June 14, 1972

[Chem. Pharm. Bull. **20**(10)2291—2292(1972)]

UDC 547.979.4.02 : 561.192

Isolation of Hexahydrocurcumin, Dihydrogingerol and Two Additional Pungent Principles from Ginger

Curcumin has attracted special attention from a biosynthetic point of view,[1,2] meanwhile gingerol has also been the subject of many investigations.[3] In our study on the pungent principles of ginger[4] we have now isolated the four new compounds (**1**, **3**, **6**, and **7**); the first of these closely relates to curcumin, while the latter three to gingerol.

The ethyl acetate soluble fraction obtained from acetone extract of Japanese commercial ginger, was successively chromatographed on silica gel column using benzene–acetone mixtures as the eluent. Compounds (**1** and **3**) were isolated from fractions more polar than gingerol (**5**), whereas **6** and **7** from crude gingerol fraction.[4]

Compound (**1**),[5] $C_{21}H_{26}O_6$, mp 90—91° (benzene), $[\alpha]_D^{24}$ +9.0°, Mass Spectrum *m/e*: 374 (M^+), IR ν_{max}^{KBr} cm^{-1}: 3380 (OH); 1705 (ketone); 1610 and 1510 (benzene ring), was obtained in 0.002% yield based on the fresh material. The compound gives a positive ferric chloride test. The NMR spectrum of **1** displays six aromatic proton signals, forming finely overlapped two, 1,2,4-substitution patterns of benzene ring (2H each at δ 6.79 d, J=8 Hz; 6.64 d, J=2 Hz; 6.6 dd, J=8 and 2 Hz), 6H singlet (3.80, $2\times C\underline{H}_3O$), overlapped multiplets (near 2.7, total 8H, four methylene groups), 2H multiplet (near 1.7, methylene) and 1H quintet (J=6 Hz) at 4.01 ppm. A broad 2H singlet also appears at 5.67 ppm; the signal diminished promptly on addition of D_2O.

Compound (**1**) upon treatment with acetic anhydride and pyridine afforded the diacetate (**2**) of anhydro derivative; the NMR spectrum of the latter shows one of the newly formed olefinic protons at 6.03 ppm as a doublet (J=17 Hz). The spectrum also exhibits 6H singlet at 2.28 due to acetyls, 6H singlet at 3.72 due to methoxyls, broad overlapped multiplets between 2.6 to 2.8 (total 8H, four methylenes) besides six aromatic and one olefinic proton

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[1] T.A. Geissman and D.H. Grout, "Organic Chemistry of Secondary Plant Metabolism," Freeman, Cooper and Company, San Fransisco, 1969, p. 169.

[2] P.J. Roughley and D.A. Whiting, *Tetrahedron Letters*, **1971**, 3741.

[3] For a histrory of studies on gingerol, see D.W. Connel and M.D. Sutherland, *Aust. J. Chem.*, **22**, 1033 (1969); They skillfully determined the absolute configuration of gingerol.

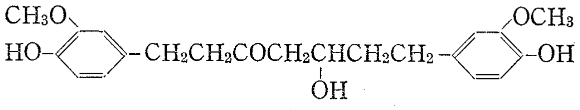
[4] We have already reported on the isolation of crystalline gingerol (**5**), mp 29—31°, $[\alpha]_D^{24}$ +25.1°; whose structure and purity were demonstrated by nuclear magnetic resonance (NMR) spectroscopy, mass spectrum and gas–liquid chromatography (GLC), trimethylsilylation method, QF-1 column). *Cf.* M. Miyamoto, M. Shinohara, and T. Murata, presented at the 88th Annual Meeting of Pharmaceutical Society of Japan, Tokyo, April, 1968, Abstract Papers, p. 231. We also suggested the presence of two minor compounds (**6** and **7**) in ginger by mass spectrum and GLC of a crude gingerol fraction; the two shogaols corresponding to **6** and **7** were detected and identified with synthetic specimens, respectively, by GLC.

[5] All melting points were measured on Kofler block and uncorrected. The specific rotations were taken on $CHCl_3$ solutions, c=1.0%. The NMR spectra were recorded with a Varian HA-100 spectrometer and calibrated against internal tetramethylsilane. Chemical shifts are expressed in ppm (δ): s, singlet; d, doublet; t, triplet; m, multiplet.

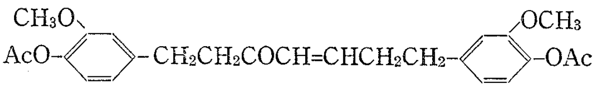
signals between 6.6 to 6.8 ppm. The infrared (IR) spectrum of compound (**2**) shows bands at 1670, 1630 (CO-C=C) and 1765 cm^{-1} (phenol acetate); no hydroxyl absorption was observed ($CHCl_3$).

On the ground of above data we assigned at this stage structures **1** and **2** to the compounds, respectively. Confirmation of the conclusion was obtained by direct comparison with the specimens derived from curcumin. Sodium borohydride reduction of tetrahydrocurcumin⁶⁾ gave hexahydrocurcumin, mp 78—80°, $[\alpha]_D^{22}$ ±0°; the melting point of the latter was not depressed by **1** of natural origin upon admixture. The IR spectra (KBr disk) were superimposable. The identity was also confirmed as **2** by IR and NMR spectra. It is interesting to note that **1** shows a choleretic action in rats and dogs, and that **1** could not be detected in commercial turmeric, *Curcuma longa* L.

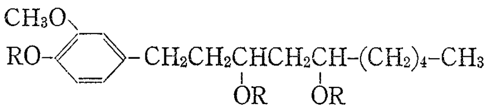
Compound (**3**), $C_{17}H_{28}O_4$, Mass Spectrum *m/e*: 296 (M^+), was obtained as an oil in 0.001% yield, and characterized as its triacetate (**4**). The triacetate (**4**), $C_{23}H_{34}O_7$, $[\alpha]_D^{23}$ −0.8°, IR $\nu_{max}^{liq.}$ cm^{-1}: 1770 and 1738 (acetyls); 1605 and 1510 (benzene ring); no OH band, displays in the NMR spectrum the following signals: 0.85 (3H t, $J=7$ Hz, $-CH_2-C\underline{H}_3$), 1.24 (6H broad s, $3\times C\underline{H}_2$), 1.5 (2H m, $C\underline{H}_2$), 1.8 (4H m, $2\times C\underline{H}_2$), 1.95 (3H s, $C\underline{H}_3COO$), 1.98 (3H s, $C\underline{H}_3COO$), 2.23 (3H s, $C\underline{H}_3COO$), 2.55 (2H broad t, $J=7$ Hz, $C\underline{H}_2$), 3.75 (3H s, $C\underline{H}_3O$), 4.88 (2H m, $2\times C\underline{H}OAc$) and 3H aromatic proton signals with spin–spin interactions characteristic of an 1,2,4-trisubstituted benzene (6.85 d, $J=8$ Hz; 6.69 broad s; 6.62 broad d, $J=8$ Hz). The IR and NMR spectra of the compound are indistinguishable from those of dihydrogingerol triacetate (**4**), $[\alpha]_D^{24}$ +1.8°, respectively, which was obtained by sodium borohydride reduction of gingerol (**5**), followed by acetylation. However, stereochemistry of the natural compounds (**1** and **3**) still remains unclarified. **3** tastes bitter rather than pungent.



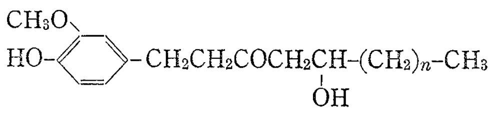
1



2



3: R=H
4: R=Ac



5: *n*=4
6: *n*=6
7: *n*=8

In addition to this, we have succeeded in isolating the two, new minor pungent principles of ginger (**6** and **7**): **6**, mp 30—32°, $[\alpha]_D^{22}$ +23.0°; O-methyl ether (dimethyl sulfate-K_2CO_3), mp 43—44°, $[\alpha]_D^{22}$ +25.0°, **7**, mp 43—44°, $[\alpha]_D^{22}$ +16.5°; O-methyl ether, mp 50—51°, $[\alpha]_D^{22}$ +23.0°. Their structures were established by NMR spectral evidence.

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Received June 20, 1972

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6) The compound was obtained by reduction of curcumin with sodium amalgam. L. Jackson and A.E. Menke, *Am. Chem. J.*, **4**, 360 (1882—1883).