原著論文

Pharmacognostic Studies on Ginger and Related Drugs – part 2 : Constituents of Zingiberis Processum Rhizome (Kankyo)

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ABSTRACT

Nineteen compounds has been isolated from the 80% methanolic extract of Kankyo (Japanese name for Zingiberis processum rhizome) made out of ginger, including a glucoside of 6 - gingerdiol (**15**), four diarylheptanoids (**16** – **19**) and the sulfonated compounds such as 6 - gingesulfonic acid (**10**) and shogasulfonic acid A (**12**) previously reported, besides twelve known compounds. This is the first isolation of compounds **15** – **19** from the Kankyo. In addition, interestingly, two kinds of Kankyo are found to be sold in the Japanese market: one contains sulfonated derivatives and the other contains no such compound.

Key words：*Zingiber officinale*, Zingiberaceae, Kankyo, Zingiberis processum rhizome, sulfonated compounds.

INTRODUCTION

Shokyo and Kankyo (Japanese names of Zingiberis rhizome and Zingiberis processum rhizome, respectively) are important crude drugs in traditional Kampo medicine made out of ginger, the rhizomes of *Zingiber officinale* Roscoe (Zingiberaceae), by different process. According to the Japanese Pharmacopeia, Shokyo is prepared simply by drying, while Kankyo is by drying after steaming. It is interest that the two crude drugs prepared from the same origin of ginger have been discriminated clinically use in Kampo medicine [1-3]. However there are no scientific evidences for the clinical discrimination between Shokyo and Kankyo. In order to clarify the chemical evidences for the discrimination between them, we started the studies on their chemical constituents.

We studied previously on the phytochemical investigation on Shokyo, and isolated, unexpectedly, six sulfonated compounds, i.e. 4- and 6-gingesulfonic acids (**10**), shogasulfonic acids A (**12**), B, C and D, together with gingerols, shogaols, diarylheptanoids [4] and five monoterpene glycosides, zingiberosides A, B, C, D and E [5]. Further on, we clarified that the sulfonated derivatives were artificial products formed by bleaching with sulfur in the preparation process [6], although the preparation procedure of Shokyo had been believed only drying without sulfur bleaching.

Kankyo is also prepared from ginger in almost same manner, only different process from Shokyo is prepared by steaming followed by drying as described above. The constituents of Kankyo have been regarded to be as the same as those of Shokyo, because their origins are same, and the previous investigations were

resulted in isolation of the same components as those from Shokyo, volatile oils consist of sesquiterpenes of bisabolane-type and pungent constituents such as gingerols, shogaols and zingerone [7].

This paper deals with the isolation and characterization of nineteen compounds from the 80% methanol extract of Kankyo as well as the comparative study on various Kankyo samples in the Japanese market.

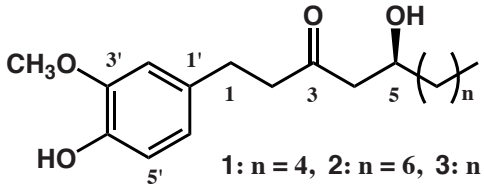
RESULTS AND DISCUSSION

The 80% methanol extract of commercial Kankyo A (imported from China, 5.0 kg) was divided into an ether- and a water-soluble fractions. By means of column chromatography (CC) and HPLC, nine compounds (**1** – **9**) were isolated from the ether-soluble fraction, and ten (**10** – **19**) were from the water-soluble fraction, as described in Experimental. Of them, the fourteen compounds were identified as follows by direct comparison with those obtained from Shokyo previously [4, 5] or by comparison of the data with those reported [8, 9]: 6-, 8-, 10-gingerols (**1 – 3**), 6-, 8-, 10-shogaols (**4 – 6**), 6-paradol (**7**), 6-gingediacetate (**8**), zingerone (**9**), 6-gingesulfonic acid (**10**), hexahydrocurcumin (**11**), shogasulfonic acid A (**12**), zingiberosides A (**13**) and B (**14**), respectively.

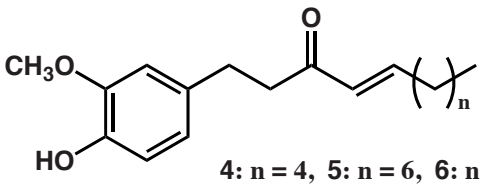
Compound **15** was isolated as a white amorphous powder, mp 123 ˚C. It showed a pseudomolecular ion ($[M+H]^+$) peak at m/z 459 ($C_{23}H_{39}O_9$) in the FAB-MS. The ^{13}C NMR spectrum of **15** revealed the presence of a 1,3,4-trisubstituted benzene, an arylic methoxyl group, two carbinyl methines, seven methylenes, an aliphatic methyl group and a β-D-glucopyranosyl moiety (Table 1-1). The signals due to the aglycone part were resembled on those of 6-gingediol [8, 10], except for the C-4' carbon signal due to the glycosylation shift. In addition, an HMBC correlation was observed between glucosyl H-1" (δ 4.82, d, J = 7.3 Hz) / C-4' (δ 146.1). The specific rotation (−37.1˚) indicated the configuration of **15** to be (3*S*,5*S*) [11]. Thus, **15** was characterized as (3*S*,5*S*)-6-gingediol 4'-*O*-β-D-glucopyranoside, which was previously isolated from the ginger rhizome [11].

Compound **16** was obtained as a pale yellowish oil, $[\alpha]_D^{16}$ −11.0˚ (*c* 1.07, EtOH). It showed a $[M+H]^+$ ion peak at m/z 407.2044 ($C_{22}H_{31}O_7$) in the HR FAB-MS, which was 31 mass unit (CH_3O) larger than that of hexahydrocurcumin (**11**) [12]. The IR spectrum of **14** showed absorption bands due to hydroxyl group at 3335 cm^{-1}. The feature of the ^1H and ^{13}C NMR spectra of **16** were similar to those of **11**, and they showed the presence of a β-glycol, a 1,3,4-trisubstituted benzene ring, and a symmetrical 1,3,4,5-tetrasubstituted benzene ring having one hydroxyl group and two methoxyl groups in **11** (Table 1-1), suggesting **16** to be 3,5-dihydroxy-1-(4-hydroxy-3-methoxyphenyl)-7-(4-hydroxy-3,5-dimethoxyphenyl)heptane. Finally, **16** was identified as (3*S*,5*S*)-3,5-dihydroxy-1-(4-hydroxy-3-methoxyphenyl)-7-(4-hydroxy-3,5-dimethoxyphenyl)-heptane by comparison of the data with those reported [13].

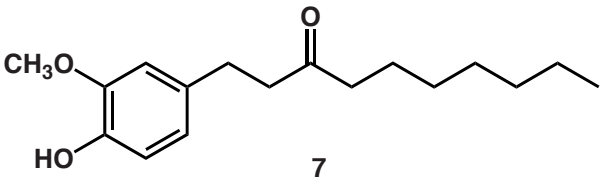
Compounds **17** and **18** were isolated as a pale yellowish oily substance, and they showed the same $[M+H]^+$ at m/z 391 in the Positive FAB-MS. Their ^1H and ^{13}C NMR spectra showed the presence of the same aromatic rings as **16**, three oxymetine and four methylen groups, and their plane structures were supposed to be 1,5-epoxy-3-hydroxy-1-(3,4-dihydroxy-5-methoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)heptane, which was recently isolated from the rhizome of ginger [10] (Table 1-1). The H-3 signal of **17** was appeared as a dddd (J = 4.6, 4.6, 11.3 and 11.6 Hz) at δ 3.80, while that of **18** was as a dddd (J = 2.1, 2.1, 2.8 and 2.8 Hz) at δ 4.21. These facts demonstrated that the orientation of the C-3 hydroxyl group must be equatorial in **17** and axial in **18**, that is, the structures of **17** and **18** were determined to be (1*R*,3*S*,5*R*)-1,5-epoxy-3-hydroxy-1-(3,4-dihydroxy-5-methoxyphe-



1: n = 4, 2: n = 6, 3: n = 8



4: n = 4, 5: n = 6, 6: n = 8



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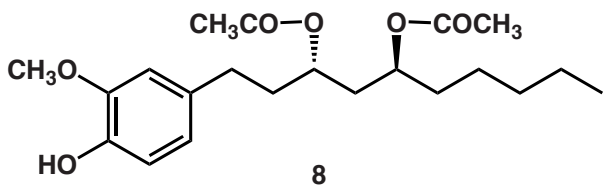

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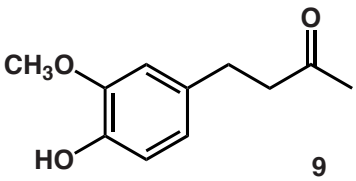

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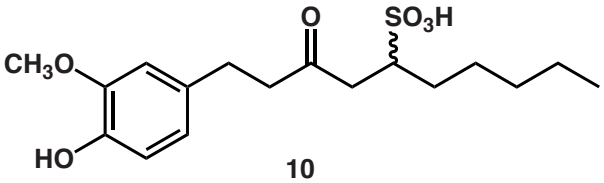

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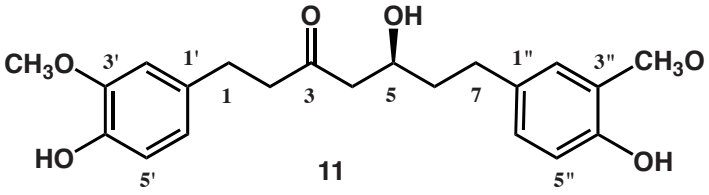

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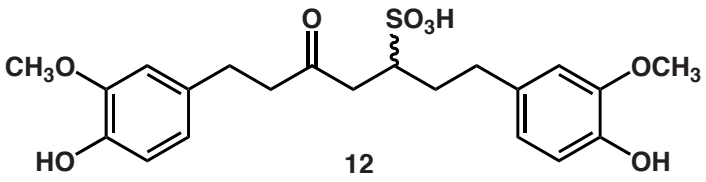

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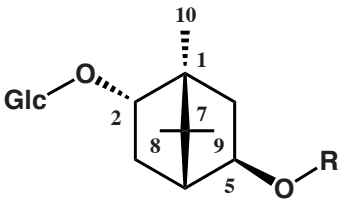
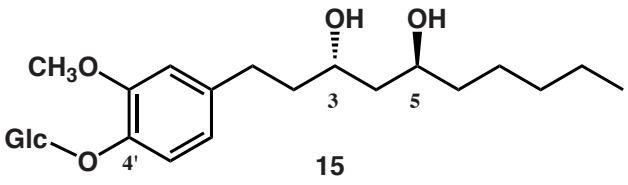


13: R=H, 14: R=Glc



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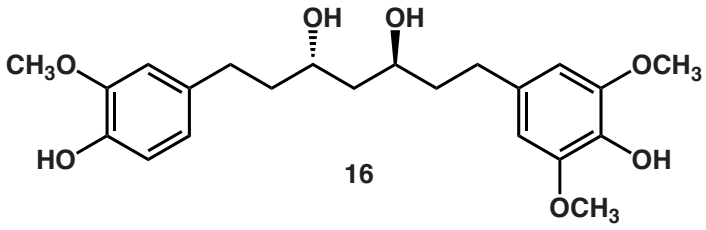
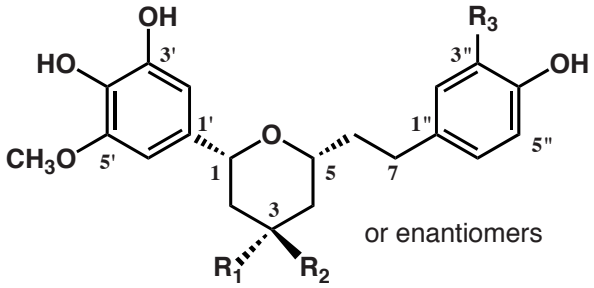


16



17: R_1=OH, R_2=H, R_3=OCH_3
18: R_1=H, R_2=OH, R_3=OCH_3
19: R_1=OH, R_2=H, R_3=H
20: R_1=OH, R_2=H, R_3=OH
21: R_1=H, R_2=OH, R_3=OH

Fig.1　Structures of **1** – **21**

Table 1-1 ^{1}H and ^{13}C NMR spectral data of **15 – 18** (in methanol-d_4, 500 and 125 MHz)

No.	15		16		17		18	
	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H
1	32.7	2.61, 1H each, dt (8.2, 14.0)	32.6	2.57, 2.68, 1H each, m	79.0	4.18, 1H, dd (2.2., 11.6)	75.2	4.63, 1H, dd (2.1, 11.6)
		2.72, 1H each, dt (7.9, 14.0)						
2	41.2	1.70, 2H, m	41.3 [a)]	1.71, 2H, m	43.8	1.40, 1H, ddd (11.6, 11.6, 12.2)	41.1	1.73, 1H, ddd (2.8, 11.6, 14.0)
	68.6	3.81, 1H, m		–	exo	2.07, 1H, dddd (2.2, 2.2, 4.6, 12.2)	exo	1.83, 1H, dddd (2.1, 2.1, 2.1, 14.0)
3	45.7	1.48, 2H, m	68.6 [b)]	3.82, 1H, m	69.0	3.80, 1H, dddd (4.6, 4.6, 11.3, 11.6)	65.6	4.21, 1H, dddd (2.1, 2.1, 2.8, 2.8)
4	69.3	3.81, 1H, m	45.7	1.56, 2H, dd (5.6, 6.7)	41.9	1.21, 1H, ddd (11.3, 11.3, 12.2)	39.3	1.53, 1H, ddd (2.8, 11.6, 14.1)
	39.2			–	exo	1.95, 1H, dddd (2.2, 2.2, 4.6, 12.2)	exo	1.68, 1H, dddd (2.1, 2.1, 2.2, 14.1)
5	26.5	1.29 - 1.43, 8H, m	68.7 [b)]	3.82, 1H, m	76.2	3.41, 1H, dddd (2.2, 4.6, 8.0, 11.3)	72.5	3.86, 1H, dddd (2.2, 4.6, 8.3, 11.6)
6	33.1		41.4 [a)]	1.71, 2H, m	39.2	1.75, 1H, dddd (4.6, 8.0, 9.2, 13.8)	39.4	1.68, 1H, dddd (4.6, 8.3, 9.5, 13.8)
	23.7					1.85, 1H, dddd (5.5, 8.0, 8.6, 13.8)		1.77, 1H, dddd (5.5, 8.3, 8.3, 13.8)
7	14.4	0.90, 3H, t (7.0)	33.1	2.57, 2.68, 1H each, m	32.3	2.62, 1H, ddd (8.0, 8.6, 13.8)	32.2	2.63, 1H, ddd (8.3, 8.3, 13.7)
						2.70, 1H, ddd (5.5, 9.2, 13.8)		2.70, 1H, ddd (5.5, 9.5, 13.7)
1'	138.9	–	135.2	–	134.5	–	134.4	–
2'	114.1	6.85, 1H, d (1.8)	113.1	6.76, 1H, d (1.8)	108.0	6.53, 1H, d (2.2)	107.9	6.53, 1H, d (2.2)
3'	150.7	–	148.8	–	146.4	–	146.4	–
4'	146.1	–	145.4	–	135.0	–	135.2	–
5'	118.3	7.06, 1H, d (8.2)	116.1	6.68, 1H, d (8.0)	149.5	–	149.5	–
6'	121.9	6.74, 1H, dd (1.8, 8.2)	121.8	6.62, 1H, dd (1.8, 8.0)	102.7	6.52, 1H, d (2.2)	102.7	6.52, 1H, d (2.2)
1"	103.2	4.82, 1H, d (7.3)	134.5	–	134.6	–	135.2	–
2"	75.0	3.46, 1H, m	106.6	6.48, 1H, s	113.3	6.75, 1H, d (1.8)	113.3	6.75, 1H, d (2.0)
3"	77.8	3.46, 1H, m	149.1	–	148.8	–	148.8	–
4"	71.4	3.40, 1H, m	134.5	–	145.5	–	145.4	–
5"	78.2	3.40, 1H, m	149.1	–	116.1	6.68, 1H, d (8.0)	116.0	6.68, 1H, d (8.0)
6"	62.5	3.68, 1H, dd (5.2, 12.2)	106.6	6.48, 1H, s	121.8	6.60, 1H, dd (1.8, 8.0)	121.9	6.61, 1H, dd (2.0, 8.0)
		3.86, 1H, dd (1.9, 12.2)						
MeO	56.7	3.84, 3H, s	56.3	3.82, 3H, s	56.6	3.83, 3H, s	56.6	3.83, 3H, s
			56.7	3.82, 3H, s	56.3	3.77, 3H, s	56.3	3.77, 3H, s
			56.7	3.82, 3H, s				

a-b) The assignments may be interchangeable within the same column.

Coupling constants (J in Hz) are given in parentheses.

Table 1-2 ^{1}H and ^{13}C NMR spectral data of **19 – 21** (in methanol-d_4, 500 and 125 MHz)

No.	19		20		21	
	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H
1	78.9	4.17, 1H, dd (2.2, 11.6)	78.9	4.19, 1H, dd (2.0, 11.3)	75.2	4.64, 1H, dd (2.2, 11.8)
2	43.6	1.41, 1H, ddd (11.6, 11.8, 12.6)	43.7	1.40, 1H, ddd (11.3, 11.6, 12.2)	41.0	1.71, 1H, ddd (2.8, 11.8, 14.0)
	exo	2.07, 1H, dddd (2.2, 2.2, 4.3, 12.6)	exo	2.07, 1H, dddd (2.0, 2.0, 4.6 12.2)	exo	1.83, 1H, dddd (2.2, 2.5, 2.7, 14.0)
3	69.0	3.79, 1H, dddd (4.3, 4.6, 11.3, 11.8)	69.0	3.81, 1H, dddd (4.6, 4.6, 11.3 , 11.6)	65.6	4.21, 1H, dddd (2.7, 2.8, 2.8, 2.8)
4	41.8	1.21, 1H, ddd (11.3, 11.3, 11.6)	41.8	1.20, 1H, ddd (11.3, 11.3, 12.2)	39.4	1.52, 1H, ddd (2.8, 11.6, 14.0)
	exo	1.93, 1H, dddd (2.2, 2.2, 4.6, 11.6)	exo	1.94, 1H, dddd (2.0, 2.0 4.6, 12.2)	exo	1.68, 1H, dddd (2.3, 2.5, 2.8, 14.0)
5	76.3	3.41, 1H, dddd (2.2, 4.6, 7.7 11.3)	76.3	3.42, 1H, dddd (2.0, 4.6, 8.0, 11.3)	72.6	3.89, 1H, dddd (2.3, 4.6, 8.6, 11.6)
6	39.2	1.71, 1H, dddd (4.6, 7.4, 9.5, 13.8)	39.1	1.70, 1H, dddd (4.6, 8.0, 9.2, 13.8)	39.2	1.64, 1H, dddd (4.6, 8.5, 9.8, 14.0)
		1.84, 1H, dddd (5.8, 7.7, 8.9, 13.8)		1.84, 1H, dddd (5.8, 8.0, 8.6, 13.8)		1.76, 1H, dddd (5.5, 8.5, 8.6, 14.0)
7	31.8	2.60, 1H, ddd (7.4, 8.9, 13.8)	32.0	2.55, 1H, ddd (8.0, 8.6, 13.8)	32.0	2.55, 1H, ddd (7.7, 8.5, 13.7)
		2.66, 1H, ddd (5.8, 9.5, 13.8)		2.61, 1H, ddd (5.8, 9.2, 13.8)		2.61, 1H, ddd (5.5, 9.8, 13.7)
1'	134.5	–	134.5	–	135.2	–
2'	108.0	6.51, 1H, d (1.6)	108.0	6.52, 1H, br d	108.0	6.52, 1H, d (1.8)
3'	146.3	–	146.3	–	146.4	–
4'	134.6	–	134.6	–	134.4	–
5'	149.4	–	149.4	–	149.5	
6'	102.8	6.52, 1H, d (1.6)	102.8	6.52, 1H, br d	102.8	6.53, 1H, d (1.8)
1"	134.2	–	134.6	–	135.2	–
2"	130.4	6.98, 1H, dd (1.8, 8.6)	116.6	6.62 1H, d (2.0)	116.7	6.62, 1H, d (2.2)
3"	116.1	6.67, 1H, dd (1.8 8.6)	146.1	–	146.1	–
4"	156.3	–	144.2	–	144.2	–
5"	116.1	6.68, 1H, dd (1.8 8.6)	116.3	6.65, 1H, d (8.0)	116.2	6.64, 1H, d (8.0)
6"	130.4	6.99, 1H, dd (1.8, 8.6)	120.7	6.50, 1H, dd (2.0, 8.0)	120.7	6.50, 1H, dd (2.2, 8.0)
MeO	56.6	3.82, 3H, s	56.6	3.83, 3H, s	56.6	3.84, 3H, s

Coupling constants (J in Hz) are given in parentheses.

nyl)-7-(4-hydroxy-3-methoxyphenyl)heptane and (1*R*,3*R*,5*R*)-1,5-epoxy-3-hydroxy-1-(3,4-dihydroxy-5-methoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl) heptane [14], or their enantiomer, respectively.

Compound **19** was obtained as a pale yellowish oily substance, and its HR FAB-MS showed a $[M+H]^+$ ion peak at m/z 361.1647 ($C_{20}H_{25}O_6$), which was 30 mass unit smaller than that of **17** corresponding to loss of CH_2O from **17**. The IR spectrum showed an absorption band at 3402 cm^{-1} due to hydroxyl group. The ^{13}C NMR spectrum was very close to that of **17**, but it showed the presence of another 4-hydroxy-3-methoxyphenyl group instead of the 4-hydroxy-3,5-dimethoxyphenyl group in **17**, indicating the structure of **17** to be 1,5-epoxy-3-hydroxy-1-(3,4-dihydroxy-5-methoxyphenyl)-7-(4-hydroxyphenyl) heptane. Whereas, the H-3 was observed a dddd (J = 4.3, 4.6, 11.3 and 11.8 Hz) at δ 3.79, and the orientation of the C-3 hydroxyl group at must be equatorial. Thus, **19** was characterized as (1*R*,3*S*,5*R*)-1,5-epoxy-3-hydroxy-1-(3,4-dihydroxy-5-methoxyphenyl)-7-(4-hydroxyphenyl)heptane [15] or its enantiomer.

The nineteen compounds were isolated from Kankyo A, and their structures were characterized as mentioned above. This is the first isolation of **10** – **19** from Kankyo (Kankyo A in Experimental), and it is noteworthy that the sulfonated derivatives (**10** and **12**) were also found as constituents of Kankyo, which had been believed to be prepared from ginger simply by steaming and then drying without sulfur bleaching. So that, this fact suggests that the sulfonated derivatives must be artifacts caused by sulfur bleaching as previously reported on Shokyo [6], and that there would be two kinds of Kankyo in the Japanese market: one is “genuine” Kankyo prepared from ginger, and another is “pseudo” Kankyo provably prepared from “sulfur-breached” ginger.

While, we examined on another Kankyo (Kankyo B in Experimental), which was prepared in traditional way without sulfur breaching, and no sulfonated derivatives have been obtained therefrom as its constituents [4, 6]. In addition to them, two compounds were isolated and identified as (1*R*,3*S*,5*R*)-1,5-epoxy-3-hydroxy-1-(3,4-dihydroxy-5-methoxyphenyl)-7-(3,4-dihydroxyphenyl)heptane (**20**) and (1*R*,3*R*,5*R*)-1,5-epoxy- 3-hydroxy-1-(3,4-dihydroxy-5-methoxyphenyl)-7-(3,4-dihydroxyphenyl)heptane (**21**) or their enantiomers, respectively, based on coincidence of their data with those reported [15].

Further, we carried out additional examination on many samples of Shokyo and Kankyo collected in the Japanese market by means of TLC method. As a result, sulfonated derivatives are contained in the almost every Shokyo samples, but in a half of Kankyo ones. On the other hand, the fresh ginger root contained no sulfonated derivatives as their constituents [6].

EXPERIMENTAL

General Procedures Melting points were determined on a Yanaco micro-melting point apparatus (hot stage type) and were uncorrected. Optical rotations were carried on a JASCO DIP 140 digital polarimeter. IR spectra were measured on a JASCO FT/IR-410 spectrometer. NMR spectra were recorded on a JEOL JNM LA-500 spectrometer (500 MHz for ^1H, 125 MHz for ^{13}C) or JEOL JNM GX-400 spectrometer (400 MHz for ^1H, 100 MHz for ^{13}C). Chemical shifts were given in a δ ppm scale from TMS used as an internal standard, and the signals were assigned by means of DEPT and 2D NMR techniques (^1H-^1H COSY, HMQC and HMBC). MS spectra were obtained on a JEOL JMS SX-120A or JMS-700 spectrometer. The matrix used for FAB-MS was shown in the parenthesis. TLC was performed on a precoated silica gel 60 F_{254} or RP-18W F_{254} plate (Merck) and the detection was achieved by spraying with 10% H_2SO_4 followed by heating. Column chromatography was performed on silica gel 60 (< 45 μm, Merck), Sephadex LH-20 (Pharmacia), or ODS (Chromatorex DM-1020T, Fuji-Silysia Co.).

Plant Material Kankyo A (Lot. No. VMFNM: imported from China) was purchased from Uchida Wakanyaku Co., Ltd., Tokyo, Japan. Kankyo B (Lot. No. 231001: imported from China) was purchased from Tochimoto-Tenkaido Co., Ltd., Osaka, Japan.

Extraction and Isolation Powdered Kankyo A (5.0 kg) was percolated with 80% MeOH (37 L) at room temperature. The 80% MeOH extract was concentrated in vacuo at 40 ˚C. The residual syrup was suspended in H_2O and extracted with ether (3 times) to afford an ether extract (164.5 g) after concentration to dryness. The ether extract was chromatographed repeatedly on silica gel column chromatography (CC) [Hexane-Acetone (4:1)] and ODS CC (80% MeOH) to give nine compounds, 6-, 8-, 10-gingerols (**1 – 3**), 6-, 8-, 10-shogaols (**4 – 6**), 6-paradol (**7**), 6-gingediacetate (**8**), zingerone (**9**), identification of which were performed by direct comparison with their authentic samples isolated from Shokyo [4]. The aqueous layer (476.4 g) was, after concentration at 40 ˚C *in vacuo*, subjected to an ODS CC with a gradient mixture of H_2O and MeOH providing the following eight fractions: Fr. A (H_2O, 266.9 g), B (H_2O, 41.3 g), C (H_2O, 10.5 g), D (50% MeOH, 26.1 g), E (50% MeOH, 7.6 g), F (50% MeOH, 3.9 g), G (50% MeOH, 2.2 g) and H (MeOH, 4.6 g). Fr. F was separated into five fractions by Sephadex LH-20 CC (MeOH): Frs. F1 (52 mg), F2 (1.5 g), F3 (1.6 g), F4 (715 mg) and F5 (42 mg). Fr. F3 was subjected to an ODS CC with a gradient mixture of H_2O and MeOH providing the following five fractions: Frs. F3-1 (20% MeOH, 53.3 mg), F3-2 (30% MeOH, 114 mg), F3-3 (30% MeOH, 55 mg), F3-4 (30% MeOH, 1.07 g) and F3-5 (MeOH, 13 mg). Fr. F3-2 was successively applied to Sephadex LH-20 CC (MeOH) to give **10** (107 mg). Fr. F4 (430 mg) was chromatographed on silica gel CC [$CHCl_3$-MeOH-H_2O (225:25:2)] to give six fractions: Frs. F4-1 (20 mg), F4-2 (77 mg), F4-3 (82 mg), F4-4 (19 mg), F4-5 (78 mg) and F4-6 (121 mg). Fr. F4-2 was successively applied to ODS (50% MeCN), Sephadex LH-20 (80% acetone) and silica gel CC [Toluene-Acetone (3:1)] to give **11** (22 mg). Fr. F4-3 was subjected to silica gel CC [$CHCl_3$-MeOH (20:1)] and silica gel CC [Toluene-Acetone (3:2)] to give **16** (10 mg). Fr. E was separated into four fractions by Sephadex LH-20 CC (80% MeOH): Frs. E1 (0.9 g), E2 (6.1 g), E3 (0.5 g) and E4 (50 mg). Fr. E2 (1.0 g) was successively applied to silica gel CC [$CHCl_3$-MeOH-AcOEt-H_2O (2:2:4:1), lower phase; $CHCl_3$-MeOH-H_2O (8:2:0.2)], Sephadex LH-20 CC (MeOH), and ODS CC (30% MeCN) to give **10** (17 mg). Fr. E3 was chromatographed on silica gel CC [$CHCl_3$-MeOH-H_2O (9:1:0.08)] to give five fractions: Frs. E3-1 (124 mg), E3-2 (189 mg), E3-3 (84 mg), E3-4 (104 mg) and E3-5 (59 mg). Fr. E3-2 was successively applied to ODS CC (45% MeOH) and HPLC (30% MeCN) to give **17** (32 mg) and **18** (10 mg). Fr. E3-4 was subjected to ODS CC (30% MeCN) to give **19** (35 mg). Fr. D (10.0 g) was separated into three fractions by Sephadex LH-20 CC (MeOH): Frs. D1 (4.1 g), D2 (6 g) and D3 (8 mg). Fr. D2 was chromatographed on ODS CC with a gradient mixture of H_2O and MeOH providing the following five fractions: Fr. D2-1 (25% MeOH, 1.5 g), D2-2 (25% MeOH, 627 mg), D2-3 (25% MeOH, 534 mg), D2-4 (30% MeOH, 1.4 g) and D2-5 (30% MeOH, 1.9 g). Fr. D2-4 was subjected to Sephadex LH-20 CC (MeOH) to give six fractions: Frs. D2-4-1 (190 mg), D2-4-2 (894 mg), D2-4-3 (193 mg), D2-4-4 (**12**, 12 mg), D2-4-5 (7 mg) and D2-4-6 (3 mg). Fr. D2-4-2 was chromatographed on silica gel CC [$CHCl_3$-MeOH-H_2O (8:2:0.2, 7:3:0.5)] to give six fractions: D2-4-2a (96 mg), D2-4-2b (80 mg), D2-4-2c (45 mg), D2-4-2d (365 mg), D2-4-2e (32 mg), D2-4-2f (264 mg). Fr. D2-4-2d was successively applied to Sephadex LH-20 CC (MeOH) and ODS CC (10% MeOH) to give **13** (73 mg). Fr. D2-4-2f was chromatographed on ODS CC (25% MeOH), and Sephadex LH-20 CC (MeOH) to give **12** (55 mg). Fr. D2-2 was successively applied to silica gel CC [$CHCl_3$-MeOH-H_2O (8:2:0.2, 7:3:0.5)], ODS CC (15% MeCN), Sephadex LH-20 CC (MeOH), silica

gel CC [$CHCl_3$-MeOH-H_2O (7:3:0.5)], Sephadex LH-20 CC (MeOH) and ODS CC (10% MeCN) to give **14** (3 mg). Fr. G was separated into two fractions by Sephadex LH-20 CC (MeOH): Frs. G1 (1.7 g) and G2 (188 mg). Fr. G2 was successively applied to ODS (40% MeCN), Sephadex LH-20 (MeOH), silica gel [$CHCl_3$-MeOH-H_2O (8:2:0.2)], Sephadex LH-20 (MeOH) and ODS CC (35% MeCN) to give **15** (15 mg).

Powdered Kankyo B (5.0 kg) was also treated as in the case of Kankyo A: the ether extract (235 g) afforded nine compounds, **1** − **9**; the aqueous extract (241 g) gave **11**, **13**, **17** − **18**, **20** − **21** [15]. But no sulfonated compounds (**10** and **12**) were obtained.

6-Gingesulfonic acid (10) [4] White amorphous powder, mp. 177 − 181 ˚C, $[\alpha]_D^{21}$ + 0.7˚ (*c* 1.00, MeOH). Positive FAB-MS (NBA) m/z: 359.1457 $[M+H]^+$ (Calcd for $C_{17}H_{27}O_6S$: 359.1528). IR ν_{max} (KBr): 3182 (OH), 1711 (C=O), 1525 (benzene ring), 1219, 1175, 1056 (SO_3H) cm^{-1}. These data were coincident with those reported for 6-gingesulfonic acid [4].

Hexahydrocurcumin (11) [12] Yellow oil, $[\alpha]_D^{17}$ + 8.3˚ (*c* 0.29, $CHCl_3$). Positive FAB-MS (NBA), m/z: 375.1815 $[M+H]^+$ (Calcd for $C_{21}H_{27}O_6$: 375.1808). The specific rotation of authentic hexahydrocurcumin was + 9.0˚, and the configuration of the 5-position of **11** must be *S* [12].

Shogasulfonic acid A (12) [4] Pale yellowish amorphous powder, mp. 205 ˚C, $[\alpha]_D^{21}$ − 0.5˚ (*c* 2.00, MeOH). Positive FAB-MS (NBA) m/z: 439.1417 $[M+H]^+$ (Calcd for $C_{21}H_{27}O_8S$: 439.1427). EI-MS, m/z: 356 ($[M-H_2SO_3]$)$^+$). IR ν_{max} (KBr): 3379 (OH), 1698 (C=O), 1523 (benzene ring), 1222, 1179, 1154, 1054 (SO_3H) cm^{-1}. These data were coincident with those reported for Shogasulfonic acid A [4].

Zingiberoside A (13) [5] White amorphous powder, mp. 99 − 103 ˚C, $[\alpha]_D^{20}$ − 18.4˚ (*c* 1.00, MeOH). Positive FAB-MS (NBA) m/z: 332.2064 $[M+H]^+$ (Calcd for $C_{16}H_{27}O_7$: 332.1835).

Zingiberoside B (14) [5] White amorphous powder, mp. 123 ˚C, $[\alpha]_D^{21}$ − 40.7˚ (*c* 1.27, MeOH). Positive FAB-MS m/z: 495.2442 $[M+H]^+$ (Calcd for $C_{22}H_{39}O_{12}$: 495.2490).

(3S,5S)-6-Gingerdiol 4'-O-β-D-glucopyranoside (15) [11] White amorphous powder, mp. 123 ˚C, $[\alpha]_D^{17}$ − 37.1˚ (*c* 1.03, MeOH). Positive FAB-MS (NBA) m/z: 459 $[M+H]^+$ (Calcd for $C_{23}H_{39}O_9$: 459). IR ν_{max} (KBr): 3335 (OH), 2858 (OCH_3), 1518 (benzene ring) cm^{-1}. ^1H, ^{13}C-NMR: Table 1-1.

(3S,5S)-3,5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-7-(4-hydroxy-3,5-dimethoxyphenyl)heptane (16) [13] Yellow oil, $[\alpha]_D^{16}$ − 11.0˚ (*c* 0.52, EtOH). Positive FAB-MS (NBA) m/z: 407.2044 $[M+H]^+$ (Calcd for $C_{22}H_{31}O_7$: 407.1992). IR ν_{max} (KBr): 3335 (OH), 2931, 2858 (OCH_3), 1635, 1515 (benzene ring) cm^{-1}. ^1H, ^{13}C-NMR: Table 1-1.

(1R,3S,5R)-1,5-epoxy-3-hydroxy-1-(3,4-dihydroxy-5-methoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)heptane or its enantiomer (17) [14] Pale yellowish oil, $[\alpha]_D^{16}$ − 65.2˚ (*c* 1.07, EtOH). Positive FAB-MS (NBA) m/z: 391 $[M+H]^+$ (Calcd for $C_{21}H_{27}O_7$: 391). IR ν_{max} (KBr): 3397 (OH), 2941, 2852 (OCH_3), 1615, 1517 (benzene ring) cm^{-1}. ^1H, ^{13}C-NMR: Table 1-1.

(1R,3R,5R)-1,5-Epoxy-3-hydroxy-1-(3,4-dihydroxy-5-methoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)heptane or its enantiomer (18) [14] Pale yellowish oil, $[\alpha]_D^{17}$ − 56.5˚ (*c* 0.84, EtOH). Positive FAB-MS (NBA) m/z: 391 $[M+H]^+$ (Calcd for $C_{21}H_{27}O_7$: 391). IR ν_{max} (KBr): 3339 (OH), 2927 (OCH_3), 1654, 1520 (benzene ring) cm^{-1}. ^1H, ^{13}C-NMR: Table 1-1.

(1R,3S,5R)-1,5-Epoxy-3-hydroxy-1-(3,4-dihydroxy-5-methoxyphenyl)-7-(4-hydroxy-phenyl)heptane or its enantiomer (19) [15] Pale yellowish oil, $[\alpha]_D^{15}$ − 87.7˚ (*c* 1.28, EtOH). Positive FAB-MS (NBA) m/z: 361.1647 $[M+H]^+$ (Calcd for $C_{20}H_{25}O_6$: 361.1651). IR ν_{max} (KBr): 3402 (OH), 2853 (OCH_3), 1615, 1516 (benzene ring) cm^{-1}. ^1H, ^{13}C-NMR: Table 1-2.

(1R,3S,5R)-1,5-Epoxy-3-hydroxy-1-(3,4-dihydroxy-5-methoxyphenyl)-7-(3,4-dihydroxyphenyl) heptane (20) **or its enantiomer** [15]　Pale yellowish oil. $[\alpha]_D^{15}$ − 58.3°(*c* 1.03, EtOH). HR FAB-MS (NBA) m/z 377.1579 $[M+H]^+$, (Calcd for $C_{20}H_{25}O_7$: 377.1600). IR ν_{max} (KBr): 3398 (OH), 1618, 1524 (benzene ring) cm^{-1}. ^1H and ^{13}C NMR：Table 1-2.

(1R,3R,5R)-1,5-Epoxy-3-hydroxy-1-(3,4-dihydroxy-5-methoxyphenyl)-7-(3,4-dihydroxyphenyl) heptane (21) **or its enantiomer** [15]　Pale yellowish oil. $[\alpha]_D^{15}$ −31.0°(*c* 0.31, EtOH). HR FAB-MS (NBA) m/z 377.1579 $[M+H]^+$, (Calcd for $C_{20}H_{25}O_7$: 377.1600). IR ν_{max} (KBr): 3398 (OH), 1618, 1524 (benzene ring) cm^{-1}. ^1H and ^{13}C NMR：Table 1-2.

ACKNOWLEDGMENT

We thank to Ms. Kimiko Shiohara (Analytical Center of in this school) for measurement of the MS spectra. This research work was supported in part by a Grant-in-aid for Scientific Research (No. 20590011) and URAKAMI Foundation.

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ショウガならびに関連薬物の生薬学的研究 (2)
カンキョウ (乾姜) の成分

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要　旨

ショウガを基原とするカンキョウ (Zingiberis processum rhizome) の80% MeOH抽出エキスから19種の化合物を単離した．これらは，既知化合物12種とgingerdiol 4'-*O*-β-D-glucopyranoside (**15**)，4種のジアリルヘプタノイド類 (**16** – **19**)，既報のスルホン化誘導体：6-gingesulfonic acid (**10**) とshogasulfonic acid A (**12**) であった．このうち，**15** – **19**はカンキョウからは初めて得られた化合物である．

また興味深いことに，本邦市場にはスルホン化誘導体を含むカンキョウと含まないカンキョウの2種類が存在することが分かった．

Key Words：ショウガ，ショウガ科，カンキョウ，Zingiberis processum rhizome, スルホン化誘導体

受付：2012年2月16日，受理：2012年3月26日