Podolactone E (**4**), $C_{18}H_{18}O_6$[5] (molecular-ion peak at *m/e* 330), m.p. 261–262°, shows hydroxyl absorption at 3500 cm^{-1} in its IR-spectrum and forms a monoacetate, $C_{20}H_{20}O_7$, m.p. 256–257°, $[\alpha]_D^{20}$ −30°. An IR-band at 1770 cm^{-1} indicates a γ-lactone group, while a band at 1720 cm^{-1} and UV-absorption at 257 nm (ε 14400) suggest the presence of a diene-lactone group similar to that found[6] in antibiotic LL-Z1271α (**5**). The NMR-spectrum of podolactone E (Table) bears an obvious similarity to that of inumakilactone B (**3**), while the differences in the spectra are accommodated by assignment of structure (**4**) to podolactone E. Thus the signal attributed to H-7 appears in the vinylic region of the spectrum (clearly seen in the spectrum of 15,16-dihydro-podolactone E acetate [see below] as a multiplet at δ 6.27), and exhibits couplings to H-6, H-11, and H-14, while H-6 shows homoallylic coupling to H-14. A vinyl side chain, as in inumakilactone B, was assigned to podolactone E on the basis of the close similarity of the appropriate regions of the NMR spectra of both compounds. This assignment was supported by hydrogenation of podolactone E acetate to the 15,16-dihydroderivative, $C_{20}H_{22}O_7$, m.p. 282° (dec.), λ_{max} 258 nm (ε 13800), which in its NMR-spectrum exhibited a 3 proton triplet (δ 1.05, J 7 Hz in pyridine) attributed to the C-16 methyl group.

The close agreement of the coupling constants found for the A-ring protons in the NMR-spectrum of (**4**) with the corresponding constants for (**3**), and for the B- and C-ring protons with those of (**5**), indicate that the stereochemistry depicted in (**4**) can be confidently assigned to podolactone E.

Podolactone E is very likely a biogenetic precursor of inumakilactone B, which can be formed by epoxidation of the 7,8-double bond: hydration of the side chain of the latter compound may then lead to inumakilactone A. The structural similarity of podolactone E and LL-Z1271α (**5**), which exhibits[6] antifungal activity, is of interest.

Résumé. Le Podolactone E, qui a la structure (**4**), empêche très activement la croissance des cellules végétales. C'est le plus actif des podolactones isolés jusqu'à présent.

M. N. GALBRAITH, D. H. S. HORN and JENNETH M. SASSE

Division of Applied Chemistry, C.S.I.R.O., Box 4331, G.P.O. Melbourne (Australia); and School of Biological Sciences, Macquarie University, Sydney (Australia), 20 September 1971.

[5] Molecular formulae of all new compounds were established by microanalysis.

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Anti-Hypercholesterolemic Effect of a Sulfur Containing Amino Acid, S-Methyl-L-Cysteine Sulfoxide, Isolated from Cabbage

S-methyl-L-cysteine sulfoxide (CH_3–S(=O)–CH_2–$CH(NH_2)$–COOH) (SMCS) is distributed abundantly in numbers of species of Cruciferae and Liliaceae plants[1–3]. For example according to the study of TSUNO[4] of our department, amounts of SMCS are 590 mg/100 g in cabbage, 650 mg/100 g in cauliflower or 60 mg/100 g in radish. The production of main Cruciferae plants in Japan represents some 7 million tons annually. Accordingly, annual production of SMCS and its analogues is estimated to be about 12,000 tons. Division of these amounts according to Japanese population results in over 300 mg of SMCS per person daily. This fact suggests that this amino acid from vegetable food may be one of the largest sources of sulfur-containing amino acids for Japanese; however, nutritional values of this amino acid are still obscure. The present report describes the anti-hypercholestrolemic effect of this amino acid.

Crystals of SMCS (m.p. 173°C) used in the experiment were isolated from cabbage and recrystallized by the method of TSUNO et al.[4], a modification of the method of MORRIS and THOMPSON[2].

Twenty-four male Wistar rats weighing about 100 g were separated into 4 groups. A synthetic diet was administered to each group and hydrogenated cocoanut oil was used as the source of fat. Composition of the basal diet is shown in Table I. Group 1 was given a basal diet, group 2 a basal diet supplemented with 1% cholesterol and 0.2% cholic acid, group 3 a basal diet supplemented with 0.25% SMCS, 1% cholesterol and 0.2% cholic acid. A diet which contained 0.5% SMCS, 1% cholesterol and 0.2% cholic acid was administered to the 4th group. A restricted diet (7–10 g) was prescribed every morning. Daily food intake amounts of each group was the same throughout the experimental period (average 8.6 g/day/rat). Dosage rates of SMCS in group 3 and group 4 were 182.2 mg and

Table I. Composition of the basal diet

	g/100 g diet
Casein	15.0
Sucrose	68.3
Hydrogenated cocoanut oil	10.0
Salt mixture[a]	4.0
Cellulose	2.0
Vitamin mixture[b]	0.5
Choline chloride	0.2

[a] The salt mixture contained: (% in the mixture) NaCl, 4.6; $Na_2HPO_4 \cdot H_2O$, 9.3; K_2HPO_4, 25.6; $CaH_4(PO_4)_2 \cdot H_2O$, 14.5; $Fe(C_6H_5O_7) \cdot 5H_2O$, 3.2; $Ca(C_3H_5O_3)_2\ 5H_2O$, 34.9; $MgSO_4$, 7.0; KI, 0.9. [b] 100 g of the vitamin mixture contained: (in mg) riboflavin, 150; thiamine, 100; nicotinic acid, 1000; pyridoxin, 100; cyanocobalamin, 1; pantothenic acid, 500; folic acid, 50; ascorbic acid, 3750; vitamin E, 100; vitamin A, 250,000 IU; vitamin D_2, 20,000 IU; and sucrose to 100 g.

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Table II. Effect of SMCS supplement on cholesterol, phospholipid levels and cholesterol phospholipid ratio in blood

Group No.	Diet	Cholesterol (mg/dl)	Phospholipid (mg/dl)	Cholesterol/phospholipid
1	Basal	145 ± 11	211 ± 7	0.69 ± 0.06
2	Basal + cholesterol	497 ± 81	236 ± 17	2.16 ± 0.34
3	Basal + cholesterol + 0.25% SMCS	395 ± 70[a]	241 ± 18	1.62 ± 0.23[a]
4	Basal + cholesterol + 0.5% SMCS	276 ± 46[b]	202 ± 8	1.38 ± 0.23[b]

Values represent mean ± S.D. of 6 rats. [a] Significant difference at $0.01 < p < 0.05$ compared with No. 2 group. [b] Significant difference at $p < 0.01$ compared with No. 2 group.

Table III. Effect of SMCS supplement on total and free cholesterol levels, total lipid level in liver and cholesterol level in aorta

Group No.	Diet	Liver			Aorta
		Total cholesterol	Free cholesterol	Total lipid	Total cholesterol
		(mg/100 g wet wt.)	(mg/100 g wet wt.)	(g/100 g wet wt.)	(mg/100 g wet wt.)
1	Basal	688 ± 151	313 ± 42	9.8 ± 3.8	146 ± 48
2	B. + chol.	3229 ± 297	449 ± 54	23.6 ± 3.6	354 ± 87
3	B. + chol. + 0.25% SMCS	2887 ± 246[a]	449 ± 45	20.1 ± 4.6	270 ± 50
4	B. + chol. + 0.5% SMCS	2758 ± 300[a]	358 ± 46	15.9 ± 2.6[a]	311 ± 68

Values represent mean ± S.D. of 6 rats. [a] $0.01 < p < 0.05$, Significant difference compared with No. 2 group.

364.4 mg/kg body wt./day, respectively. After 2 weeks of this dietary regimen, the animals were killed by decapitation. The blood, liver and aorta were removed immediately and portions of these tissues were examined to determine cholesterol, phospholipid or total lipid levels. Levels of blood and aorta cholesterol were determined by the procedure of ABELL et al.[5]. Free and total cholesterol levels in liver were determined by the method of SPERRY and WEBB[6]. To determine the phospholipid level in the blood, the method of KING[7] was used after extraction with chloroform: methanol (2:1). Total lipid level in liver was determined by the method of LEVEILLE and SAUBERLICH[8].

As shown in Table II, the blood cholesterol level in rats fed 1% cholesterol added diet was elevated to approx. 500 mg/dl and supplementation of SMCS to the cholesterol diet depressed this elevation significantly. In contrast, phospholipid levels revealed no significant change in the experimental groups. The elevated cholesterol-phospholipid ratio in the cholesterol feeding group was alleviated markedly by the supplementation of SMCS to the diet. The addition of 0.5% SMCS appeared to be more effective than 0.25% SMCS.

Table III reveals the free and total cholesterol levels and total lipid level in the liver and total cholesterol level in the aorta. Total cholesterol and total lipid of the liver decreased significantly by the addition of SMCS to hypercholesterolemic diet but free cholesterol in liver and total cholesterol in aorta revealed no significant change.

Although further study is necessary to elucidate the mechanism in the animal body, it is certain that SMCS has the potent anti-hypercholesterolemic effect. This effect of SMCS concerning nutrition of vegetables showed the given consideration.

Zusammenfassung. Die Antihypercholesterinwirkung der aus dem Kohl isolierten S-Methylcysteinsulfoxide (SMCS) wurde untersucht. Bei Ratten mit experimentell induzierter Hypercholesterinämie kam es zu einem Abfall der Cholesterinwerte im Blut und in der Leber.

M. FUJIWARA, Y. ITOKAWA, H. UCHINO and K. INOUE

Department of Hygiene, Faculty of Medicine, Kyoto University, Kyoto (Japan), 5 August 1971.

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