Metabolism of Alginic Acid and Its Salts and Their Effects on Serum Concentrations of Na, K and Ca in the Rat

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The metabolism of alginic acid, sodium alginate, potassium alginate and calcium alginate, and their effect on the serum concentrations of Na, K and Ca in the rat were investigated by single-dose oral administration. Rats were orally given 90.4 mg/kg (50 times of the daily intake of alginates of Japanese) of alginic acid, sodium alginate, potassium alginate or calcium alginate as a solution or suspension in water. No significant differences were observed in fecal excretion or the pattern of contents of alginates in the gastrointestinal tract as a function of time: 1) 72.7~79.3% of the administered alginates were excreted into feces within 3 days; 2) administered alginates remained in the stomach for 2 hours, then gradually moved to the small intestine after 4 hours and to the large intestine after 8 hours, and most of the alginates remained in the large intestine after 24 hours; 3) there were no significant differences in the serum concentrations of Na, K and Ca caused by the administration of alginates.

Key words: alginic acid; sodium alginate; potassium alginate; calcium alginate; high performance liquid chromatography; atomic absorption spectrophotometry; electrolyte in serum

Introduction

Alginates were extracted from brown seaweeds in 1881 for the first time¹⁾. They are linear glycuronoglycan polymers that contain 1:4 linked β -D-mannuronic and α -L-guluronic acid residues²⁾. Sodium alginate and propylene glycol ester of alginic acid are permitted food additives for use as thickening agents or stabilizers in Japan³⁾, while in U. S. A., the ammonium, calcium, potassium and sodium salts, and the propylene glycol ester of alginic acid are used as emulsifiers and stabilizers in the food, cosmetic and pharmaceutical industries⁴⁾.

Ito *et al.*⁵⁾ estimated that the daily intake of alginate of Japanese was 1.808 mg/kg, whereas the acceptable daily intake (ADI) for man was estimated by the WHO to be 0~25 mg/kg of body weight (calculated as alginic acid)⁶⁾. In contrast, there is no available information on the ammonium, calcium, potassium, sodium and propylene glycol esters of alginic acid^{4), 6)}.

The doses for oral administration were set at 90.4 mg/kg (50 times the daily intake of algi-

nate of Japanese) because 1.808 mg/kg was too small to investigate the fate of administered alginates. The metabolism of alginic acid, sodium alginate, potassium alginate and calcium alginate and their effects on the serum concentrations of Na^+ , K^+ and Ca^{2+} were investigated in the rat.

Materials and Methods

Alginic acid, sodium alginate (viscosity (1%) 160 cps), potassium alginate (viscosity (1%) 123 cps) and calcium alginate were purchased from Kimitsu Chemical Industries Co., Ltd. (Tokyo). Naphthoresorcinol (extra pure reagent) was purchased from Nakarai Chemicals, Ltd. (Kyoto). Standard solutions for atomic absorption spectrophotometry of Na, K and Ca (1,000 ppm, respectively) were purchased from Ishizu Pharmaceutical Co., Ltd. (Osaka). Other reagents were of special or guaranteed grade.

A system consisting of a Shimadzu LC-6A and Shimadzu SPD-6AV (Shimadzu Seisakusho, Kyoto), Finepak SIL C₁₈P and Finepak SIL C₁₈₋₅ (ϕ 4.6 $\times$ 250 mm) (Japan Spectroscopic Co., Ltd.,

Tokyo) was used for the analysis of alginate by HPLC. For filtration of HPLC samples, a CHROMATODISC 13N (nonaqueous, $0.45\mu\text{m}$) was purchased from Biofield Inc. (Tokyo). An atomic absorption & flame emission spectrophotometer AA-845 (Nippon Jarrel Ash, Kyoto) was used for analysis of Na, K and Ca by the atomic absorption method.

Male Slc: Wistar rats (Shizuoka Laboratory Animal Center), 4 weeks old, were acclimated in an air-conditioned room for more than 1 week before use. Rats were allowed free access to the pelleted diet (F-2, a commercial chow of Funahashi Farm, Chiba) and distilled water was provided *ad libitum* from the day before the experiment.

Experiment 1. Determination and recovery test of alginates

Each sample (dried feces (0.2 g), the diet (0.2 g), or gastrointestinal homogenates including their contents (5 ml)) was defatted with 7 ml of diethylether twice, then soluble protein, pectin and minerals were removed by extraction with 7 ml of 1 N hydrochloric acid twice⁷⁾. The residue was dissolved in 4 ml of 5 N sodium hydroxide and heated for 30 min in boiling water. The suspension was adjusted to pH 7~8 and centrifuged at 3,000 rpm for 10 min. The water layer was collected and adjusted to 20 ml with water. Using 5 ml of this solution, alginate was determined by the method of Toyoda *et al.*⁸⁾.

Briefly, alginate was precipitated selectively as Cu-alginate complex by addition of 1.5 ml of 10% copper sulfate. The precipitate was dissolved in 0.5 ml of 1 N ammonia solution and adjusted to 5 ml with water. To 1 ml of this solution were added 1 ml of 0.4% naphthoresorcinol solution and 2 ml of hydrochloric acid solution containing copper sulfate (prepared by mixing 40 ml of conc. hydrochloric acid, 9 ml of water and 1 ml of 1% copper sulfate). The mixture was heated for 1 hr in boiling water, and the reaction product was extracted with 4 ml of *n*-butyl acetate, washed with 3 ml of 20% sodium chloride and filtered using the CHROMATODISC 13N. Twenty μl of filtrate was injected into the HPLC column.

Conditions of HPLC were as follows:

Apparatus: Shimadzu LC-6A

Detector: Shimadzu SPD-6AV, 565 nm

Column: Finepak SIL C₁₈₋₅ $\phi 4.6 \times 250$ mm attached to Finepak SIL C₁₈P

Mobile phase: acetonitrile-water-*n*-butyl acetate (75:20:5, v/v/v)

Flow rate: 2.0 ml/min

Injection volume: 20 μl

No alginates were found in any of the samples. The recovery test for alginate was performed by adding 1.808 mg of sodium alginate to each sample and taking it through the above-mentioned method.

Experiment 2. Fecal and urinary excretions of alginate, Na, K and Ca

Alginic acid, sodium alginate, potassium alginate and calcium alginate were dissolved or suspended in water and samples for oral administration of 90.4 mg/kg/10 ml were prepared. The relative contents of alginates determined by the HPLC method were as follows: alginic acid-sodium alginate-potassium alginate-calcium alginate=134:113:100:103.

Fifteen rats weighing 130~150 g were divided into 5 groups of 3 each. Rats were housed individually in metabolic cages after oral administration of the samples. Distilled water was administered orally to the 3 rats of the control group. The diet and distilled water were provided *ad libitum*. Urine and feces were collected for 3 days individually. Feces were dried at 60°C for more than 4 hours and ground into powder. Alginate in the dried feces was analyzed by the method described in *Experiment 1* and determined as sodium alginate.

Sodium, K and Ca in dried feces and urine were extracted with 1 N hydrochloric acid, filtered, then diluted with distilled water so as to give concentrations of Na, K and Ca of 1~10 ppm, respectively. Contents of Na, K and Ca in each extract were determined by the atomic absorption method.

Experiment 3. Serum concentrations of Na, K and Ca and distribution of alginates in the gastrointestinal tract as a function of time

Twenty-five rats weighing 180~200 g were divided into 5 groups of 5 each. Rats were housed individually in metabolic cages after the oral administration of 4 kinds of samples as

Table 1. Recovery Tests for Sodium Alginate by HPLC Method

Sample	No.	Alginate (mg)		Recovery (%)
		Added	Detected	
Feces		0	0	—
	1	1.808	0.831	46.0
	2	1.808	1.023	56.6
	3	1.808	0.840	46.5
	Mean $\pm$ SD			49.7 $\pm$ 6.0
F-2 pellet		0	0	—
	1	1.808	0.972	53.6
	2	1.808	1.024	56.6
	3	1.808	1.074	59.4
	4	1.808	1.256	69.5
	Mean $\pm$ SD			59.8 $\pm$ 6.9
Stomach ¹⁾		0	0	—
	1	1.808	1.112	61.5
	2	1.808	0.928	51.3
	3	1.808	1.172	64.8
	Mean $\pm$ SD			59.2 $\pm$ 7.1
Small intestine ¹⁾		0	0	—
	1	1.808	0.915	50.6
	2	1.808	1.037	57.4
	3	1.808	0.939	51.9
	Mean $\pm$ SD			53.3 $\pm$ 3.6
Large intestine ¹⁾		0	0	—
	1	1.808	1.021	56.5
	2	1.808	0.943	52.2
	3	1.808	0.886	49.0
	Mean $\pm$ SD			52.6 $\pm$ 3.8

Sodium alginate was reacted with naphthoresorcinol and analyzed by the HPLC method.

¹⁾ Both tissue and content were included.

described in *Experiment 2*. Distilled water was administered orally to the 5 rats of the control group. The diet and distilled water were provided *ad libitum*. At 1, 2, 4, 8 and 24 hours after the oral administration of alginates, rats of each group were killed by decapitation one by one. The stomach, small intestine and large intestine (including their contents) were removed immediately. Serum concentrations of Na, K and Ca were determined by the atomic absorption method.

The stomach, small intestine and large intestine, including their contents, were homogenized with 5 volumes of water. The homogenates were adjusted to 50 ml with water and alginates in 5 ml of these homogenates were

determined by the above-mentioned method.

Results

Experiment 1. Determination and recovery test of alginates

Recoveries of sodium alginate in several samples are shown in Table 1.

Alginate was not detected in any sample when no alginate was added.

Recovery of sodium alginate was 49.7% (46.0~56.6) in the dried feces, 59.8% (53.6~69.5) in the diet, 59.2% (51.3~64.8) in the homogenate of stomach, 53.3% (50.6~57.4) in the homogenate of small intestine and 52.6% (49.0~56.5) in the homogenate of large intestine. Similar results were obtained with alginic acid, potassi-

Table 2. Relative Content of Alginates and Concentrations of Na, K and Ca in the Administered Samples

Sample	Relative content of alginates ¹⁾	Concentration (mg/ml)		
		Na	K	Ca
Na-Alginate ²⁾	100	0.949	0.096	0.081
K-Alginate ²⁾	113	0.120	1.69	0.047
Alginic acid ²⁾	134	0.094	0.038	0.098
Ca-Alginate ²⁾	103	0.310	0.064	2.75

Data are the means for 3 experiments.

¹⁾ Relative content of alginate in each solution or suspension is indicated on the basis that of sodium alginate was 100.

²⁾ A solution or suspension of each alginate (90.4 mg/kg/10 ml) was orally administered to the rats.

Table 3. Body Weight, Food Intake and the Amounts of Excreted Feces and Urine

Group	Control	Alginic acid	Na-Alginate	K-Alginate	Ca-Alginate
Body weight (g)					
Initial	142 ± 7 ¹⁾	140 ± 8	145 ± 5	145 ± 2	134 ± 2
1 days	150 ± 3	146 ± 7	152 ± 1	149 ± 2	148 ± 3
2	157 ± 3	153 ± 7	159 ± 1	152 ± 3	154 ± 4
3	161 ± 3	158 ± 6	161 ± 3	153 ± 1*	143 ± 3*
Food intake (g)					
0~1 days	15.0 ± 0.6	13.7 ± 0.7	14.7 ± 1.2	14.7 ± 0.3	17.5 ± 0.5
1~2	15.7 ± 0.3	14.0 ± 0.6	15.3 ± 0.3	16.0 ± 0.6	16.0 ± 1.0
2~3	15.0 ± 0.0	15.3 ± 0.7	15.7 ± 0.3	16.3 ± 0.7	10.5 ± 0.5
Total	45.7 ± 0.7	43.0 ± 1.7	45.7 ± 0.7	47.0 ± 1.2	44.0 ± 2.0
Dry weight of feces (g)					
0~1 days	2.03 ± 0.22	2.06 ± 0.16	1.51 ± 0.50	2.35 ± 0.33	2.56 ± 0.15
1~2	2.13 ± 0.37	1.84 ± 0.24	2.04 ± 0.16	2.98 ± 0.60	2.56 ± 0.23
2~3	2.43 ± 0.18	2.73 ± 0.19	2.94 ± 0.27	2.83 ± 0.33	2.11 ± 0.10
Total	6.59 ± 0.58	6.64 ± 0.53	6.49 ± 0.28	8.16 ± 0.20	7.22 ± 0.48
Volume of urine (ml)					
0~1 days	3.25 ± 0.75	4.67 ± 0.33	5.00 ± 1.04	4.50 ± 0.50	3.00 ± 0.50
1~2	2.75 ± 0.75	4.53 ± 1.16	4.40 ± 0.90	4.07 ± 0.47	3.75 ± 0.75
2~3	5.50 ± 0.50	8.30 ± 0.90	6.67 ± 2.17	5.33 ± 1.17	0.50 ± 0.00
Total	11.50 ± 2.00	17.50 ± 0.66*	16.07 ± 4.03	13.90 ± 1.80	7.25 ± 1.25

Solutions or suspensions of alginates (90.4 mg/kg/10 ml) were orally administered to rats.

Distilled water and F-2 pellet were provided *ad libitum*.

¹⁾ Data are represented as mean ± SEM for 3 rats of each group.

* Differs significantly from the control group ($p < 0.05$).

um alginate and calcium alginate (data not shown). The results of analysis of alginates were corrected on the basis of the recovery tests.

Experiment 2. Fecal and urinary excretions of alginate, Na, K and Ca

Table 2 indicates the relative content of alginates and concentrations of Na, K and Ca in the diets and the 4 kinds of solutions or suspensions

of alginates administered to the rats.

Contents of Na, K and Ca in the diet were much higher than those in the 4 kinds of solutions or suspensions of alginates administered to the rats. It was found that trace amounts of Na, K and Ca were contained in alginic acid suspension. The contents of Na, K and Ca in the diet was 2.48, 8.57, 6.97 mg/g, respectively.

Body weight, food intake and amounts of

Table 4. Fecal Excretion of Alginates

Group	Control	Alginic acid	Na-Alginate	K-Alginate	Ca-Alginate
Alginates administered ¹⁾	0	16.9 ± 0.9 ²⁾	12.9 ± 0.7	14.9 ± 0.2	12.5 ± 0.2
Fecal excretion of alginate (mg) ¹⁾					
0~1 days	0	3.57 ± 2.60	3.44 ± 1.59	1.99 ± 1.09	7.01 ± 0.60
1~2	0	3.29 ± 1.39	3.94 ± 1.10	5.21 ± 2.23	0.60 ± 0.60
2~3	0	5.72 ± 1.71	2.50 ± 0.10	3.59 ± 0.39	2.14 ± 0.55
Total	0	12.58 ± 1.02	9.87 ± 0.39	10.79 ± 1.34	9.75 ± 0.55
Apparent excretion rate (%) ³⁾					
0~1 days	-	21.8 ± 15.6	27.4 ± 13.8	13.5 ± 7.5	56.9 ± 3.2
1~2	-	19.1 ± 7.6	30.1 ± 6.9	35.0 ± 14.7	5.1 ± 5.1
2~3	-	33.2 ± 8.5	19.4 ± 0.4	24.2 ± 2.6	17.3 ± 4.0
Total	-	74.2 ± 2.1	76.8 ± 7.3	72.7 ± 9.0	79.3 ± 2.2

Solutions or suspensions of alginates (90.4 mg/kg/10 ml) were orally administered to rats.

Distilled water and F-2 pellet were provided *ad libitum*.

¹⁾ Alginate was determined as sodium alginate. Analysis of alginate was performed in duplicate for each sample.

²⁾ Data are represented as mean ± SEM for 3 rats of each group.

³⁾ Apparent excretion rate (%) = (Excretion/Intake) × 100

feces and urine excreted are shown in Table 3. There were no major differences among groups. The volume of urine increased slightly in the rats administered sodium alginate or alginic acid and decreased slightly in the rats administered calcium alginate.

Fecal excretion of alginates and the apparent excretion rate of alginates (ratio of the excreted alginates to the intake of alginate) are shown in Table 4. There was no significant difference in fecal excretion of alginates among the groups; 29.3~72.7% of the alginates were excreted into feces within 3 days after administration.

Urinary and fecal excretions of Na, K and Ca are shown in Table 5. Fecal and urinary excretions of Na were increased in the rats administered sodium alginate, potassium alginate and calcium alginate, but not significantly. Fecal and urinary excretions of K were also increased in the rats administered sodium alginate, potassium alginate, alginic acid and calcium alginate, but not significantly. There was no significant difference in the intake, or fecal or urinary excretion of Ca.

Experiment 3. Serum concentrations of Na, K and Ca and distribution of alginates in the gastrointestinal tract as a function of time

Table 6 summarizes the serum concentrations

of Na, K and Ca. All the rats were administered one of the 4 kinds of alginates or distilled water at AM 9 to AM 10. No significant differences were observed among serum concentrations of Na, K and Ca.

The time courses of the distribution of administered alginates in stomach, small intestine and large intestine are shown in Fig. 1.

The administered alginates remained in the stomach during the first 2 hours after oral administration, and were found in the small intestine after 4 hours and in the large intestine after 8 hours. Most of the administered alginates remained in the large intestine after 24 hours.

The sum of the alginates in the stomach, small intestine and large intestine tended to decrease as a function of time. There was no significant difference depending on the kinds of administered alginates in the contents of alginates in the gastrointestinal tract at any time.

Discussion

Alginic acid and its salts have specific physicochemical properties^{9)~14)}. Sodium alginate and potassium alginate are soluble in water, but alginic acid and calcium alginate are insoluble. Alginic acid forms an insoluble calcium salt with calcium ion and several studies have been done from the viewpoint of calcium balance³⁾.

Table 5. Fecal and Urinary Excretions of Na, K and Ca

Group	Control	Alginic acid	Na-Alginate	K-Alginate	Ca-Alginate
Urinary excretion of Na (mg)					
0~1 days	14.1±0.4 ¹⁾	23.8±5.4	6.6±5.7	17.5±1.6	25.9±0.9*
1~2	18.4±7.8	17.0±2.7	14.5±1.4	27.7±3.6	35.5±1.4
2~3	15.0±1.9	12.9±2.0	14.5±0.5	16.9±1.0	12.3±4.1
Total	47.5±6.4	53.6±3.1	55.6±1.7	62.1±4.6	73.7±6.5
Fecal excretion of Na (mg)					
0~1 days	5.16±0.50	5.98±0.52	8.35±2.85	6.38±1.08	7.69±0.10*
1~2	4.28±0.48	5.11±0.86	9.01±0.17*	7.56±1.19	7.16±1.01
2~3	6.15±1.37	5.13±0.55	9.20±1.23	7.19±1.81	9.27±6.06
Total	15.58±1.76	15.82±1.30	26.56±4.16	21.13±1.59	24.11±6.98
Urinary excretion of K (mg)					
0~1 days	55.6± 0.4	61.9±0.8*	57.2±1.3	64.9±1.9*	59.3± 0.9
1~2	53.8± 6.3	58.9±2.8	53.7±5.7	66.3±2.3	70.1± 5.2
2~3	65.3± 4.1	58.0±4.9	62.3±1.7	68.9±2.1	48.3±12.3
Total	160.4±14.8	178.8±7.0	174.9±6.5	200.1±5.9	177.6± 7.7
Fecal excretion of K (mg)					
0~1 days	19.8±1.0	18.1±3.0	23.2± 9.3	25.0±3.6	25.6± 3.8
1~2	16.8±3.7	17.1±1.6	30.4± 4.1	26.8±2.5	23.1± 0.8
2~3	23.5±5.6	17.4±5.4	29.4± 4.8	22.7±4.7	28.3±19.8
Total	60.1±9.3	52.6±9.0	71.5±10.1	74.5±2.9	76.9±16.9
Urinary excretion of Ca (mg)					
0~1 days	0.125±0.039	0.078±0.030	0.105±0.013	0.088±0.008	0.049±0.005
1~2	0.108±0.010	0.088±0.015	0.082±0.012	0.083±0.007	0.108±0.006
2~3	0.073±0.013	0.095±0.010	0.082±0.005	0.058±0.013	0.046±0.006
Total	0.305±0.024	0.271±0.032	0.269±0.028	0.229±0.013	0.202±0.007
Fecal excretion of Ca (mg)					
0~1 days	37.9± 4.2	34.4± 3.3	27.7±10.1	49.3±7.5	49.1± 6.7
1~2	44.8± 9.7	32.0± 3.6	52.1±13.1	63.2±2.4	53.3±10.0
2~3	52.0± 3.7	47.3±12.5	61.8± 8.3	60.4±5.6	43.2± 5.6
Total	134.7±13.1	113.7±18.0	141.6±23.9	172.9±4.4	145.6±22.2

Solutions or suspensions of alginates (90.4 mg/kg/10 ml) were orally administered to rats.

Distilled water and F-2 pellet were provided *ad libitum*.

¹⁾ Data are represented as mean±SEM for 3 rats of each group.

* Differs significantly from the control group ($p < 0.05$).

Sodium alginate is soluble in water and forms a viscous solution which has excellent thickening or stabilizing properties; its use as a food additive has been permitted since 1957 in Japan³⁾.

Various studies on the effect of alginates in several species have been done from the viewpoint of toxicology or nutritional science.

The values of lethal dose 50 (LD₅₀) of alginates are very high on oral administration^{1), 3), 15)} in mice or rats. No remarkable change was observed in the organs after the administration of alginates either macroscopically or microscopically¹⁵⁾. Alginic acid was well tolerated in humans when ingested in quantities of 45 g per

day, but was mildly laxative¹⁶⁾. Carcinogenicity was not detected when alginic acid was injected subcutaneously into mice¹⁷⁾.

A literature review showed a weak inhibition of some digestive enzymes by alginates *in vitro* or in rat feeding experiments¹⁸⁾. Concerning the effects on utilization of nutrients, the intestinal absorptions of glucose and maltose hardly decreased and the absorptions of folic acid and riboflavin were not affected by alginate ingestion¹⁸⁾. Alginates increase the moisture content and the volume of stools, decrease the transit time and cause cecal enlargement¹⁸⁾. It was found that 7.5% of sodium alginate caused

Table 6. Serum Concentrations of Na, K and Ca

Group	Time after administration (hr)	Serum concentration (mg/100 ml)		
		Na	K	Ca
Control	1	404.3	28.8	20.3
	2	385.7	36.5	20.4
	4	406.1	29.7	21.0
	8	411.3	33.6	20.4
	24	381.0	33.5	20.9
Na-Alginate	1	395.9	35.5	19.6
	2	407.1	33.0	22.9
	4	419.6	33.2	18.3
	8	350.8	35.3	19.4
	24	377.8	32.9	19.9
K-Alginate	1	368.0	34.7	19.3
	2	325.7	30.0	19.3
	4	383.8	30.3	20.1
	8	381.9	33.2	20.0
	24	352.6	35.4	19.0
Alginic acid	1	359.6	33.2	18.8
	2	416.4	31.6	19.0
	4	331.2	33.4	17.3
	8	358.7	36.5	20.3
	24	328.0	34.9	17.6
Ca-Alginate	1	364.7	35.4	20.0
	2	408.9	40.0	21.2
	4	342.9	34.3	21.6
	8	362.9	30.6	22.0
	24	374.0	33.2	21.3

Rats of each group were killed at the same time after the oral administration of alginates (90.4 mg/kg/10 ml).

a decrease in dietary fat digestibility¹⁹⁾. The inhibition of increase in serum and hepatic cholesterol contents in rats was observed when the animals were fed the semi-purified lithogenic diet containing 1% cholesterol and 0.25% sodium cholate supplemented with 5% sodium alginate²⁰⁾.

Sodium alginate decreases the intestinal absorption of strontium (Sr) and to a lesser extent, those of several other metal ions^{4), 21)}. In man, alginic acid increases fecal sodium (Na) and potassium (K) excretions¹⁶⁾.

There is some uncertainty concerning the digestion and absorption of alginates in experimental animals; the question relates to the degree of "digestion" by intestinal enzymes or degradation by intestinal flora and subsequent absorption⁴⁾. Viola *et al.*²²⁾ concluded that

sodium alginate was digested and absorbed by rats. On the other hand, studies using ¹⁴C-labeled sodium alginate revealed no digestion or absorption in rat feeding trials²³⁾.

The dose administered to the rats (90.4 mg/kg) in our experiment was significantly lower than the dose used in the above-mentioned reports.

Contents of Na, K and Ca in the administered alginate solutions or suspensions were less than 5% of those derived from the diets (Tables 2 and 3), and this fact seems consistent with the results that the urinary and fecal excretions of Na, K and Ca did not change significantly in any of the groups (Table 5), which was different from the result in previous reports^{16), 21)}. No significant differences were observed in serum concentrations of Na, K and Ca among the groups

Fig. 1. Distribution of alginate in the gastrointestinal tract as a function of time

Rats of each group were killed by decapitation at a given time after the oral administration of alginates (90 mg/kg/10 ml). Alginate in each tissue including its content was determined as sodium alginate. Analysis was performed in duplicate for each sample.

(Table 6).

There were no significant differences in body weight, food intake and the volume of urinary and fecal excretions owing to the administration of alginates among the rats of all the groups (Table 3).

Significant changes in the patterns of fecal excretion of alginates were not observed (Table 4). The apparent excretion rate of alginate during 3 days was in the range of 72.7~79.3% (Table 4). This is roughly consistent with the results of Humphrey *et al.*,²³⁾ who found that more than 85% of the administered ¹⁴C-labeled sodium alginate was excreted into feces within 17 hours.

Patterns of the contents of alginates in gastrointestinal tract as a function of time were similar in the rats administered the 4 kinds of alginates (Fig. 1). Administered alginates remained in the stomach 2 hours after the oral administration, then were gradually transferred to the small

intestine after 4 hours and to the large intestine after 8 hours (Fig. 1). Most of the alginates remained in the large intestine after 24 hours (Fig. 1). Table 4 shows that 13.5~56.9% of administered alginates were excreted into feces within 24 hours. So, although the possibility of the decomposition of alginates in the intestine could not be ruled out completely, it was considered that most of the alginates administered orally are excreted into feces in the rat.

Therefore, it is suggested that alginic acid, sodium alginate, potassium alginate and calcium alginate are not a hazard to man at the levels currently ingested through foods.

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