[Chem. Pharm. Bull.
26(6)1846—1851(1978)]

UDC 615.453.2.011.3.014 : 546.284'46.02.09

The Silicate Structure Analysis of Magnesium Silicate Antacid by the Trimethylsilylation Method

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(Received November 28, 1977)

Composition and degree of polymerization of polysilicic acids in magnesium silicates were studied by the trimethylsilylation method. The trimethylsilylated derivatives of silicic acids obtained by acid hydrolysis of the silicates were separated into soluble and insoluble fractions. Orthosilicic acid and a few species of polysilicic acids were determined by gas-liquid chromatography in the soluble fraction. The results are as follows: monosilicic acids (0.16—0.96%), disilicic acids (0.02—0.31%), trisilicic acids (−0.06%), cyclic tetrasilicic acids (−0.11%), the other soluble polysilicic acids (0.35—1.45%), and insoluble polysilicic acids (75.78—82.07%). These results apparently suggest that, when magnesium silicate is hydrolyzed in gastric juice, most of silicic acids produced may lead to insoluble silica gel and the other, such as orthosilicic acid and several polysilicic acids with low degree of polymerization, may disperse in gastric juice. Possible absorption of silicic acids from digestive tracts following oral administration of the antacid was discussed.

Keywords——structure analysis; trimethylsilylation; magnesium silicate; antacid; trimethylsilylated polysilicate; soluble silicate; intestinal absorption

Magnesium silicate is widely used in the treatment of hyperacidity and gastric and duodenal ulcers. The absorption of silicates from digestive tracts following the oral administration has been known.[2,3] Cases of nephrolithiasis were reported in the patients given oral doses of antacid containing silicates.[4,5] Furthermore, Lagergren[6] has reported urinary calculi containing silicic acid as major component in 5 patients. All of them had received tablets of magnesium silicate over a few years.

On the other hand, trimethylsilylation was studied by several authors on silicates, such as sodium zeolite, tobermorite, and sodium silicate, and the structures of the silicates were speculated through the trimethylsilylated derivatives.[7-10]

In the present report, the trimethylsilylation method after Lentz[7] and Masson *et al.*[10] was modified to determine the composition of a magnesium silicate, an antacid. Significant information on polymerization of the silicate was obtained by the method. Total soluble silicates in the magnesium silicate were also determined gravimetric analysis and were compared with those from the trimethylsilylation method.

Experimental

Magnesium Silicates——The following five preparations of commercially available magnesium silicate were used: sample 1 (lot 8492) and sample 2 (lot 8839) produced by Kyowa Chemical Ind., Tokyo, sample 3

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[1] Location: *3190 Gofuku, Toyama-shi, Toyama.*
[2] R.R. Heffner, R.C. Page, and A. Frey, *Am. J. Digest. Diseases*, **8**, 219 (1941).
[3] Federal Register, 39, No. 108, 19875 (1974).
[4] G. Hammarsten, I. Helldorff, W. Magnusson, and T. Rilton, *Svensk Lakartidning*, **50**, 1242 (1953).
[5] J.R. Herman and A.S. Goldberg, *J. Am. M. A.*, **174**, 1206 (1960).
[6] C. Lagergren, *J. Urology*, **87**, 994 (1962).
[7] C.W. Lentz, *Inorg. Chem.*, **3**, 574 (1964).
[8] C.W. Lentz, *Mag. Concre. Research*, **18**, 231 (1966).
[9] K. Komatsu, I. Tohyama, A. Kawahara, and T. Nakamura, *Kogyo Kagaku Zasshi*, **74**, 160 (1971).
[10] S.K. Sharma, L.S. Dent Glasser, and C.R. Masson, *J. Chem. Soc. Dalton*, **1973**, 1324.

(lot 209497) and sample 4 (lot 209495) produced by Tomita Pharm. Co., Tokushima, and sample 5 (lot 9YC110K1) produced by Iwaki Pharm. Co., Tokyo.

Trimethylsilylation[11]——A mixture of 50 g of ice, 30 ml of concentrated HCl, 100 ml of isopropyl alcohol, and 100 ml of hexamethyldisiloxane (HMDS) was stirred for 1 hour at 18—20°. To the solution obtained was added magnesium silicate, 10 g, suspended in about 50 ml of water and the mixture was stirred thoroughly for another one hour. The mixture was transferred into a separatory funnel to remove aqueous phase. After centrifugation of the HMDS layer at 3000—3500 rpm, the precipitate obtained was washed with about 100 ml of HMDS, followed by washing with distilled water and isopropyl alcohol successively. The precipitate was dried at 150° for about 5 hours. The precipitate was named "insoluble component." The supernate and HMDS used for the washing were pooled and then washed with distilled water until no more chloride was detectable. After separation of water, to the HMDS was added 10 g of ion-exchange resin for nonaqueous used, Amberlyst 15, and the mixture was shaken vigorously for 2 hours. The resin separated from HMDS by filtration was washed with about 50 ml of HMDS. The filtrate and HMDS used for the washing were pooled and then distilled at atmospheric pressure to remove excess HMDS. The volatile fraction of the condensate was analyzed by gas-liquid chromatography. The condensate was distilled again under reduced pressure of 17 mmHg in the temperature range from 160 to 180°. Thus, the non-volatile fraction of the trimethylsilylated derivatives was obtained.

Gas-Liquid Chromatography——Gas-liquid chromatography was performed on a Model 063 produced by Hitachi Co., Ltd. Solvent used was HMDS. Silicon gum SE 30, 10 ml, produced by Wako Junyaku Co. Ltd. was packed in a column. The elevation rate of the temperature during the operation was programmed at 7.5°/min. The quantity of the trimethylsilylated derivatives were converted to weight percent values of SiO_2 using calibration curves. The calibration curves were prepared using pure specimens which derived from various silicates.

Composition of Insoluble Component and Determination of Silanol——The morphology of the insoluble component was observed by a scanning electron microscope. For the determination of the hydroxyl groups, the insoluble component was treated at 500° in an atmosphere of argon and then water produced was determined by Karl Fischer's Method.

Gravimetric Analysis of Silicic Acids Soluble in Acid——To an accurately weighed magnesium silicate, 1—2 g, was added 100 ml of 0.5 N HCl. The magnesium silicate in 0.5 N HCl was kept at 36—37° for 1 hour and filtered with a filter paper for the use of quantitative determination. To a definite amount of the filtrate, concentrated HCl was added, and the mixture was evaporated to dryness. The silicic acids in the residue were determined as soluble silicic acids by gravimetric analysis with hydrofluoric acid.

Results and Discussion

Magnesium Silicate

Results of the physico-chemical analysis are shown in Table I.

Trimethylsilylation

The results of trimethylsilylation are shown in Tables II and III.

The mole ratio of H/C, about 3, for the non-volatile component was estimated by elemental analysis, suggesting that the component contains about 27—29% of carbon. Among the molecular structures of the polysilicates, linear structures of $Si_nO_{3n+1}{}^{2(n+1)-}$, $Si_{4n+2}O_{11n+7}{}^{(6n+1)-}$ or $Si_{2n}O_{5n+2}{}^{2(n+2)-}$, and several plane and steric network structures are considered. With the carbon contents calculated for each trimethylsilylated derivative of the polysilicic acids, one fraction corresponding to $Si_nO_{3n+1}{}^{2(n+1)-}$ contains higher than 32.39% and another fraction corresponding to $Si_{4n+2}O_{11n+7}{}^{6(n+1)-}$ contains higher than 29.72%. Therefore these two are excluded from the structure study. Carbon content is controllable over the 25.51 to 32.39% range in the trimethylsilylated derivatives from the polysilicic acids corresponding to $S_{2n}O_{5n+2}{}^{2(n+2)-}$. Although polysilicate molecules having plane and steric network structures with less silicon can theoretically contain larger amount of carbon atoms, the increase in the degree of polymerization decreases markedly the carbon content. Andrianov[12] and Komatsu *et al.*[9] proposed Formula (I) for a trimethylsilylated derivative of calcium silicate as a molecular model of non-volatile fraction.

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[11] All chemicals were analytical grade commercial materials and used without further purification.

[12] K.A. Andrianov, "Metalorganic Polymer," Interscience Pub. Inc., 1965, p. 276.

Table I. Physico-chemical Analysis of Magnesium Silicate

Samples		1	2	3	4	5
Average particle size[a] (μm)		7.6	3.4	5.2	2.8	7.1
Bulk density (g/cc)		0.386	0.213	0.375	0.200	0.376
Slurry pH (4% aqueous suspension)		10.2	9.7	10.4	10.1	10.3
Acid consuming capacity[b] (ml/g)		157.7	155.4	157.5	158.2	162.1
Loss on drying (105°, 1 hr, %)		16.72	14.14	17.58	15.03	15.77
Ignition loss[b] (%)		29.13	27.30	28.18	27.06	27.88
Component[b] (%)	MgO	20.59	21.73	21.81	22.14	21.35
	SiO_2	47.76	48.60	49.03	49.67	47.21
	Al_2O_3	0.65	0.57	0.76	0.28	0.33
	Na	0.99	0.53	0.82	0.64	0.07

a) Determined by light transmission method.
b) J.P. IX, The Ministry of Welfare, 1976, p. 279.

Table II. Composition of Silicic Acids in Magnesium Silicate

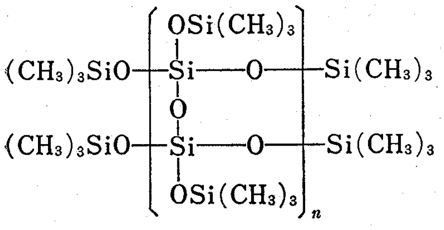
as SiO_2 (%)

Samples	SiO_4^{4-}	$Si_2O_7^{6-}$	$Si_3O_{10}^{8-}$	$Si_4O_{12}^{8-}$	Soluble polysilicate	Insoluble polysilicate	Total recovered
1[a]	0.80±0.17	0.09±0.03	0.04±0.02	0.09±0.02	0.68±0.14	79.61±3.16	81.31±3.22
2	0.68	0.02	0.02	0.06	0.82	79.60	81.20
3	0.54	0.14	0.01	0.02	0.86	75.78	77.36
4	0.75	0.31	0.02	0.11	1.40	77.87	80.46
5	0.16	0.11	—	—	0.35	82.07	82.69

a) The value represents the mean ± S.E. of three experiments of the trimethylsilylation.

Table III. The Results of Elemental Analysis of Soluble and Insoluble Trimethylsilylated Polysilicate

Samples	Soluble polysilicate (Residual fraction)				Insoluble polysilicate			
	C (%)	H (%)	H/C	n	C (%)	H (%)	H/C	Silanol as H %
1	28.34	7.38	3.10	6.50	12.28	4.71	4.57	1.09
2	26.95	6.82	3.02	13.85	11.04	3.62	3.91	0.79
3	28.67	7.01	2.95	5.70	13.79	4.40	3.80	0.91
4	27.04	7.22	3.18	12.97	5.35	2.18	4.85	0.79
5	28.73	7.70	3.19	5.57	13.48	5.42	4.79	0.93



formula (I)

However, neither plane nor steric network structure can be excluded, because of the reason mentioned above. In order to estimate the average degree of polymerization of the silicates, the non-volatile fraction of the silicates tentatively assumed to be $Si_{2n}O_{5n+2}^{2(n+2)-}$ in this study, of which carbon content is similar to that of formula (I). The n for the polysilicates with average molecular size was calculated from carbon content obtained by elemental analysis.

Gas–liquid chromatographic examination of the volatile trimethylsilylated derivatives of the silicic acids in magnesium silicate indicated the presence of $[(CH_3)_3Si]_4SiO_4$, $[(CH_3)_3Si]_6Si_2O_7$, $[(CH_3)_3Si]_8Si_3O_{10}$, and $\{[(CH_3)_3SiO]_2SiO\}_4$ and they correspond to the monomer, the dimer, the trimer, and the cyclic tetramer, respectively. A typical gas–liquid chromatogram for the volatile trimethylsilylated derivatives is shown in Fig. 1. All of the unknown peaks are minor components.

The elemental analysis of the insoluble component suggests that the silicate may include considerable amount of silanols. It appears that silanols remaining unchanged are either shielded by trimethylsilyl groups or directing towards inside the particles.

Species of Silicic Acid Molecules and Their Contents in Magnesium Silicate

Volatile fraction was analyzed by gas–liquid chromatography. The presence of small amount of anions, such as SiO_4^{4-}, $Si_2O_7^{6-}$, $Si_3O_{10}^{8-}$, and $Si_4O_{12}^{8-}$ was demonstrated. Elemental analysis of the non-volatile fraction demonstrated the presence of polysilicate which is soluble in acid solution and designated by $Si_{2n}O_{5n+2}^{2(n+2)-}$. Possible model for molecule is shown in Fig. 2. The *n*'s estimated range from 5.57 to 13.85. These results apparently suggest that a magnesium silicate may contain various silicic acids ranging from monomers to those highly polymerized. However, most of the silicic acids may be polymers insoluble in acid, having structures of steric networks. A scanning electron microphotograph of an insoluble trimethylsilylated polysilicic acid is shown in Fig. 3. This trimethylsilylated polysilicic acid has essentially the same structure as that of the magnesium silicate. These particles may be the secondary aggregation particles of the primary particles with particle size over the 50—160 nm range. X-ray refractometry of the powder gave only broad halos similar to those of magnesium silicates, suggesting that the powder is amorphous.

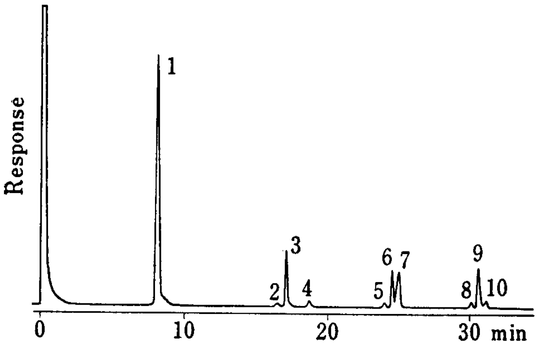


Fig. 1. Typical Gas–liquid Chromatogram for the Volatile Trimethylsilylated Derivatives (Sample 1)

1, $[(CH_3)_3Si]_4SiO_4$;
3, $[(CH_3)_3Si]_6Si_2O_7$;
6, $\{[(CH_3)_3SiO_2]SiO\}_4$;
7, $[(CH_3)_3Si]_8Si_3O_{10}$;
2,4,5,8—10, unknown.

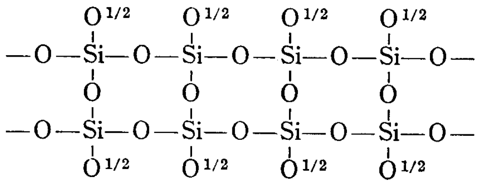


Fig. 2. Structure Model for the Molecule of Soluble Polysilicate

Fig. 3. Scanning Electron Micrograph of Insoluble Trimethylsililated Polysilicic Acids (Sample 5)

The distribution of particle sizes of the trimethylsilylated derivatives suggests that most of the magnesium silicate particles are composed of complex of amorphous silica and magnesium hydroxide. On the other hand, the silicic acids are partially soluble in HCl and almost insoluble in water. Therefore, the silicic acids may be bonded to magnesium ion, forming metallsiloxane bond (≡Si-O-Mg-O-Si≡) on the surface of the polysilicate particles which are not soluble in acid.

Silicic acid composition of magnesium silicates varies a bit with individual preparation. For example, sample 5 contains remarkably small amount of soluble fraction, compared with the other samples. Neither trimer nor cyclic tetramer was detected in the preparation. The reasons why each preparation contains different amount of soluble silicates are as follows: 1) the difference in the degree of polymerization of sodium silicate used for the preparation of magnesium silicate, 2) the difference in the variables for the synthesis, such as temperature, concentration, pH and so on, and 3) the difference in remaining ions, such as Na^+ and Al^{3+} in magnesium silicate.

Most of silicic acids in sodium silicate (Na_2O/SiO_2 molar ratio is 0.32) generally used for the preparation of magnesium silicate are soluble in acid, whereas most of silicic acids in magnesium silicate are insoluble. The finding suggest occurrence of binding between polysilicate molecules during the synthesis of magnesium silicate by double decomposition between sodium silicates and magnesium salts. As an activation energy for the polymerization of silicates lower than that for the formation of metallsiloxane bond, polymerization of silicates proceeds in association with neutralization of sodium silicate by the addition of magnesium salts. Thus, after gelation of silicates is mostly completed, magnesium ions are converted into magnesium hydroxides which precipitate to form complex with the silica gel.

Comparison between the Results obtained by the Trimethylsilylation Method and Gravimetric Analysis

Total soluble components of the silicic acids determined by gravimetric analysis are shown in Table IV. The values of soluble fraction determined by the trimethylsilylation method are related to those determined by gravimetric analysis with some difference in yields. The difference may be attributed to the difference in variables for the decomposition process, such as pH, solvent used and so on.

Table IV. Total Soluble Components of the Silicic Acids in Magnesium Silicates

Samples	1	2	3	4	5
Soluble silica (%)	2.38	1.66	1.82	2.05	1.49

The value represents the mean of two experiments.

Absorption of Silicic Acids from Digestive Tract following Oral Administration of Magnesium Silicate

Page *et al.*[2] demonstrated *in vivo* absorption of magnesium silicate and excretion of silica into urine. They considered that colloidal silica was produced by the reaction between magnesium silicates and acid. The colloidal silica includes soluble orthosilicic acid (H_4SiO_4), partially soluble metasilicic acid (H_2SiO_3), trisilicic acid ($H_4Si_3O_8$) and insoluble disilicic acid ($H_2Si_2O_5$). Lagergren[6] and Hammarsten *et al.*[4] discussed absorption of silicic acids based on the theory proposed by Page *et al.*

The present experiment with trimethylsililylation demonstrated that not only orthosilicic acid, but also the oligomers and even more highly polymerized silicic acids are soluble. The soluble silicic acids mainly consist of orthosilicic acid (ionized form), and polysilicic acids designated by $Si_{2n}O_{5n+2}^{2(n+2)-}$. Although silicic acid molecules being able to be absorbed from digestive tracts seems to be primarily limited by the molecular size, the molecular size and form permitting absorption from digestive tract and effects of polysilicic acid absorbed from digestive tract on renal filtration remain yet to be elucidated. Although acid soluble silicic acids present only by 1—2% in magnesium silicate, soluble and partially insoluble polysilicic acids should be formed by the reaction of magnesium silicate with stomach juice and splitting their siloxane bonds to form low molecular weight polysilicic acid in intestinal alkaline solution. The low molecular weight polysilicates may contribute to the increase in the amount of silicates to be absorbed from digestive tract.

Acknowledgement The authors express their deep gratitudes to Prof. H. Takahashi of University of Tokyo for his kind encouragement, and to Prof. M. Saito of Toyama University for his useful suggestions and the measurement of Karl Fischer aquametry.

The authors are also indebted to Dr. M. Inoue and Dr. H. Kashiwagi for valuable discussion, and to Miss. Y. Yamada for her technical assistance of the experiments.