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25. Hisashi Nogami, Tsuneji Nagai,*1 Takao Kasai, and Toshio Kajima*2 : Studies on Powdered Preparations. XV.*3 Aging of Dried Aluminum Hydroxide Gel under Humidity and in Water.*4

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Many observations have been made on the excellent properties of dried aluminum hydroxide gel (DAHG) as a gastric antacid, as well as on the diverse physico-chemical behaviors. Especially, a validity of DAHG as medicinal preparations is influenced by the antacidic reactivity, which was discussed in the previous paper1) from the standpoint of a reaction kinetics.

One of the important factors which may control the antacidic reactivity is considered to be a shape and especially it is necessary to be amorphous. Many reports2~10) have been found on this fact, which is known even empirically, as well on the manufacturing methods. As to the aging phenomenon, Funaki,2) Santos, *et al.*,5) Moscou and Vlies,10) Marboe and Bentur,11) and Yamaguchi12) studied and presented the concurrent conclusions that, though a slight difference may be observed depending on the aging conditions, bayerite-like crystalline body was once produced, examined, by X-ray crystallographical methods. However, the details on the conditions and processes of the aging phenomenon have not been completely examined, based on a premise of using as medicinal preparations.

The present study was attempted to observe the aging processes of commercial DAHG, which was kept in various atmosphere under relative humidity and in distilled water at 30°, by the measurements of neutralizing rate, X-ray powder diffraction and infrared absorption spectra.

Experimental

Samples——a) DAHG J.P. : Two kinds of commercial products (G-A and G-B), which were both amorphous by X-ray observations, were chosen and dried for 24 hr. under the reduced pressure of $10^{-2}\sim10^{-3}$ mm. Hg. Loss on drying of both samples were found to be about 4%. Specific surface area was 80 m^2/g. for G-A and 34 m^2/g. for G-B by the BET method using nitrogen, and the total CO_2 content13) was found to be approximately 3% for G-A and about 7% for G-B. The acid-consuming capacity by the J.P. method was 305 ml. respectively. It was known that both G-A and G-B was prepared from the reaction between sodium aluminate in aqueous solution and carbon dioxide gas, but

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[*3] Part XIV. H. Nogami, T. Nagai, H. Uchida : This Bulletin, **14**, 152 (1966).
[*4] Presented at the Kanto Branch Meeting of Pharmaceutical Society of Japan, Tokyo, June 1964.
1) Part VII. H. Nogami, T. Nagai : This Bulletin, **10**, 728 (1962).
2) K. Funaki : Kogyo Kagaku Zasshi, **45**, 103 (1942).
3) I.G. Ferbenind : Ger. Pat. No. 735073 (1944).
4) K. Suzuki : Kogyo Kagaku Zasshi, **47**, 30 (1944).
5) P.S. Santos, A. Vallejo-Freire, H.L.S. Santos : Kolloid-Z., **133**, 101 (1953).
6) T. Okazawa, J. Ishigame, H. Sano : Japan Pat. Showa-30-3529 (1955).
7) P.S. Roller : U.S. Pat. No. 2667454 (1954).
8) J.H.L. Watson, J. Parsons, A. Vallejo-Freire, P.S. Santos : Kolloid-Z., **140**, 102 (1955).
9) H. Matsumaru : Yakuzaigaku, **16**, 17 (1956).
10) L. Moscou, G.S. van der Vlies : Kolloid-Z., **163**, 35 (1959).
11) E.C. Marboe, S. Bentur : Silicates Industrials, **26**, 389 (1961).
12) G. Yamaguchi : Kogyo Kagaku Zasshi, **61**, 307 (1958).
13) Y. Imai, Y. Hirasaka : Yakugaku Zasshi, **81**, 1109 (1961).

the details of the properties of the solution and temperature in the reaction, rinsing method and drying conditions were unknown. No difference was observed between both samples by electron microscope at the magnification of 10,000 ×.

b) Bayerite: 100 g. of Al_2O_3 was suspended in 1 L. of distilled water, to this 140 g. of NaOH in 1 L. of water was added with stirring, and it was kept stirring for 5 days to dissolve completely, Being decolored with nolite, the reaction solution was continued to stir slowly for crystallization. After a complete precipitation of the crystals, they were filtered, washed with boiled distilled water and dried *in vacuo*. The crystals obtained were dissolved again in NaOH solution and the similar operations were repeated for a pure crystallization. The 2θ value and relative intensities obtained from X-ray powder diffraction pattern were wholely coincident with data in ASTM cards.

c) Boehmite: Hg was painted over polished aluminum plate, to the white powder produced was added distilled water and it was boiled, filtered and dried for 5 hr. at 100°. The X-ray powder diffraction pattern was wholely coincident with the result by Yamaguchi.[12)]

d) Gibbsite: Commercial sample was used. The X-ray powder diffraction pattern was coincident wholely with data in ASTM cards.

Apparatus for Controlling Humidity and Procedure for Moistening and Aging of Dried Aluminum Hydroxide Gel——In this series of experiments, saturated inorganic salt solutions were put to use for maintaining constant humidities as described in Table I. The solution was placed in the desiccator, which was kept in a vessel of stainless steel and they were placed in the temperature constant bath at 30°, as shown in Fig. 1. 2 g. of DAHG samples in 20 ml. weighing bottles were kept over the solution in the desiccator for moistening and aging.

TABLE I. Conditions for Obtaining the Adsorption Isotherm of Water on Dried Aluminum Hydroxide Gel

Salt used	Relative humidity[a)] (%)	Keep-standing period[b)] (day)
LiBr	5.9	7
LiCl	11.8	8
$MgCl_2$	31.4	9
CrO_3	44.6	10
$Mg(NO_3)$	50.9	11
$NaNO_2$	63.0	11
NaCl	75.1	12
KCl	84.5	23
K_2SO_4	97.0	32

a) International Critical Table, **3**, 291 (1928).
b) Reference *5

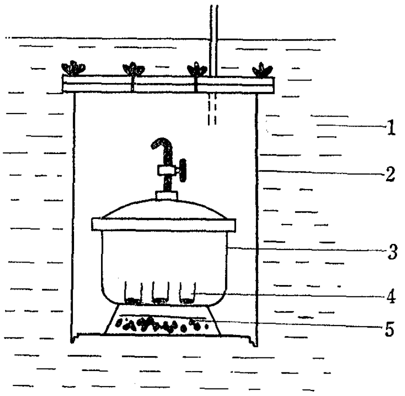

Fig. 1. Apparatus for Moistening and Aging of Dried Aluminum Hydroxide Gel

1: constant temperature water with stirring
2: vessel of stainless steel
3: desiccator
4: sample in a small beaker
5: saturated solution of inorganic salt

Measurements——a) Neutralizing rate[1)]: 600 mg. of DAHG sample and 200 ml. of 0.015*N* HCl containing 0.05% of Tween 80 were employed for the measurement of pH change at 38° with a Hitachi-Horiba Model P pH meter.

b) X-ray powder diffraction: Samples were made into a very fine powder in a small agate mortar and the patterns were measured with a Toshiba X-Ray Diffractometer Model ADX-102.

c) IR absorption spectra: The spectra were measured in NaCl prism region with a Hitachi IR Spectrophotometer Model EPI-II according to the KBr disk method.

Results and Discussion

Adsorption Isotherm of Water and Specific Surface Area

Puri, *et al.*[14)] reported on the measurements of the specific surface area of various porous powders by the adsorption of water. In this study, allowing sufficient time[*5]

[*5] A period of time necessary for complete saturated adsorption was examined preliminarily.

14) B.R. Puri, L.R. Sharma: J. Sci. Ind. Research, **15B**, 178 (1956).

for a complete saturated adsorption of water under relative humidity at 30°, the isotherms were obtained as shown in Fig. 2. These curves showed a typical BET II type and the specific surface area[15] was obtained to be 114 m^2/g. for G-A and 90 m^2/g. for G-B, assuming a section area of one molecule of H_2O being 10.5 Å^2. These values showed some difference from those measured using nitrogen. Assuming the facts that the interaction of H_2O molecule may be much stronger than that of nitrogen, and that a capillary condensation may occur in a small cavity of gel under comparatively high relative humidity, the values obtained from the adsorption isotherm of water are considered to be appropriate. The difference between the value by water adsorption and that by nitrogen adsorption was especially remarkable with G-B. It is considered to have some relationship to the fact that G-B would age much faster, observed by the experiments of keep-standing on moistening, as described later.

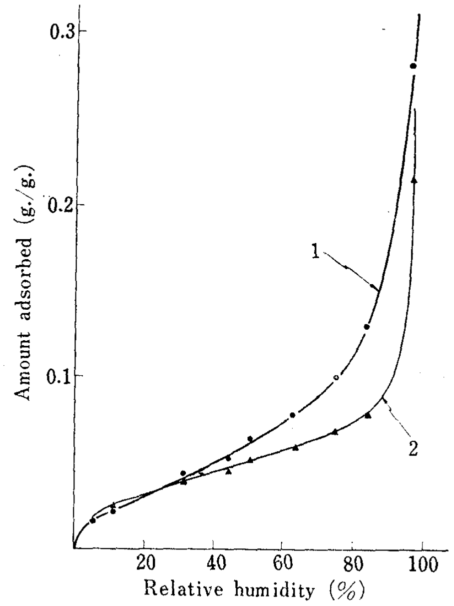

Fig. 2. Adsorption Isotherm of water on Dried Aluminum Hydroxide Gel
1 : G-A 2 : G-B

Neutralizing Rate of the Aged Dried Aluminum Hydroxide Gel

About the samples of G-A and G-B aged under various relative humidities at 30°, typical pH-time curves are shown in Figs. 3 and 4, each curve being for the sample aged for a period up to the completion of saturated adsorption.[*5] A changing process of neutralizing rate was dependent on the relative humidity when then aging was taken place on keep-standing. One interesting fact is that the sample kept standing in a similar way under more than 90% of relative humidity, *e.g.*, Figs. 3-4 and 4-4, showed almost the same or as fast a neutralizing rate as the untreated sample. Furthermore, both samples were aged with the lapse of time under 97% relative humidity and the change of neutralizing rate was measured, as shown in Figs. 5 and 6.

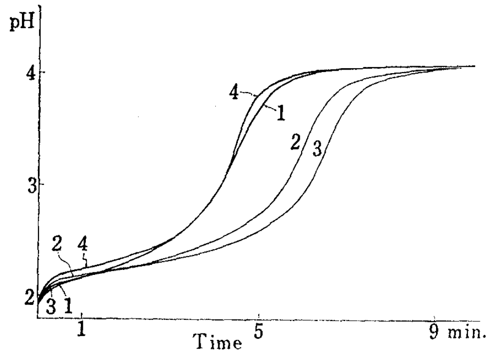

Fig. 3. Reaction between G-A and Hydrochloric Acid at 38° under 600 mg. of Test Sample and 200 ml. of Acid

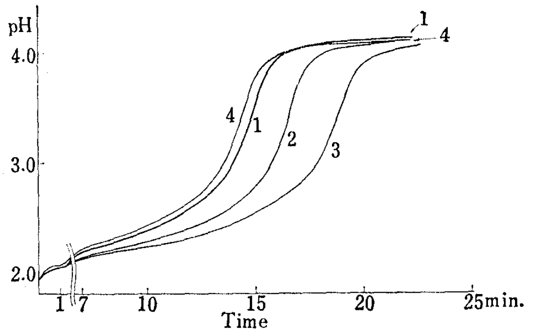

Fig. 4. Reaction between G-B and Hydrochloric Acid at 38° under 600 mg. of Test Sample and 200 ml. of Acid

1 : untreated sample
2 : kept standing under 11.8% relative humidity at 30° for 7 days
3 : kept standing under 84.5% relative humidity at 30° for 23 days
4 : kept standing under 97.0% relative humidity at 30° for 30 days

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15) S. Brunauer, P.H. Emmett, E. Teller : J. Am. Chem. Soc., **60**, 309 (1938).

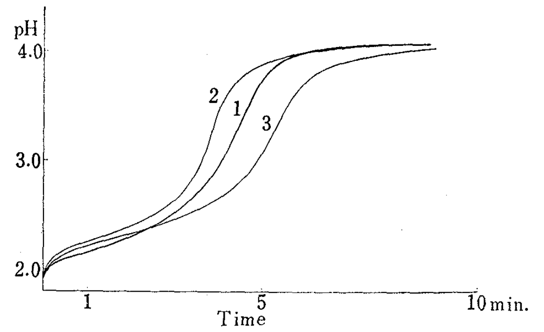

Fig. 5. Reaction between G-A and Hydrochloric Acid at 38° under 600 mg. of Test Sample and 200 ml. of Acid

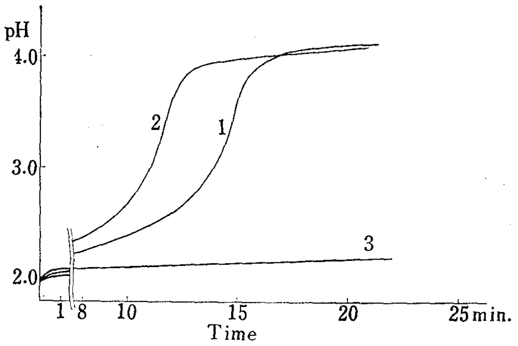

Fig. 6. Reaction between G-B and Hydrochloric Acid at 38° under 600 mg. of Test Sample and 200 ml. of Acid

1: untreated sample
2: kept standing under 97% relative humidity at 30° for 14 days
3: kept standing under 97% relative humidity at 30° for 55 days

In both cases, the rate became maximum around the time when the adsorption would become saturated. Being kept for 55 days, the pH flexional time[1] of G-A became about one minute slower than untreated sample and it still held a neutralizing reactivity, but G-B showed no neutralizing reactivity. This fact confirmed that, even if preparations of DAHG are approved to be of the same quality as an antacid according to the experiment of acid-consuming capacity in J. P., they may have different aging properties. The reason of these differences of aging is considered to be caused perhaps by difference of chemical structure and surface structure depending upon the fine difference of manufacturing conditions.

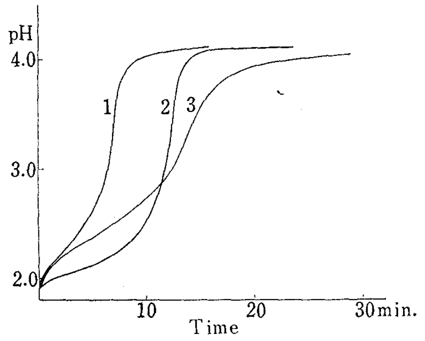

Fig. 7. Reaction between G-B and Hydrochloric Acid at 38° under 600 mg. of Test sample and 200 ml. of Acid

1: untreated sample
2: kept standing in water at 30° for 7 days
3: kept standing in water at 30° for 55 days

In the case of measurement of neutralizing rate, when the sample was added to the acid solution, such a phenomenon that the pH rises a little rapidly was reported,[1,16] and the degree of the rise of G-A was observed to be usually larger and the largest rise with both sample was found when the adsorption of water arrived at the saturation.

Next, the samples were kept in distilled water, *i.e.*, under the moistening condition supposed to arrive at the limit, and the aging was observed. The changing process of neutralizing rate showed a similar tendency to the case of keep-standing under 97% relative humidity, but, as shown in Fig. 7, the neutralizing reactivity of G-B had not been lost after 55 days' keep-standing. This shows that it was more difficultly aged than the case under 97% relative humidity.

The neutralizing rate of the sample aged under relative humidity for a period up to the completion of saturated adsorption became minimum around 84% relative humidity and remarkably faster under more than about 90% relative humidity. This fact will be explained that the adsorption behavior of water on DAHG and an ionic atmosphere around the particles may be different between the cases of

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16) Part XIII. H. Nogami, T. Nagai, A. Suzuki: This Bulletin, 13, 1387 (1965).

more than and less than 90% relative humidity, as discussed from the standpoint of adsorption site for water on silica.[17]

X-Ray Observations of the Aged Dried Aluminum Hydroxide Gel

Both G-A and G-B, aged more than the days of arriving at the saturated adsorption under 97% relative humidity, showed slower neutralizing rate, *e.g.*, in Figs. 5-3 and 6-3, especially G-B lost the neutralizing reactivity when kept standing for 55 days as mentioned above. The X-ray powder diffraction analysis showed a clear difference between the samples.

In Fig. 8-2, G-B which indicated no neutralizing reactivity any more after 55 days' keep-standing, had been in crystallization. On the other hand, Fig. 8-1 showed to be amorphous when G-A was aged under the similar conditions. Fig. 8-3 showed the diffraction pattern of bayerite, to which Fig. 8-2 was pretty resemble, and so this aged G-B might be called bayerite-like crystal. Paying an attention on the X-ray diffraction of aluminum hydroxide crystals, the characteristic difference was around 18° as 2θ value by Cu-$K\alpha$ radiation and so this portion was enlarged, and it was found that the tip of the peak were clearly separated into two peaks as shown in Fig. 9, being 18.8° (d=4.72 Å) and 18.4° (d=4.82 Å). The former value corresponded to bayerite and the latter to gibbsite and G-B aged for 55 days under 97% relative humidity was

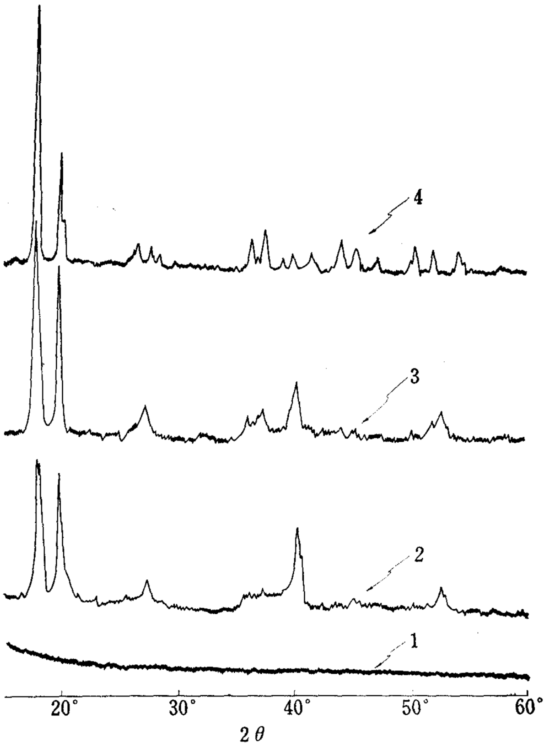

Fig. 8. X-Ray Powder Diffraction Patterns of Aged Dried Aluminum Hydroxide Gel, Bayerite and Gibbsite, by Cu-$K\alpha$ Radiation at a Scanning Speed of 2° per min.

1: G-A kept standing under 97% relative humidity at 30° for 55 days
2: G-B kept standing under 97% relative humidity at 30° for 55 days
3: bayerite
4: gibbsite

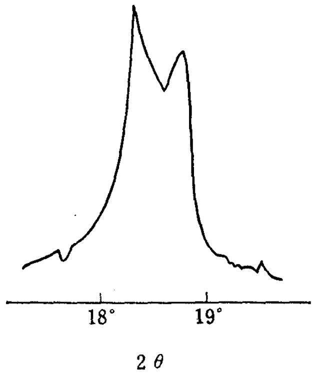

Fig. 9. X-Ray Powder Diffraction Pattern of G-B Aged under 97% Relative Humidity at 30° for 55 Days, by Cu-$K\alpha$ Radiation at a Scanning Speed of 1/2° per min.

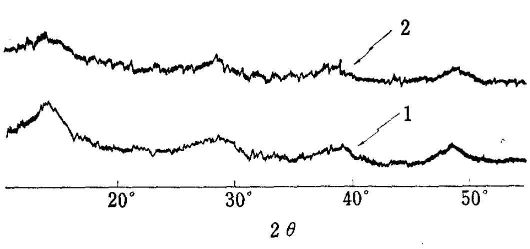

Fig. 10. X-Ray Powder Diffraction Patterns of Aged Dried Aluminum Hydroxide Gel and Boehmite.

1: boehmite
2: G-B aged in water at 30° for 55 days

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[17] K. Kawasaki, I. Tsuchiya: Presented at the 8th Sekigai-Raman Supekutoru Tōronkai (Symposium on IR and Raman Spectra), Tokyo, October 1961.

considered to be a mixture of bayerite and gibbsite. Fig. 8-4 shows the diffraction of gibbsite.

The diffraction of G-B aged in distilled water is shown in Fig. 10-2 which is in good agreement with that of boehmite in Fig. 10-1, while the former had the neutralizing reactivity as shown in Fig. 7-3 and the latter boehmite had no neutralizing reactivity. Therefore, even though the X-ray diffraction would be in accordance each other, they are considered to be different in the other physico-chemical properties.

It is quite certain that the aged sample kept for elongated days under humidity was found to be a mixture of bayerite and gibbsite. Therefore, the aged sample kept for elongated days in water, which was found to be boehmite-like substance and had the neutralizing reactivity, would be transferred to such a mixture, if it would be kept for much longer period of time.

Infrared Observations of the Aged Dried Aluminum Hydroxide Gel

The infrared absorption spectra of the samples aged under 97% relative humidity for a period up to the completion of saturated adsorption are shown in Fig. 11. As shown in Fig. 11-1, both untreated samples showed very resembling absorptions, though there are some difference in intensity. The big broad absorption band around 3700~3400 cm^{-1} and the two step broad absorption around 1600~1400 cm^{-1} with about 1/2 extent of intensity of the former have been recognized to be specific. The absorption around 3700~3400 cm^{-1} is due to ν_{O-H} and it it considered to be overlapping because of an asymmetric absorption. The band around 1600 cm^{-1} would be assigned to δ_{O-H}.[18] Though the absorption around 1400 cm^{-1} is usually assigned to be attributable to carbonate, it is better to interpret that the absorption around 1400 cm^{-1} in Fig. 11 is considered to be a overtone of δ_{Al-O} recognizable around 750~700 cm^{-1},[19] because of its pretty strong intensity comparing with the quantitaive value of carbon dioxide of the samples.

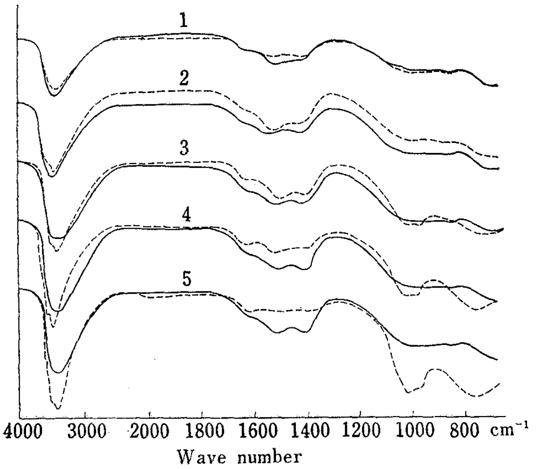

Fig. 11. Infrared Absorption Spectra of Dried Aluminum Hydroxide Aged under 97% Relative Humidity at 30°, According to the Potassium Bromide Disk Method

——— G-A ------ G-B

1: untreated sample
2: kept standing for 7 days
3: kept standing for 21 days
4: kept standing for 34 days
5: kept standing for 70 days

The curves of the aged G-A and G-B under 97% relative humidity with a lapse of time are shown in Figs. 11-2 to 11-5. On the aged G-A no remarkable change had been recognized and this fact is quite in accord with the observations by neutralizing rate and X-ray diffraction. However, G-B showed such a clear difference with the lapse of time that the absorption band of ν_{O-H} around 3700~3400 cm^{-1} became narrower in its width to appear as a sharp band around 3650 cm^{-1}, together with the absorption around 3750 cm^{-1}. The absorption shifted toward higher frequency according to the process of aging, indicating that the hydrogen bond in the structure of DAHG was considered to decrease depending on the aging. The intensity of the absorption

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[18] T. Motooka, G. Hashizume, Y. Inoue: Presentation No. 2T11 at the Annual Meeting of Chemical Society of Japan, Tokyo, April 1964.

[19] T. Sato, Y. Iwai: Presentation No. 2T12 at the Annual Meeting of Chemical Society of Japan, Tokyo, April 1964.

around 1600~1400 cm^{-1} decreased as the aging proceeded and instead of that a broad absorption with comparatively strong intensity was appeared around 1020~960 cm^{-1}. The absorption around 1000 cm^{-1} or lower frequency has been similarly observed with metal complexes in which water is co-ordinated.[20]

Though it is still unknown in detail why the neutralizing rate of DAHG became faster temporarily while aged under high relative humidity or in water, it seems possible as an explanation for this phenomenon that the distortion formed by unhomogeneous crystallization in the solid particles made the packing loose and until the crystallization proceed to a certain extent, specific surface area was increased temporarily,[21] and that, since the decrease of hydrogen bond in the structure could be assumed from the change of infrared spectra, at the beginning in the transfer process of the disordered atoms or atomic group to the ordered arrangement for a certain crystal structure, structural portions of atom or atom pair to increase the basicity of solid were supposed to increase temporarily in the surface to hasten the neutralizing rate. Furthermore, as the aging was proceeded, and also an orientation of molecular structure would be restrained toward uniformity, it is supposed that the neutralizing reactivity would be lost when finally crystallization was completed. Anyway, a temporary increase of neutralizing rate is considered to be a process towards aging, and both G-A and G-B go through a similar process, even if there is a difference in the rate.

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Summary

Commercial DAHG J. P. (G-A and G-B) were kept in various atmosphere under relative humidity and in distilled water at 30° and the following results were obtained.

1. BET specific surface area by the adsorption of water was a little larger than that by the adsorption of nitrogen and the difference between both values of G-B, which had less specific surface area and inferior anti-aging properties, was larger.
2. When both samples were kept standing under high humidity or in water, at an early stage of the aging process, their neutralizing rates became faster temporarily. This phenomenon was observed remarkably with G-B.
3. The sample aged under high humidity with the lapse of time were considered to change in the following process:

Amorphous→boehmite-like substance→bayerite+gibbsite;

i.e., finally transferred to a mixture of bayerite and gibbsite.

4. Infrared absorption spectra of the aged samples, which lost the neutralizing reactivity, showed their characteristic absorption band around 1020~960 cm^{-1}.

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20) J. Fujita, K. Nakamoto, M. Kobayashi: J. Am. Chem. Soc., **78**, 3963 (1956).

21) H. D. Bale, P. W. Schmidt: J. Phys. Chem., **62**, 1179 (1958); J. Chem. Phys., **31**, 1612 (1959).