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# Influence of Particle Size on Physicochemical Properties of Pharmaceutical Powders. VII.[1] Fluidity and Packing Property of Binary Mixtures

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Influence of particle size of boric acid, aspirin or magnesium alumino silicate on fluidity and packing property of the binary mixtures of starch was investigated.

For the mixtures of starch and boric acid or aspirin, angle of repose decreases gradually with the increase of proportion of boric acid or aspirin above critical size, while minimum angle is obtained for the mixture containing a certain proportion of smaller particles. It is suggested that cohesion of starch particles is scarcely influenced by adhesion of starch to particles above critical size, and that it decreases by the adhesion to them below critical size. Porosity of the mixture is a little larger than the arithmetic mean value of porosity of starch and boric acid or aspirin.

Remarkably small values of angle of repose and porosity are obtained for the mixture of starch and magnesium alumino silicate. Magnesium alumino silicate particle is suggested to take moisture away from starch particle.

Several workers reported remarkably small values for angles of repose of starch and some other sticky powders by addition of small proportion of fine powders, such as magnesium oxide.[3,4,5] This phenomenon is very interesting from consideration that, in general, fine powders are sticky. Furthermore, Aoki, *et al.* reported that large particles of magnesium stearate powders were poor lubricants, though small particles of them were used very often as excellent lubricants for tablet compression.[6]

In the previous papers,[1,7] the authors reported that particles below critical size had a tendency to cohere each other or to adhere to a solid surface. The above phenomena may be related to this tendency. Common powders might be expected to have lubrication effect like lublicants, if the particle size would be adjusted adequetly.

In this work, influence of particle size on fluidity and loosest packing of binary mixtures of potato starch and boric acid, aspirin or magnesium alumino silicate is investigated.

## Experimental

One hundred grams of the samples tabulated in Table I were mixed in a cubic-type mixer for twenty minutes. Samples of large particles were sieved by sieves standarized by JIS. Arithmetic mean values were taken as mean particle diameters for boric acid and magnesium alumino silicate larger than 100 $\mu$ and aspirin larger than 300 $\mu$. For the other samples, surface mean diameters or linear mean diameters were obtained by optical microscopic examination. Specific gravity was measured in liquids. Samples were

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[1] Part VI: N. Kaneniwa and A. Ikekawa, *Yakuzaigaku*, **28**, 29(1968).

[2] Location: *Hatanodai, Shinagawa-ku, Tokyo.*

[3] D.J. Craik, *J. Pharm. Pharmacol.*, **10**, 73 (1958). D.J. Craik and B.F. Miller, *J. Pharm. Pharmacol.*, **10**, 136T(1958).

[4] M. Noda, C. Hayashi, M. Ito, S. Fukui and S. Fujita, *Yakuzaigaku*, **20**, 50 (1960).

[5] M.Aoki, S. Ogawa, S. Hayashi and M. Hirayama, *Yakuzaigaku*, **27**, 18 (1967).

[6] M. Aoki and S. Hayashi, *Yakugaku Zasshi*, **87**, 1164 (1967).

[7] A. Ikekawa and N. Kaneniwa, *Zairyo*, **16**, 314 (1967); N. Kaneniwa, A. Ikekawa and H. Aoki, *Chem. Pharm. Bull.* (Tokyo), **15**, 1441 (1967); A. Ikekawa, H. Aoki, K. Masukawa and N. Kaneniwa, *Chem. Pharm. Bull.* (Tokyo), **15**, 1626 (1967).

degassed for seven hours at 80° with a vacuum pump. Moisture content in Table I stands for the ratio of the difference of the weight of a sample before and after drying to the initial weight. Angle of repose was measured by Nogami -Sugiwara's method with a plate of 3 × 10 cm.[1,8] Porosity was measured by JIS standard funnel method.[9] Measurement of surface area was made by air permeability method.[10] Contact angle of liquid to a sample was obtained by capillary rise method.

Table I

| Sample | Informal sign | Mean particle diameter | Specific gravity | Moisture content | Tangent of angle of repose | Porosity in loosest packing |
|---|---|---|---|---|---|---|
| Potato starch | | 30.7$\mu$ | 1.45 | 17.7% | 1.14 | 0.69 |
| Boric acid | | 35.9—324 | 1.44 | | 0.67—1.05 | 0.49—0.75 |
| Crushed aspirin | | 38.9 | 1.35 | | 1.12 | 0.70 |
| Aspirin | | 293—545 | 1.35 | | 0.63—0.76 | 0.45—0.48 |
| Magnesium alumino silicate powder | NFL1 | 1—2[a] | 1.92 | 15.2 | 1.14 | 0.92 |
| | NFL2 | 1—2[a] | 2.27 | 4.3 | 0.98 | 0.93 |
| | NFH1 | 1—2[a] | 2.05 | 15.0 | 0.92 | 0.88 |
| | NFH2 | 1—2[a] | 2.24 | 8.2 | 0.83 | 0.90 |
| Spray dried magnesium alumino silicate | NS1 | 140—324 | 1.93 | 17.8 | 0.64—0.73 | 0.71—0.86 |
| | NS2 | 235 | 2.25 | 8.4 | 0.55 | 0.85 |
| | NSG | 163—385 | 2.09 | 14.0 | 0.49—0.51 | 0.82—0.83 |

a) Agglomerates of magnesium alumino silicate powder particles are too small to measure the size of them correctly but they seem to be approximately 1—2 $\mu$, by optical microscopy.

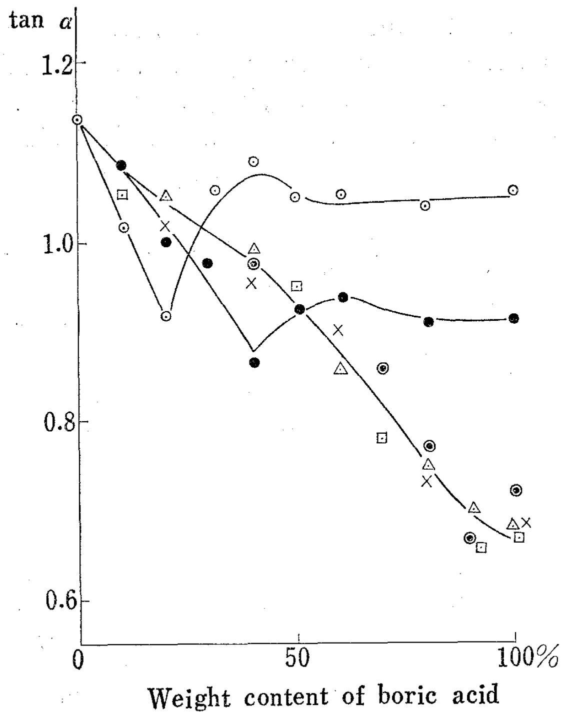

Fig. 1. Angles of Repose of Mixture of Potato Starch and Boric Acid in Various Proportions

particle size of boric acid
—⊙— 35.9 $\mu$ (surface mean diameter)
—●— 67.6 (surface mean diameter)
—◉— 90.0 (surface mean diameter)
—△— 115 —×— 214 $\mu$ —⊡— 324 $\mu$

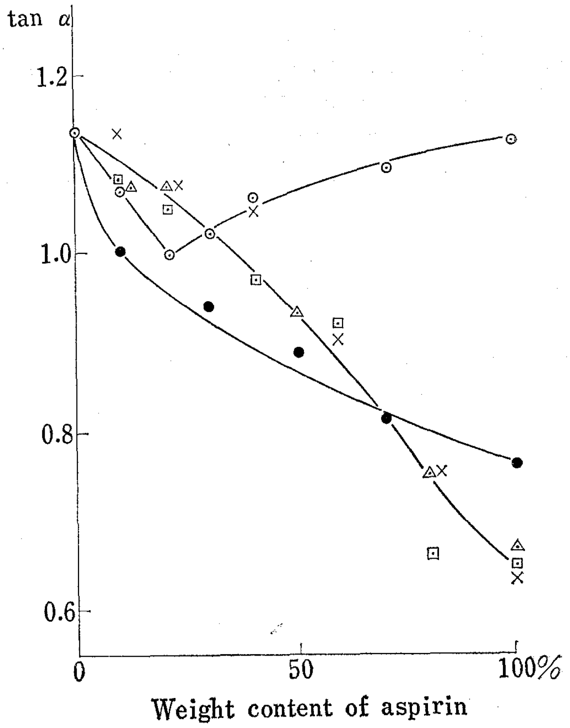

Fig. 2. Angles of Repose of Mixture of Potato Starch and Aspirin in Various Proportions

particle size of aspirin
—⊙— 38.9 $\mu$ (surface mean diameter)
—●— {379 (surface mean diameter) / 293 (linear mean diameter)}
—△— 324 —×— 460 $\mu$ —⊡— 545 $\mu$

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8) H. Nogami, M. Sugiwara, and S.Kimura, *Yakuzaigaku*, **25**, 260 (1965).
9) JIS Z 2502-1958.
10) E. Suito, M. Arakawa, and M. Takahashi, *Kogyo Kagaku Zasshi*, **59**, 307 (1956).

## Results and Discussion

Fig. 1 and 2 show angles of repose of the mixtures of starch and boric acid or aspirin in various proportions. The angle decreases gradually with the increase of the proportion of boric acid larger than 100 μ, while minimum angle is obtained for the mixture containing a certain proportion of smaller particles. When boric acid content is small, the angle of the mixture of boric acid below 100 μ is smaller than that of boric acid above 100 μ. The same tendency is also found for the mixtures of starch and aspirin.

As shown in Fig. 3 and 4, addition of small amount of magnesium alumino silicate gets starch to flow freely, with the exception of NSG. The larger the angle of repose of mixed magnesium alumino silicate is, the smaller is the weight content of that for the mixture showing minimum angle. The value of the minimum angle for the mixture of magnesium alumino silicate is much smaller than that for the mixture of boric acid or aspirin, and a little smaller than that of common coarse particles.

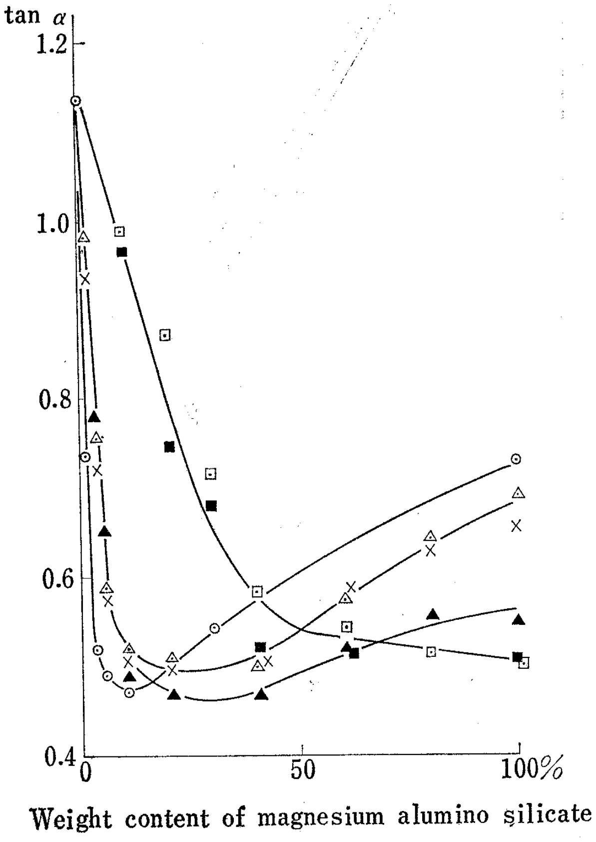

Fig. 3. Angles of Repose of Mixture of Potato Starch and Magnesium Alumino Silicate in Various Proportions

particle size of magnesium alumino silicate
—⊙— NS1 140 μ —▲— NS2 235 μ
—△— NS1 324 —■— NSG 163
—×— NS1 214 —□— NSG 385

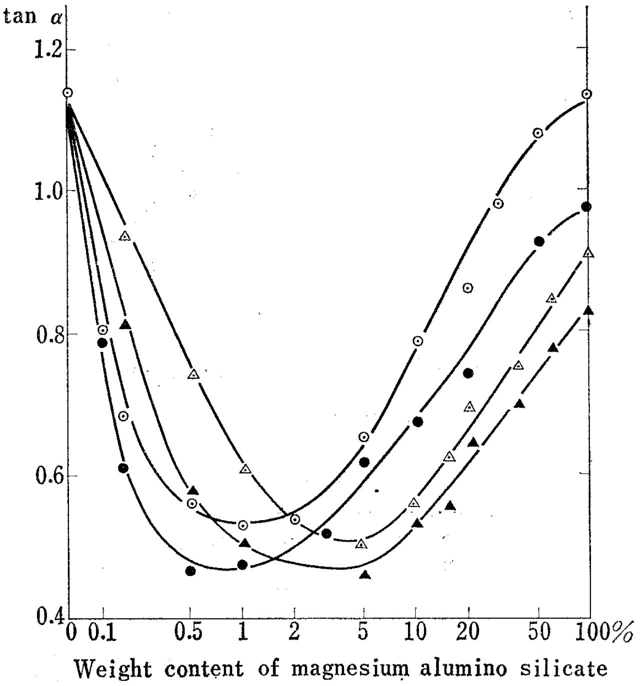

Fig. 4. Angles of Repose of Mixture of Potato Starch and Magnesium Alumino Silicate in Various Proportions

—△— NFH1
—▲— NFH2
—⊙— NFL1
—●— NFL2

It is shown from the data of angle of repose and porosity in loosest packing that critical diameters for boric acid, aspirin and magnesium alumino silicate are 100 μ, 300 μ, and around or below 100 μ, respectively.[7] Angles of mixtures of particles above critical size are independent of the size of component particles of the mixture, while those of particles below critical size are influenced by them. It is suggested from the above facts that adhesive or cohesive force of boric acid, aspirin or magnesium alumino silicate particles has some relation to fluidity of the mixtures.

Porosity in loosest packing of binary mixtures are investigated. Fig. 5 and 6 show porosity of mixtures of starch and boric acid or aspirin in various proportions. In the case of boric acid, the plotted lines of porosity *vs* weight content of boric acid are above the straight lines drawn between the porosity of starch and that of boric acid. This tendency is more remarkable for small particles. The same phenomenon is also found for aspirin.

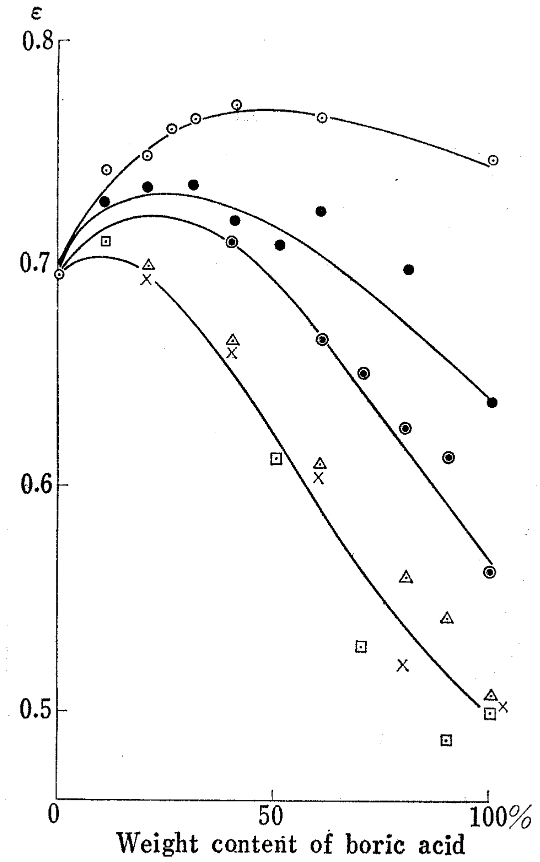

Fig. 5. Porosity in Loosest Packing of Mixture of Potato Starch and Boric Acid in Varying Proportions

particle size of boric acid
—⊙— 35.9 μ —◉— 90.0 μ
—×— 214 —●— 67.6
—△— 115 —⊡— 324

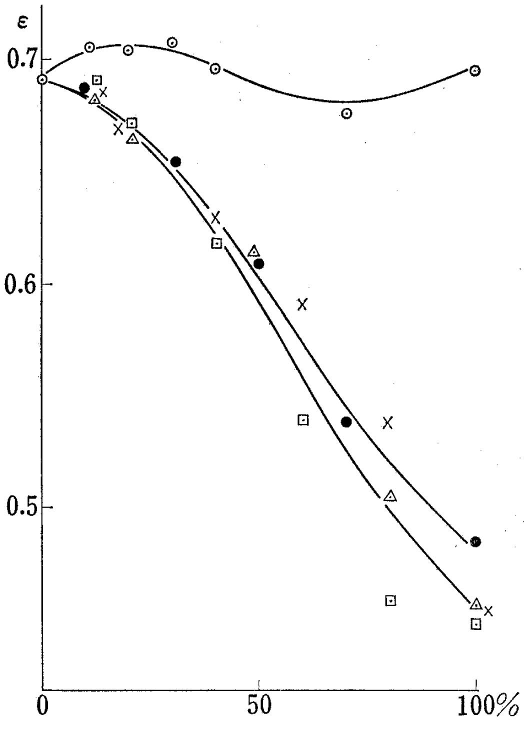

Fig. 6. Porosity in Loosest Packing of Mixture of Potato Starch and Aspirin in Varying Proportions

particle size of aspirin
—⊙— 38.9 μ —×— 460 μ
—●— 293 —⊡— 545
—△— 324

Westman, *et al.* reported the following facts for sands and some other powders. When same kind of different sized particles were mixed, minimum porosity was obtained for the binary mixture containing 30 v/v % of large particles. Closer packing was obtained as the ratio of the size of large particles to that of small ones increased.[11]

By discharging boric acid powders on the metal plate of foil galvanoscope, two foils separate each other. This fact suggests that boric acid particles carry frictional electricity. Small particles of aspirin are also suggested to carry static electricity by the tendency of remarkable adhesion to paper. Static electricity might be related to the fact that porosity of the mixture of starch and boric acid or aspirin is large, in spite of small value of angle of repose.

As shown in Fig. 7 and 8, porosities of the mixtures of starch and magnesium alumino silicate in various proportions are pararell to angles of repose of them. The larger is the angle of repose of mixed magnesium alumino silicate, the smaller is the value of the minimum

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11) A.E.R. Westman and H.R. Hugill, *J. Am. Ceram. Soc.*, **13**, 767 (1930); C.C. Furnas, *Ind. Eng. Chem.*, **33**, 1052 (1931).

porosity for the mixture. The numerical values of the minimum porosity are 0.47—0.58, with the exception of NSG. This value is similar to that for common coarse particles. Considering that magnesium alumino silicate granules are porous and have intraparticle void, remarkably close packing is made by the mixture.

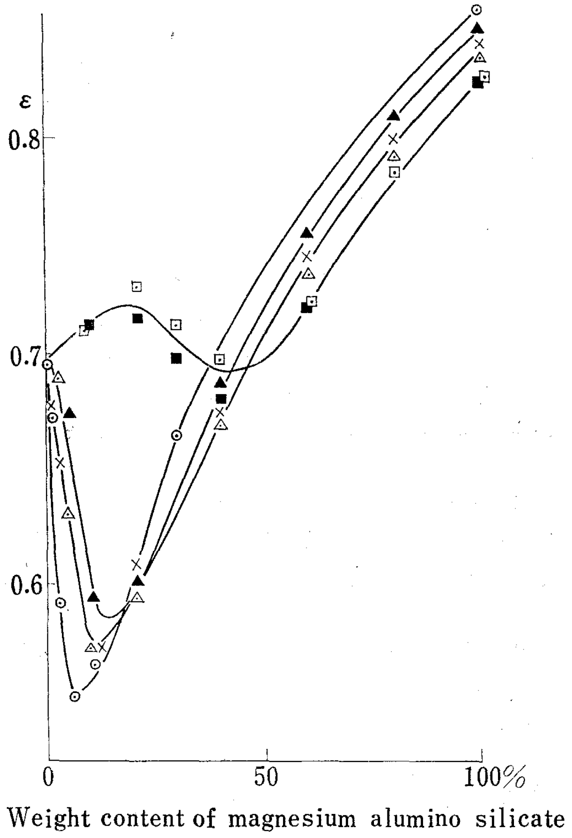

Fig. 7. Porosty in Loosest Packing of Mixture of Potato Starch and Magnesium Alumino Silicate in Varying Proportions

—⊙— NS1 140μ —▲— NS2 235μ
—×— NS1 214 —△— NSI 324
—⊡— NSG 385 —■— NSG 163

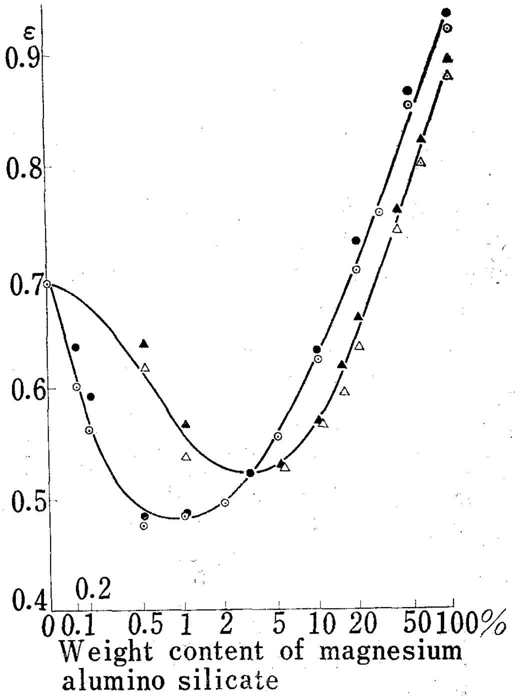

Fig. 8. Porosity in Loosest Packing of Mixture of Potato Starch and Magnesium Alumino Silicate in Varying Proportions

—△— NFH1 —⊙— NFL1
—▲— NFH2 —●— NFL2

Surface area of all the mixtures of starch and magnesium alumino silicate could be measured, since magnesium alumino silicate granules were porous and had large surface area. When no interaction exists between starch and magnesium alumino silicate particles, surface area of the mixture of them is expected to be equal to the arithmetic mean value of the surface area of them. However, the found values of the surface area of the mixtures are much smaller than the expected values. It may be suggested from this finding that osculating plane exists between starch and magnesium alumino silicate particle. Air permeability method may be unsuitable for porous powders, but the same phenomenon has been found for the mixture of starch and fine particles, such as magnesium stearate, talc and magnesium oxide. These fine particles were proved to adhere to the surface of starch particles by microscopic observation.[12] Craik, *et al.* also confirmed that magnesium oxide particles were adsorbed on the surface of starch grains and the remarkable fluidity of starch by the addition of small amount of magnesium oxide were attributed to this fact.[3]

Mixtures are now observed by optical microscopy. As shown in Fig. 9, fine particles of magnesium alumino silicate adhere to the surface of starch particles and starch particles adhere to large particles of magnesium alumino silicate.

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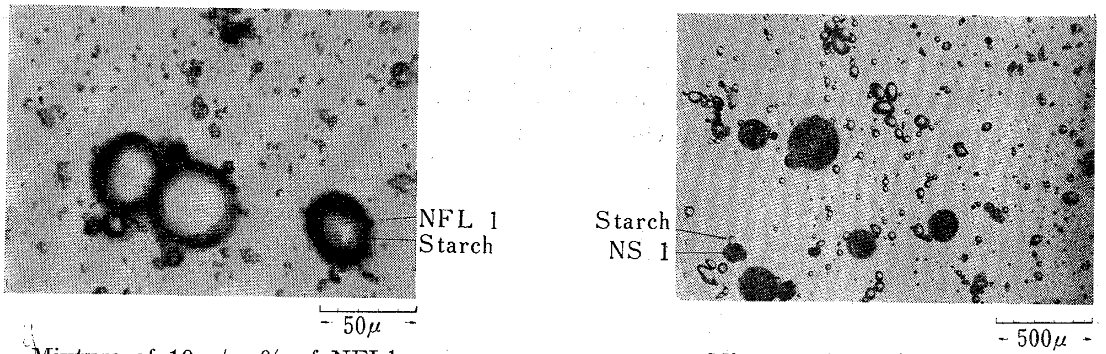
[12] O. Ohodaira, *Yakuzaigaku*, **25**, 195 (1965).



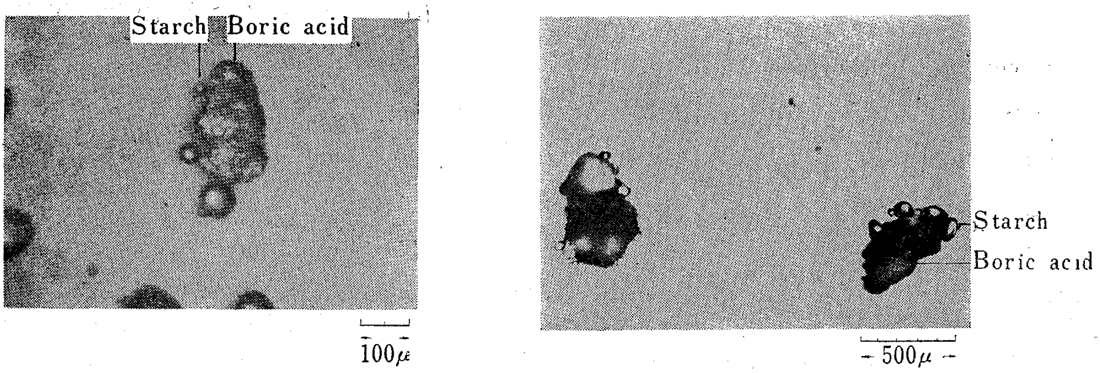
Mixture of 10 w/w % of NFL1 Mixture of 20 w/w % of NS1

Fig. 9. Photograph of Mixture of Potato Starch and Magnesium Alumino Silicate

The following fact is shown by Craik from electron microscopic studies. The added magnesium oxide is all adsorbed on starch surface over the range where angle of repose falls rapidly and adsorption reaches maximum for the mixture of minimum angle of repose. At higher concentrations, the additional magnesium oxide is no longer adsorbed and the angle begins to increase.[3] The similar phenomenon is also observed for the mixture of fine magnesium alumino silicate powders.

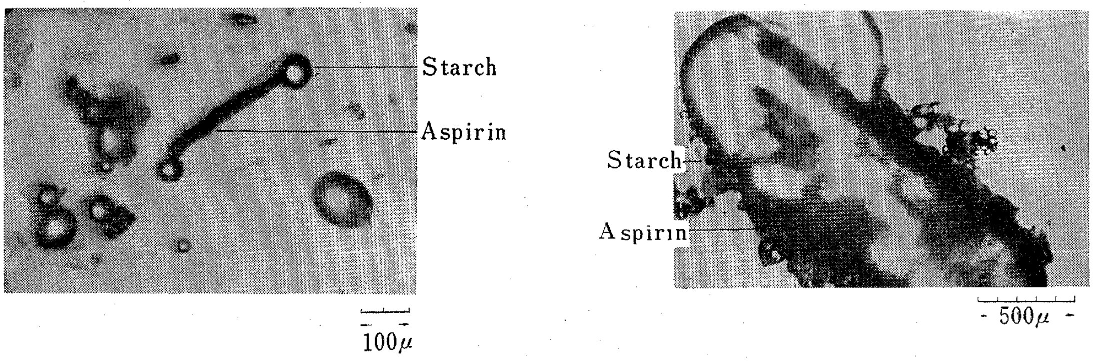
Starch particles and boric acid or aspirin particles adhere to each other, as shown in Fig. 10 and 11. The surface area of the mixture of small particles of boric acid or aspirin doesn't seem to be much smaller than the arithmetic mean values of the surface area of starch and boric or aspirin, though the data are not reproducible.

For boric acid and aspirin, the following suggestion is made from the above findings. Cohesion of starch particles is scarcely influenced by adhesion of starch to the particles above critical size, but it decreases by the adhesion to particles below critical size.



Mixture of 30 w/w % of boric acid Mixture of 60 w/w % of boric acid

Fig. 10. Photograph of Mixture of Potato Starch and Boric Acid



Mixture of 30 w/w % of crushed aspirin Mixture of 80 w/w % of aspirin

Fig. 11. Photograph of Mixture of Potato Starch and Aspirin

Remarkably small values of angle of repose and porosity in loosest packing of the mixture of magnesium alumino silicate and starch are probably due to the dehydration action of magnesium alumino silicate. Fig. 3 and 4 suggest that moisture content of magnesium alumino silicate is one of the parameters controlling fluidity of the mixtures.

Noda, *et al.* reported that angle of repose of starch mixed with 0.5% of synth. aluminium silicate was similar to that of dry starch grains. They also found that angle of repose of the mixture of dry starch and synth. aluminium silicate didn't increase after the mixture was kept in the dessicator containing water and maintaining 100% of R.H. for three days.[4]

As shown in Table II, the contact angles of several kinds of liquid to starch mixed with 1% of NFL1 are similar to those to dry starch, rather than those to starch or NFL1. This finding suggests that magnesium alumino silicate particle takes moisture away from starch particle.

TABLE II. Consine of Cotact Angle of Liquid to Powder[a)]

| | Potato starch mixed with 1% of NFL1 | Starch | Dry starch | NFL1 |
|---|---|---|---|---|
| Water | 0.09 | 0.10 | 0.02 | 0.02 |
| Acetone | 0.72 | 0.39 | 0.91 | 0.72 |
| Diethyl ether | 0.85 | 0.81 | 0.88 | 0.89 |
| Toluene | 1.0 | 1.0 | 1.0 | 0.86 |
| *n*-Hexane | 0.92 | 0.96 | 0.94 | 1.0 |
| Carbon tetrachloride | 0.99 | 0.92 | 1.0 | 0.75 |

*a*) The cosine of the contact angle of the liquid showing the largest value of $r. \cos\theta$ is reckoned to be one, where $r$ is the radius of the capillary tube and $\theta$ is contact angle.

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