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Effect of geometric structure and surface wettability of glidant on tablet hardness

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Abstract

The aim of this study is to investigate the effect of geometric structure and surface wettability of glidant on tablet hardness. Geometric structure is defined, in this work, as three-dimensional structure such as porosity, particle size and specific surface area. A variety of silica was incorporated in direct compressive fillers as glidant and mixed powder was compressed in single punch tablet machine with and without 0.5 wt.% magnesium stearate. Flowability of mixed powder was evaluated with Carr's index measurement. In the case of unlubricated compression, tablet hardness decreased as a function of additional concentration of silica. Reduction rate directly depended on surface coverage of silica over filler surface and hydrophobicity. Since surface coverage is related to geometric structure, it can be concluded that structural influence plays an important role to determine tablet hardness. While, in the case of lubricated compression, either water adsorption amount or geometric structure effects on tablet hardness. Increase of tablet hardness was observed only when hydrophilic porous and small size nonporous silica were added. All the other silica had deleterious effect on tablet hardness and in particular hydrophobicity strongly reduced tablet hardness.

Keywords: Tablet hardness; Glidant; Geometric structure; Surface wettability; Silica

1. Introduction

Glidant is usually incorporated in solid formulations to improve the flowability of granules or powders (Sindel et al., 1998). It is widely known that addition of glidant increases the hardness of tablet, especially in the process of direct compression. The possible mechanism for increasing tablet hardness is (a) suppressing the deleterious effect of magnesium stearate and (b) facilitating densification of powder mixture because of glidant action (Alderborn and Nyström, 1996; Chang et al., 1999).

A number of studies have been carried out for finding an optimum concentration of glidant to give the optimum compactability and hardness by means of varying formulations. Lubner and Ricciardiello (1977) investigated the effect of several types of glidant on tablet hardness and concluded that silica is only effective to increase hardness, if used at the optimum concentration. Another study (Hollenbach et al., 1983) demonstrated that effective concentration depends on the surface affinity between host filler and glidant. In

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spite of these numerous studies, effect of geometric structure and wettability of glidant on hardness has not been fully investigated.

In this study, several types of silica were incorporated in direct compressive fillers as glidant and mixed powder was compressed in single punch tablet machine with and without magnesium stearate. How geometric structure and surface wettability of glidant influence on tablet hardness is discussed, dividing the case when compressed with and without magnesium stearate.

2. Materials and methods

2.1. Materials

The following silica were purchased from commercial suppliers and used as received: Aerosil 50, Aerosil 200 and Aerosil R974 (Nippon Aerosil Co., Ltd., Tokyo, Japan); SO-C1 and SO-C5 (Admatechs Co., Ltd., Aichi, Japan); Carplex CS-5 and Carplex CS-7 (Shionogi & Co., Ltd., Osaka, Japan); Adsolider 101 (Freund Industrial Co., Ltd., Tokyo, Japan); Nipsil SS-50 (Nippon Silica Industrial Co., Ltd., Tokyo, Japan). Tablettose 80 (MEGGLE GmbH, Wasserburg, Germany) and Avicel PH101 (Asahi Kasei Corporation, Osaka, Japan) were used as directly compressible fillers. Magnesium stearate (TAIHEI CHEMICAL INDUSTRIAL CO., LTD., Osaka, Japan) was incorporated as lubricant.

2.2. Determination of geometric structure

Specific surface area and porosity of silica and fillers were determined by gas adsorption method. Adsorption and desorption isotherms of nitrogen at −196 °C were measured by FlowSorb 2300 and TriStar 3000 (SHIMADZU CORPORATION, Kyoto, Japan). Specific surface area S_{N_2} was calculated by the BET method and pore volume was figured out by the BJH Desorption Pore Distribution method (Kondo et al., 1991).

Laser diffraction analysis was used for the determination of particle size distribution except Aerosil samples. In advance of measurement, hydrophilic silica particles were dispersed into distilled water with adding Polysorbate80 as surfactant. In the case of hydrophobic silica, 20% ethanol was used as dispersion media. Prepared dispersion was exposed to super ultrasonic for 10 min in order to avoid the aggregation of single particles and these samples were set to diffraction analyzer (HEROS&RODOS, Sympatec GmbH, Clausthal-Zellerfeld, Germany). Mean particle size of Aerosil samples was quoted from the Aerosil catalog.

2.3. Characterization of surface wettability

Surface wettability of silica was classified into hydrophilic group and hydrophobic group by preferential dispersion test (Fuji et al., 1999). Preferential dispersion test was conducted by dispersing silica particles in water, hexane and a two-phase medium of water and hexane. Prepared slurry solution was placed overnight and the state of dispersion was confirmed visually.

Besides preferential dispersion test, contact angle measurement and water vapor adsorption experiment were conducted, with a view to evaluating surface wettability more quantitatively. Quasi-static contact angles were measured by placing a drop of 0.9 μl purified water on the pellet formed silica particles and imaging it with a video camera (Contact Angle Meter, KYOWA INTERFACE SCIENCE CO., LTD., Saitama, Japan). The angles were calculated directly from the video monitor, taking the average of three times measurements (Engquist et al., 1995). Water adsorption was performed using a volumetric method. The amount of water vapor adsorption was measured up to a relative pressure of ca. 0.4 at 0 or 25 °C. The water was introduced into a vacuum line after removing the dissolved gas by several repetitions of a freeze–melting cycle (Fuji et al., 1999).

2.4. Tablet preparation

Tablettose 80 and Avicel PH101 were premixed in the ratio of 7:3 in drum mixture (NISIDA CHEMICAL EQUIPMENT MFG. LTD, Osaka, Japan) for 30 min and screened with 1 mm mesh sieve. Sieved mixture was poured into silica particles, which were pre-screened with 500 μm mesh sieve, and mixed in a Turbula mixer (T2C Willy A. Bachofen AG Maschinenfabrik, Basel, Switzerland) for 20 min. The total amount of mixed powder was fixed at 350 g and prepared mixtures were stored at 18–26 °C and 30–60% RH.

The compression of mixed powder was carried out by single-punch tablet press (Korsch AG, Berlin, Germany) at 1000 kg compression force. The amount of 340 mg mixture was compacted into flat-faced tablets with a diameter of 10 mm. For the production of lubricated tablets, 0.5 wt.% magnesium stearate was added and mixed in a 1 l stainless container. Since mixing time and particle size of lubricant influence on tablet hardness (Hölzer and Sjögren, 1979; v.d.Watt, 1987), these two factors were fixed at 5 min and 15 μm throughout the experiments. For unlubricated tablets, the die was prelubricated with magnesium stearate before compression (Zuurman et al., 1999).

2.5. Tablet hardness

Crushing strength of tablets ($n = 40$) was measured immediately after compression using a Schleuniger strength tester (Dr. Schleuniger Pharmatron AG, Solothurn, Switzerland).

2.6. Evaluation of flowability of mixed powder

Flowability of mixed powder was expressed as Carr’s index. This total index was obtained from particle size uniformity, repose angle, compressibility and spatula angle. Particle size uniformity was calculated from undersize distribution of initial mixed powder and the value 4.3 was used for all the samples. The other indices were measured by Powder Characteristics Tester (HOSOKAWAMICRON CORPORATION, Osaka, Japan).

3. Results and discussions

3.1. Geometric structure

Three-dimensional structure of silica was determined by gas adsorption method and laser diffraction analysis. Fig. 1 shows nitrogen gas adsorption and desorption isotherms of Adsolider 101 as an example. Hysteresis loop of isotherms was observed typically in porous samples. For porous samples, pore volume can be calculated from desorption isotherm (Kondo et al., 1991). Obtained results were summarized with mean particle size in Table 1. Four samples are porous and the other five samples have nonporous structure. Specific surface area of nonporous samples decreased in inverse proportion to particle size, as nonporous silica has no internal surface area. Whereas, porous samples which include large internal surface area revealed high surface area independent of size (Gregg and Sing, 1982).

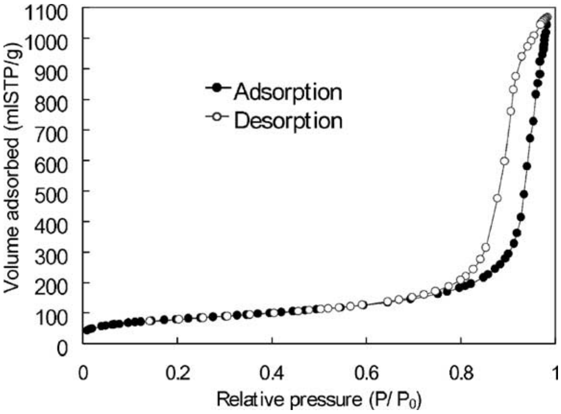

Fig. 1. Adsorption and desorption isotherms of Adsolider 101. Hysterisis loop was typically appeared in porous samples.

3.2. Surface wettability

The result of preferential dispersion tests is listed in Table 2. All samples except Aerosil R974 and Nipsil SS-50 dispersed both in water and hexane and alternatively in water phase for the two phase solution. On the other hand, Aerosil R974 and Nipsil SS-50 floated on the water surface and dispersed only in hexane phase. According to this result, surface wettability of Aerosil R974 and Nipsil SS-50 can be classified as hydrophobic and the residual seven samples are categorized into hydrophilic group.

The result of contact angle was divided into two trends subjected to surface wettability (Table 2). Contact angle for hydrophobic group was ca. 140°, whereas all hydrophilic group samples showed zero. Contact angle for totally methylated silica is 110 ± 2° (Crawford et al., 1987), therefore contact angle even over 140° is considered as the reveal of highly non-wettable surface or the emphasize of hydrophobicity from surface roughness which was described by Wenzel equation (Busscher et al., 1984).

The order of hydrophilicity was determined by water vapor adsorption. The monolayer capacity of

Table 1
Surface geometric structure of silica samples

	Mean particle size (μm)	Specific surface area (m^2/g)	Pore volume (ml/g)
Aerosil 200	0.012[a]	194	Nonporous
Aerosil 50	0.030[a]	53.2	Nonporous
SO-C1	0.42	13.6	Nonporous
SO-C5	1.0	3.62	Nonporous
Aerosil R974	0.012[a]	153	Nonporous
Adsolider 101	0.97	289	1.65
Carplex CS-5	2.0	132	0.96
Carplex CS-7	2.5	120	1.24
Nipsil SS-50	2.5	107	0.56

[a] Mean particle size of Aerosil samples was quoted from the Aerosil catalog.

water vapor adsorption was calculated by the BET equation from the adsorption isotherms and shown as the amount of water adsorbed per square meter and gram in Table 2. Behavior of water adsorption on bare silica surface depends on several factors, such as SiOH density, SiOH type and porous structure (Iler, 1979; Takei and Chikazawa, 1998). Therefore, wettability is generally assessed by amount of water adsorbed per square meter, as it can minimize the effect of pore or surface specific area (Fuji et al., 1999; Muster et al., 2001). Wettability of all samples is placed in order in Table 2.

Porous silica exhibited higher hydrophilic surface more than the other nonporous silica and Aerosil 200 was the least hydrophilic samples. However, owning to the effect of surface area, capacity to water adsorption per gram has different trend. In addition to porous sample, Aerosil 200 is also effective to hold water over its surface (8.07 ml STP/g) because of its large surface area.

3.3. Hardness of unlubricated tablet

In order to assess the effect of hydrophilic silica on hardness when tabletted without magnesium stearate, Fig. 2 depicts the relation between additional concentration of hydrophilic silica and tablet hardness. All the samples, especially in the cases of nonporous small silica particles such as Aerosil 200 and Aerosil 50, caused the deleterious effect on tablet hardness.

Table 2
Result of preferential dispersion test, contact angle and water vapor adsorption

	Dispersion medium			Contact angle (°)	Amount of water adsorbed		Wettability
	Water	Hexane	Water/hexane[a]		(ml STP/m^2)	(ml STP/g)	
Aerosil 200	D	D	D/F	0	0.0416	8.07	Hydrophilic
Aerosil 50	D	D	D/F	0	0.0481	2.56	Hydrophilic
SO-C1	D	D	D/F	0	0.0732	0.995	Hydrophilic
SO-C5	D	D	D/F	0	0.0519	0.188	Hydrophilic
Aerosil R974	F	D	F/D	143	–	–	Hydrophobic
Adsolider 101	D	D	D/F	0	0.138	39.8	Hydrophilic
Carplex CS-5	D	D	D/F	0	0.174	23.0	Hydrophilic
Carplex CS-7	D	D	D/F	0	0.0983	11.8	Hydrophilic
Nipsil SS-50	F	D	F/D	138	–	–	Hydrophobic

Hydrophilic[b] ↔ Hydrophobic
Carplex CS-5 > Adsolider 101 > Carplex CS-7 > SO-C1 > SO-C5 > Aerosil 50 > Aerosil 200 ≫ Nipsil SS-50 > Aerosil R974

[a] Water/hexane indicates silica was poured into water and then dispersed in hexane. D and F indicate dispersion and floatation, respectively.

[b] The order of hydrophilicity was determined by the monolayer capacity of water vapor adsorption divided by S_{N_2}.

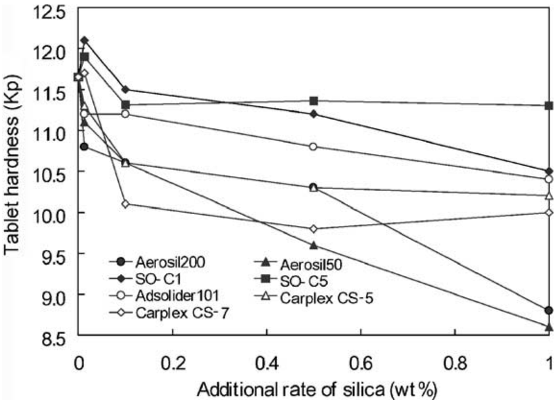

Fig. 2. Additional concentration of hydrophilic silica and tablet hardness when tabletted without magnesium stearate. Four closed symbols belonged to nonporous silica and three open symbols to porous silica. Addition of Aerosil 200 and Aerosil 50 severely reduced tablet hardness.

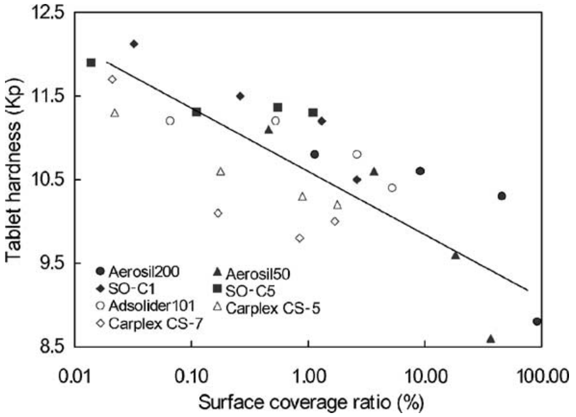

Fig. 3. Calculated surface coverage of silica over filler surface and tablet hardness. Closed symbol is nonporous silica and open symbol is porous silica. Hardness decreased logarithmly with the increase of surface coverage.

No clear relation between hardness and hydrophilicity of samples was observed. Behavior of Adsolider 101 and SO-C1 is similar, though there is difference in the degree of hydrophilicity. These results are considered as follows; the decrease in tablet hardness regarding hydrophilic silica has been influenced by geometric structure and not by surface wettability. Reduction rate of tablet hardness might be related to the surface coverage of silica over filler surface.

For the purpose of proving this hypothesis, surface coverage by silica was calculated from the following equations. Cover area of one silica particle S (m^2) over filler surface and weight of one silica particle W (g) is

$$S = \pi r^2 \tag{1}$$

$$W = \frac{4}{3}\pi r^3 \rho (1 - \varepsilon) \tag{2}$$

where r (m) is silica particle mean radius, ρ (g/m^3) is true density and ε is porosity. True density is quoted from each silica catalog and porosity is calculated from pore volume listed in Table 1. Using the value of S and W, surface coverage ratio R (%) when silica additional concentration is C (%) is determined from the following equation.

$$R = \frac{CS}{0.62W} \tag{3}$$

where 0.62 (m^2/g) is the specific surface area of filler measured by gas adsorption method.

Table 3
Coverage ratio of filler surface when the additional concentration of silica is 1.0 wt.%

	Mean particle size (μm)	Cover area of one silica particle (m^2)	Weight of one silica particle (g)	True density[a] (g/m^3)	Porosity	Apparent density (g/m^3)	Coverage ratio (%)
Aerosil 200	0.012	1.1×10^{-16}	2.0×10^{-18}	2.2×10^6	0	2.2×10^6	89
Aerosil 50	0.030	7.1×10^{-16}	3.1×10^{-17}	2.2×10^6	0	2.2×10^6	37
SO-C1	0.42	1.4×10^{-13}	8.5×10^{-14}	2.2×10^6	0	2.2×10^6	2.7
SO-C5	1.0	8.2×10^{-13}	1.2×10^{-12}	2.2×10^6	0	2.2×10^6	1.1
Adsolider 101	0.97	7.4×10^{-13}	2.3×10^{-13}	2.2×10^6	0.78	0.47×10^6	5.2
Carplex CS-5	2.0	3.1×10^{-12}	3.1×10^{-12}	2.0×10^6	0.66	0.68×10^6	1.8
Carplex CS-7	2.5	4.9×10^{-12}	4.7×10^{-12}	2.0×10^6	0.71	0.59×10^6	1.7

[a] True density is quoted from each catalog.

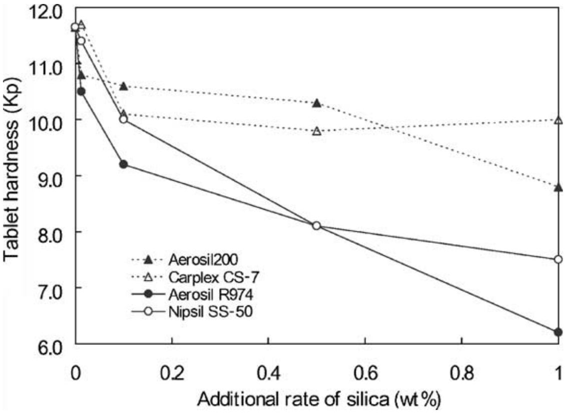

Fig. 4. Additional concentration of hydrophobic silica and hardness of unlubricated tablet. Aerosil R974 is nonporous silica and Nipsil SS-50 is porous silica. Aerosil 200 and Carplex CS-7 are also shown as comparison.

Coverage ratio of filler surface, when the additional concentration of silica is 1.0 wt.%, is summarized in Table 3. In the case of nonporous silica, particle size dominates surface coverage ratio, since porosity and true density are equal and negligible. Consequently surface coverage increase with the reduction of particle size. While in the case of porous silica, both porosity and true density differ from each sample. Therefore surface coverage ratio is not simply related to particle size.

Obtained surface coverage ratio and tablet hardness is plotted in Fig. 3. Tablet hardness logarithmly decreased with increase of surface coverage. Nonporous small particles that reveal high surface coverage significantly weaken the tablet hardness. This result corresponded to the hypothesis and it can be concluded that tablet hardness depends directly on coverage of silica over filler surface and on the geometric structure of silica particles.

Secondly, effect of hydrophobic samples on hardness was evaluated. Additional concentration of hydrophobic silica and tablet hardness is plotted in Fig. 4. The tendency that addition of silica deteriorates the tablet hardness was as common as hydrophilic silica, but the effect was more severe than that of hydrophilic silica. For example, Table 1 indicates that geometric structure of Aerosil 200 and Aerosil R974 is almost the same. However, tablet that contains 1.0 wt.% hydrophobic Aerosil R974 was 6.2 kp, compared to that of hydrophilic Aerosil 200 was 8.8 kp. Wada et al. (1989) investigated the effect of hydrophobic glass beads on tablet hardness and explained that decrease of hardness is related the reduction of adhesive ability of glass beads. Based on this report, it is considered that hydrophobic silica–filler affinity is weaker compared to that of hydrophilic silica–filler. From this result, it is determined hydrophobicity directly influences on tablet hardness and that hydrophobic silica severely decreases tablet hardness.

3.4. Hardness of lubricated tablet

Presence of magnesium stearate changes the effect of silica on tablet hardness. Opposite to unlubricated tablet, four in seven hydrophilic samples increased tablet hardness. Those samples are nonporous Aerosil 200 and three porous samples. This result corresponded to the previous study. Lerk et al. (1977) reported that addition of 0.2 wt.% Aerosil 200 suppressed the deleterious effect of magnesium stearate bonding. On the contrary to above four samples, the residual three nonporous samples have little effect and the tablet hardness was almost constant throughout up to 1.0 wt.%.

To clarify the mechanism to cause this difference, flowability of mixed powder was measured. Flowability of mixed powder has similar tendency to tablet hardness. Nonporous Aerosil 200 and all three porous samples had highly improved flowability, contrary to the residual three nonporous samples. In case of nonporous structure, effect of flowability is restricted only to small size silica, though all porous silica is effective regardless of particle size. This result also indicated that enhancement of flowability varies depending on the geometric structure of silica particles.

The coincident behavior between tablet hardness and flowability implies that enhancement of flowability and tablet hardness is correlated. Carr’s index of mixed powder and tablet hardness was shown in Fig. 5. Linear curve was obtained only regarding effective four samples and the residual three samples have no relation between hardness and flowability. Approximated liner curve was calculated based on these effective samples and depicted in the Fig. 5. Chang et al. (1999) described that higher flowability promotes compaction of powder bed and it is assumed

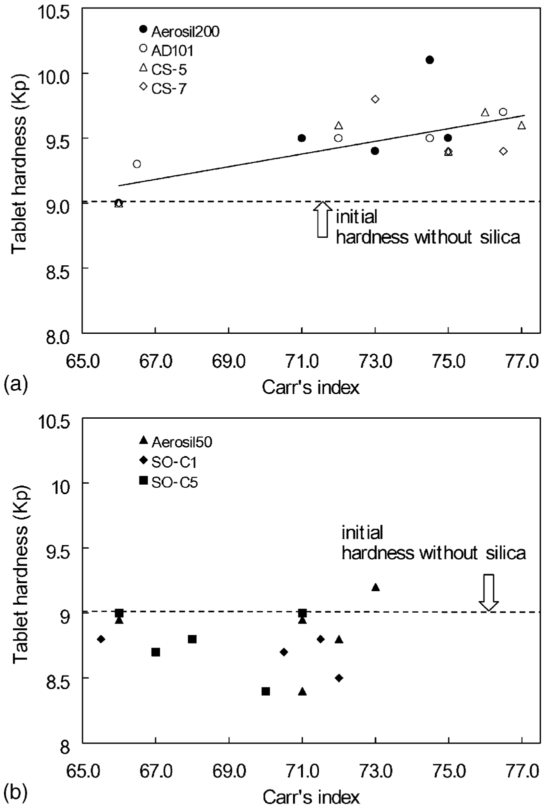

Fig. 5. (a) Relationship between Carr's index and tablet hardness. Tablet hardness increased proportionally to Carr's index particularly to Aerosil 200 and three porous samples, which were effective to increase tablet hardness. Approximated liner curve was calculated based on these effective samples and depicted in the figure. (b) The residual three were not related to Carr's index.

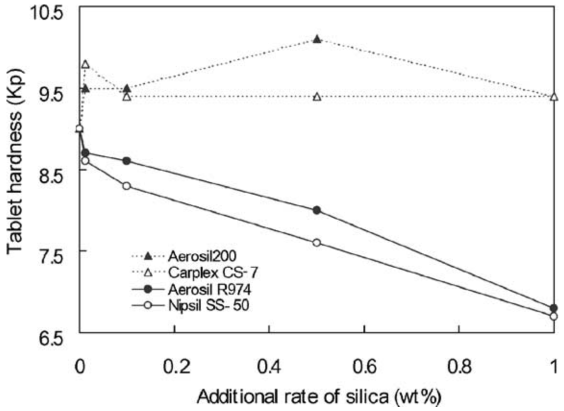

Fig. 6. Additional concentration of hydrophobic silica and hardness of lubricated tablet. Aerosil R974 is nonporous silica and Nipsil SS-50 is porous silica. Aerosil 200 and Carplex CS-7 are shown as comparison. Tablet was softened in proportion to the additional concentration, of which tendency was commonly observed in unlubricated tablet.

that increase of tablet hardness is due to the facilitated densification via addition of silica. However, this theory is only true for effective four samples and it remains questionable for other nonporous silica samples. In light of hydrophilicity shown in Table 2, surface wettability seems to have no impact on tablet hardness. Aerosil 200 is the least hydrophilic sample though it is one of the four effective silica samples. However, in other aspect, Aerosil 200 possesses ample capacity of water adsorption and it could be linked to the consolidation of tablet. Table 2 indicates that porous three samples and Aerosil 200 have higher water-retention capacity compared to the other three samples. It is widely known that moisture content is one of the fatal factors to determine the tablet hardness. Amidon and Houghton (1995) reported that significant changes in tablet were observed as the moisture level and water acts as a plasticizer. Therefore, it is considered that total amount of water adsorbed as well as moisture content is also related to the intensification of internal bonding.

In conclusion, addition of hydrophilic porous and small size nonporous silica is effective to increase tablet hardness, when added with magnesium stearate. It is considered that either flowability or amount of water retention capacity over silica surface is related to tablet hardness, and hydrophilicity has no direct effect. Enhancement of flowability is dependent on the geometric structure, and structural influence works to determine tablet hardness. However relation between flowability and hardness could not be fully resolved in this study and further investigation is needed.

Secondly, effect of hydrophobic sample was evaluated and shown in Fig. 6 in comparison with hydrophilic samples. Different from the case of hydrophilic silica, presence of magnesium stearate hardly had impact on tablet hardness. That is to say, tablet was softened in proportion to the additional concentration of hydrophobic silica, of which tendency was commonly observed in unlubricated tablet. Tablet hardness, which contains 1.0 wt.%, was converged ca. 7 kp as seen in unlubricated tablet. This means that hydrophobic silica does not suppress the deleterious effect of magnesium stearate and rather works like magnesium stearate itself, since hydrophobic silica–filler affinity is weaker to filler–filler affinity which has been mentioned above. Based on this result, it can be stated that hydrophobicity directly influences on the tablet hardness regardless of tabletting method.

4. Conclusions

Effect of geometric structure and surface wettability of glidant on tablet hardness was investigated by means of adding several kinds of silica into direct compressible fillers as glidant. With respect to hydrophilic silica, it is not hydrophilicity but geometric structure which has a decisive impact on tablet hardness both in unlubricated and lubricated tablets. In addition, amount of water adsorbed over silica surface is also related, when tabletted with magnesium stearate. On the contrary, hydrophobicity has a direct effect and hydrophobic silica weakens tablet hardness regardless of presence of magnesium stearate.

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