eye on excipients

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This edition of the column—a follow-up to John McCarty's three-part series on using silica in pharmaceutical solid dosage forms—focuses on Cab-O-Sil M-5P fumed silica [1, 2]. It cites the results of several laboratory tests to demonstrate how the excipient makes powder formulations flow better, thus improving tablet quality and manufacturability.

M-5P fumed silica is a high-purity excipient classified as a flow aid and glidant. It has a surface area of 200 square meters per gram and a bulk density of less than 60 grams per liter.

Its main function is to improve the flow of pharmaceutical powders and dietary supplements. It does this in three ways. It can act as a "spacer" between particles in the powder formulation, thereby reducing the attraction between particles and allowing the powder to flow more easily and clump less. Hydrophilic fumed silica can also act as a "sponge," absorbing moisture that would otherwise create liquid bridges between powder particles. This also improves powder flow. Last, fumed silica particles easily develop a negative electrostatic charge through friction (triboelectricity), creating a repulsive force between powder particles. That minimizes interaction between the particles, thus promoting powder flow.

TABLE 1

Correlation of angle of repose to powder flowability

Angle of repose (degrees)	Flowability
25-30	Very free flowing
30-38	Free flowing
38-45	Fair/passable flow
45-55	Cohesive
>55	Very cohesive

Source: Bodhmage, A. (2006). Correlation between physical properties and flowability indicators for fine powders. Unpublished doctoral dissertation, University of Saskatchewan.

During tablet and capsule manufacture, fumed silica prevents powder formulations from building up along the walls of hoppers. That, in turn, prevents irregular flow, agglomeration, and segregation, all of which impair productivity and quality. Its properties also ensure the powder flows as it should into the dies on the tablet press and/or into capsules, preventing the API from segregating from the excipients, which could create content uniformity issues and off-spec weights. Fumed silica also helps particles rearrange as they fill the die and during the early stages of compression, which enables them to form strong bonds to one another. Strong bonds prevent or reduce broken or chipped tablets, capping, and lamination. Fumed silica can also help in the spray drying process.

Powder flow

Angle of repose provides a useful correlation to powder flow properties. See Table 1.

To demonstrate how fumed silica improves flow, it was tested at differ-

FIGURE 1

Effect of M-5P fumed silica on the flowability of APAP, ibuprofen, and aspirin formulations at different use levels

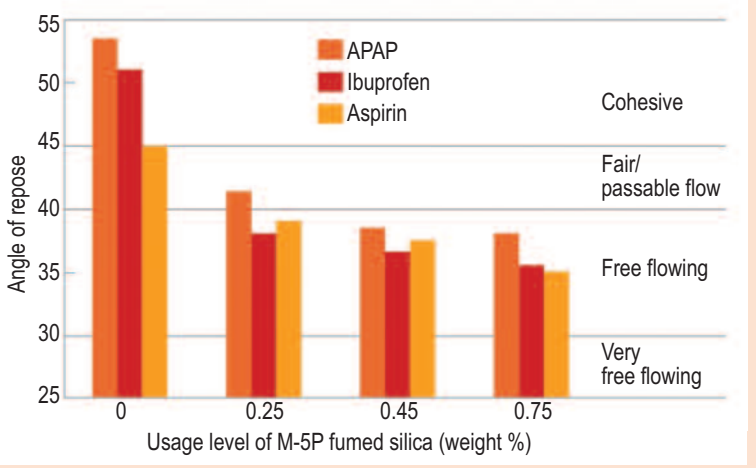
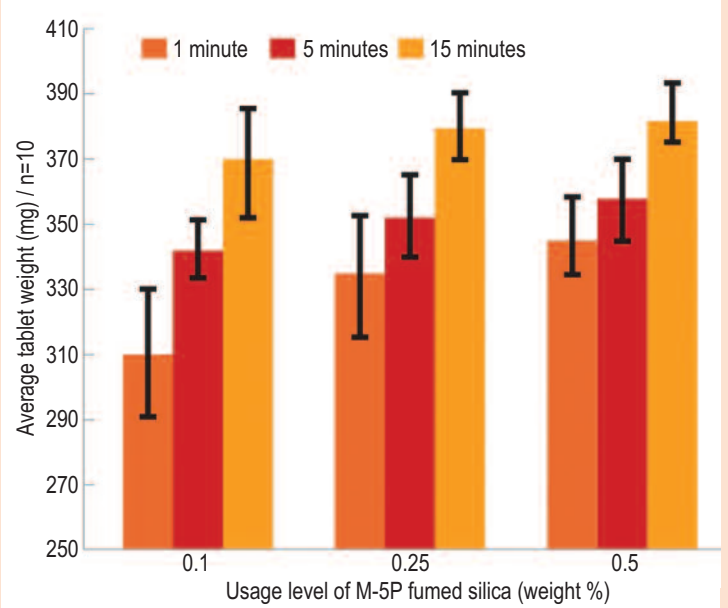


Figure 2

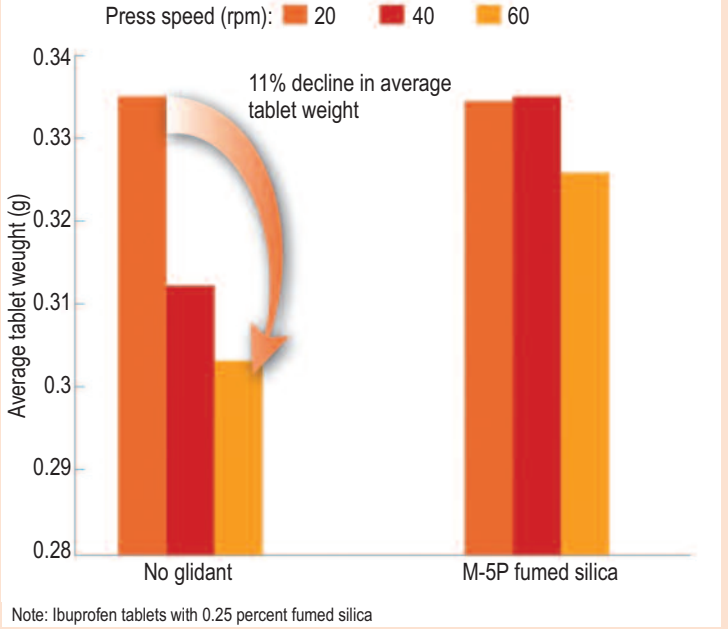
Effect of M-5P fumed silica on tablet weight at different use levels and mixing times



Note: Formulation includes 10 percent APAP and balance is lactose. Bars correspond to minimum and maximum tablet weight.

Figure 3

Effect of M-5P fumed silica and press speed on tablet weight



Note: Ibuprofen tablets with 0.25 percent fumed silica

ent use levels in formulations that included three different active pharmaceutical ingredients (APIs): acetaminophen (APAP), ibuprofen, and acetylsalicylic acid (aspirin). The results presented in Figure 1 show that as the use level of M-5P fumed silica increased, the flowability of all three powder formulations improved, going from "cohesive" to "passable flow" to "free flowing." Note: For highly hygroscopic materials or for materials that exhibit poor flow due to static charge, the amount of fumed silica required may increase by three to four times over what would otherwise be needed.

Die filling

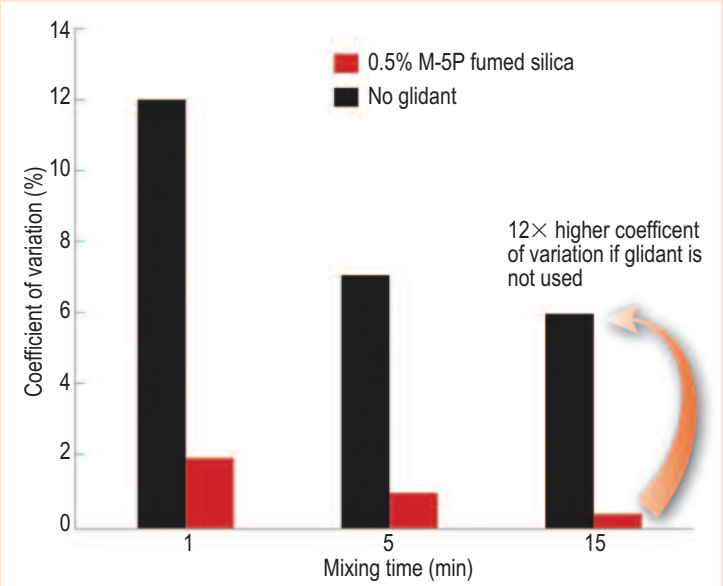
One requirement of manufacturing uniform tablets is getting the powder into the dies in a reproducible manner. For that to occur, the powder must flow reliably and not clump, bridge, or build up a static charge. Adding fumed silica to a powder formulation makes it flow better. It also allows particles to rearrange within the die during die filling and in the early stages of compression. Figure 2 illustrates that the average weight of APAP tablets correlates positively to the use levels of M-5P fumed silica in the formulation and the length of mixing time. (More consistent tablet weights indicate an improvement in die filling.)

The addition of fumed silica has also been shown to help tablet manufacturers produce high-quality tablets of uniform weight at higher tablet press speeds than would be possible without fumed silica. This improves productivity and throughput. As Figure 3 shows, without the addition of fumed silica, the average weight of ibuprofen tablets decreased by 11 percent when made at high production speeds. This indicates that the powder had difficulty filling the die cavity. In contrast, tablets made from a powder that included 0.25 percent M-5P fumed silica exhibited more consistent weights at high press speeds. Indeed, when ibuprofen tablets are made at high speed, the addition of fumed silica to the formulation has been shown to reduce tablet weight variation by 30 to 40 percent compared to the same formulation without it.

Furthermore, the addition of fumed silica has been shown to decrease the coefficient of variation of API content in a tablet batch. Tests showed that tablets made from a powder containing 0.5 percent of M-5P fumed silica—when mixed for 1, 5, and 15 minutes—had little variation in API content. Tablets made from the same powder mixed for 15 minutes—but without the addition fumed silica—had a coefficient of variation of 6 percent. That is 12 times higher than the variation

Figure 4

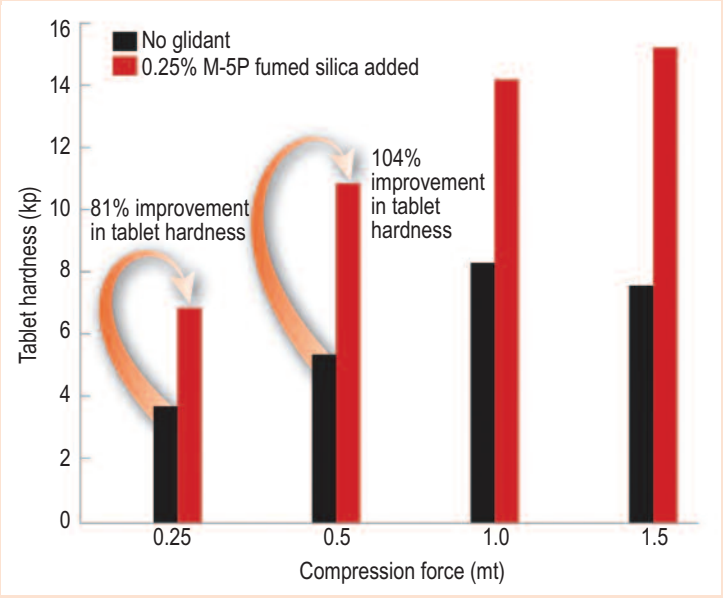
Effect of M-5P fumed silica on coefficient of variation of API in tablet formulations



Note: Tablets contained 10 percent APAP and 90 percent lactose or 10 percent APAP, 89.5 percent lactose, and 0.5 percent M-5P fumed silica.

Figure 5

Effect of M-5P fumed silica on tablet hardness at different compression forces



observed in tablets that contained fumed silica (Figure 4).

Compaction

The addition of fumed silica facilitates particle flow and rearrangement during the early stages of tablet compression, which can increase the bonding strength between particles in the tablet. This leads to better tablet/capsule compaction and higher tablet hardness at lower compression forces. Higher hardness can also add strength and prevent or decrease chipped, broken, capped, and laminated tablets. Tests showed that the addition of 0.25 percent of M-5P fumed silica to a powder compressed at 0.25 metric tons (mt) facilitated an 81 percent improvement in tablet hardness when compared to tablets formulated without fumed silica. When the compression force reached 0.5 mt, tablet hardness was shown to improve by 104 percent (Figure 5).

Spray drying

Spray drying is commonly used to microencapsulate ingredients, coprocess multiple ingredients, granulate formulations, and change the morphology and liquid state of materials. The addition of fumed silica to ingredients and formulations can help alleviate clogs in the spray dryer's atomizer. It can also decrease the amount of product that sticks to the walls and thereby increase throughput. It has also been shown to improve the drying profile of tacky materials and to serve as a nucleation aid. *T&C*

References

1. CAB-O-SIL is a registered trademark of Cabot Corp.

2. John McCarty's columns appeared in the January, March, and April issues of 2015. They're available at www.tabletscapsules.com.

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