



Applications of CAB-O-SIL® M-5P Fumed Silica in the Formulation and Design of Solid Dosage Forms

Introduction

Glidants are excipient materials that are added to tablet formulations to improve the flow properties of a granulation from the hopper into the feed mechanism and, ultimately, into the tablet die. CAB-O-SIL® M-5P fumed silica is a white, free-flowing powder of extremely high purity. It is widely used as a glidant in tablet and capsule formulations. The basic physical and chemical properties of CAB-O-SIL M-5P are discussed in the scientific report, *Properties of CAB-O-SIL® M-5P Fumed Silica*.¹ The impact of CAB-O-SIL M-5P on tablet properties is presented in this scientific report.

Hardness and Tensile Strength

The failure of some powders to compact favorably when compressed into tablets is often due to the amount of pressure which can be safely applied to the compacts and to the distribution of the forces within the compact itself. In addition, the presence of lubricants or glidants in a formulation will affect the strength of the compacts.² In the production of tablets, glidants are added to the granulation to be compressed, in order to improve flow; lubricants are added to reduce friction between the tablet granulation and the die wall during compression and ejection of the tablet. Lubricants and glidants are present by necessity in most pharmaceutical solid dosage formulations and are predominantly hydrophobic in nature. Their presence in the formulation will generally produce weakened bonding between host particles, since strong bonds are formed between clean surfaces.

To investigate the influence of the time of mixing and the concentration of CAB-O-SIL M-5P on tablet hardness, acetaminophen (APAP) tablets containing 50% microcrystalline cellulose (Avicel® PH 101) were compressed. As the time of mixing increased, there was an increase in the

hardness of the tablet compacts (Figure 1). It is also interesting to note that as the level of glidant in the granulation was increased from 0.1% to 0.5% CAB-O-SIL M-5P, the hardness of the tablets increased. The addition of a lubricant or a glidant to host particles or granules generally results in a weakened tablet since the additive functions as a contaminant on the granule surface to interfere with bond formation. The results in Figure 1 clearly demonstrate that the addition of the fumed silica (colloidal silicon dioxide) to the APAP:Avicel PH 101 granulation caused an increase in bond strength, and after 15 minutes, the CAB-O-SIL M-5P was distributed evenly over the surface of the larger particles in the granulation.

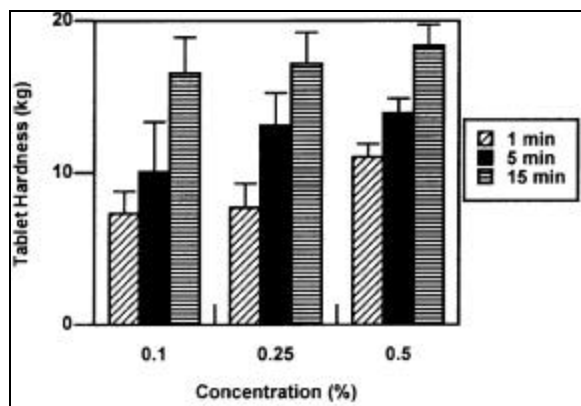


Figure 1

Influence of mixing time and the concentration of CAB-O-SIL M-5P on the hardness of acetaminophen tablets (n = 10)

The influence of CAB-O-SIL M-5P and magnesium stearate on the tensile strength of compacts of anhydrous lactose is illustrated in Figure 2. Both CAB-O-SIL M-5P and magnesium stearate have been widely used as glidants. There was a trend towards stronger compacts when the lactose was blended with the CAB-O-SIL M-5P and a decrease in the tensile strength with magnesium stearate present in the formulation. Previous studies had also demonstrated this

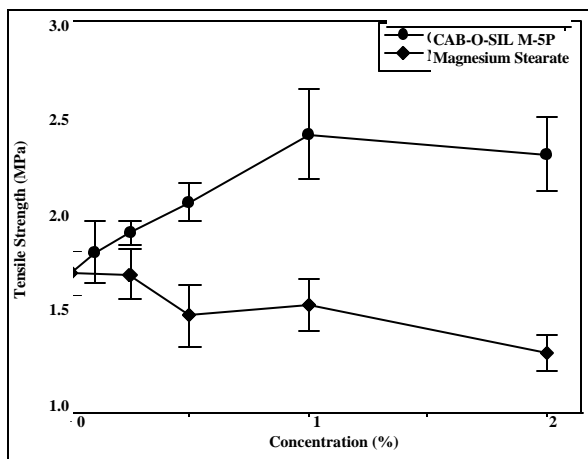


Figure 2

Influence of glidant concentrations on the tensile strength of lactose compacts (solid fraction = 0.8 and mixing time = 15 min)

increase in the tensile strength of lactose tablets upon the addition of 1% fumed silica.³ A similar trend for the magnesium stearate was previously reported by Williams and McGinity for compacts containing either microcrystalline cellulose or sodium sulfathiazole with the magnesium stearate.² Weaker compacts were formed and a decrease in the bonding index was seen as the level of magnesium stearate in the compact was increased.

Piracetam undergoes plastic deformation during compression. Van Aerde and co-workers⁴ reported a dramatic reduction in the mechanical strength of piracetam tablets in the presence of magnesium stearate. However, they reported an increase in the tensile strength of piracetam tablets when fumed silica was present in the compacts. By incorporating the fumed silica before the lubricant, the increase in tensile strength of the piracetam tablets was unaffected by the addition of magnesium stearate.

Tablet Weight and Content Uniformity

Uniform tablet weights and uniform doses of active ingredients, as well as production rate, are dependent on the ability of particulate matter to feed into the dies in a reproducible manner.⁵ Glidants are added to the formulation in order to improve the flow properties of the material and

to aid particle rearrangement within the die during the early stages of compression. Formulations that flow evenly into the die cavity during the tableting operation will result in uniformity in tablet weight and drug content. Figure 3 demonstrates that the weight of acetaminophen tablets will be influenced by both the concentration of CAB-O-SIL[®] M-5P in the formulation as well as the time of mixing. Uniformity in tablet weight was achieved after 15 minutes of mixing. An ordered powder mixture was then formed with the fine component having sufficient

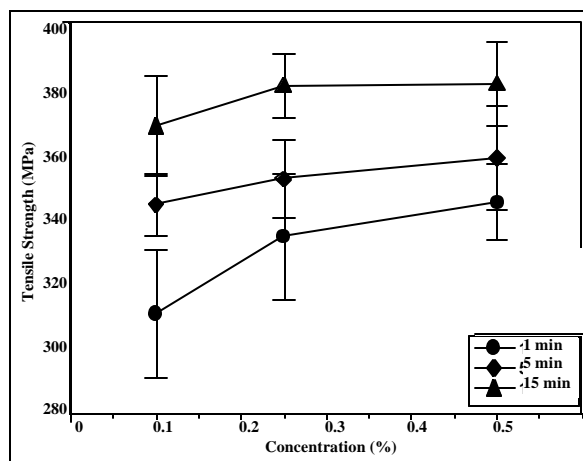


Figure 3

Influence of mixing time and concentration of CAB-O-SIL M-5P on the weight of acetaminophen tablets (n = 10)

intrinsic cohesiveness to adhere to the surface of the granules of the APAP.

Augsburger and Shangraw⁵ had previously reported in their manuscript, entitled "Effect of Glidants in Tableting," that CAB-O-SIL M-5 was the most effective glidant in terms of overall performance of the materials tested. They reported that CAB-O-SIL M-5 was found effective in concentrations as low as 0.1% by weight when added to microcrystalline cellulose and showed an optimum glidant activity at a concentration of about 0.5% by weight.⁵ Their studies showed that no increase in glidant activity was observed with concentrations higher than 0.5% by weight in the tablet formulations.

The data in Figure 4 are in agreement with previously published results⁵ and demonstrate that

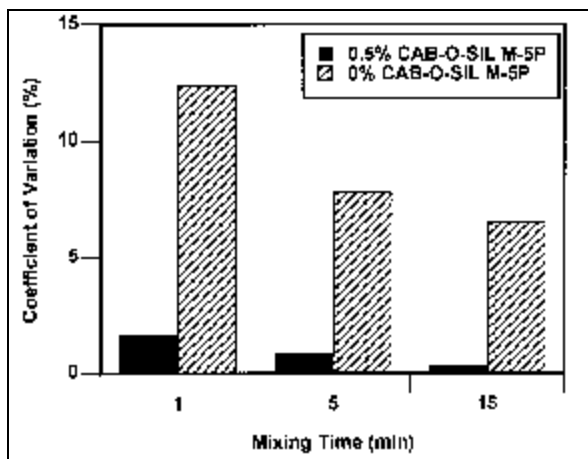


Figure 4

Influence of mixing time on the coefficient of variation of acetaminophen in tablets containing either 0.5% or 0% CAB-O-SIL M-5P (n = 6)

the presence of CAB-O-SIL M-5P in a tablet formulation will decrease the coefficient of variation of drug content in a batch of tablets. The longer mixing times for tablet formulations with or without the CAB-O-SIL® M-5P caused a decrease in the coefficient of variation. However, very low variations in drug content were observed with acetaminophen tablet formulations containing 0.5% CAB-O-SIL M-5P after blending for 15 minutes. These tablets contained 10% drug, 89.5% lactose and 0.5% CAB-O-SIL M-5P. The tablet formulation without the glidant contained 90% lactose. Varthalis and Pilpel⁶ demonstrated in their studies that the efficiency of the glidant in a tablet formulation was influenced by the hydrophilic nature of the surfaces of the glidant and the host powder or granulation. The extent to which CAB-O-SIL M-5P adhered to and coated the surface of a powder was influenced by the chemical property of the powder mixture. These studies indicated that since the chemical surface of fumed silica was hydrophilic in nature, it was more compatible with the hydrophilic surface of materials such as lactose and acetaminophen. The flow properties were superior to other more hydrophobic materials such as oxytetracycline.

Dissolution Studies

Monkhouse and Lach⁷ successfully increased the dissolution rates of poorly soluble drugs by adsorbing the active ingredient onto CAB-O-SIL

M-5P. The adsorbents had a higher surface area of drug in contact with the dissolution medium. This was accomplished by equilibrating the drug in an organic solvent with the fumed silica and evaporating the mixture to dryness. Rapid dissolution of indomethacin and aspirin was reported by these authors. Micronization of hydrophobic drugs to reduce particle size and increase surface area will increase the cohesive energy of particles which may result in clumping or aggregates to form when in contact with an aqueous medium. Powder adsorbates of drugs and fine carrier materials can be formulated to circumvent such problems. CAB-O-SIL M-5P will adsorb moisture readily. It has the ability to scavenge water in formulations that are moisture sensitive and may also function as a wicking agent in higher concentrations.

The addition of glidants and lubricants to tablet formulations to improve flow and to decrease die wall friction in the die will influence tablet properties, including disintegration and drug dissolution. During the final blending steps, these adjuvants will coat the surface of the granules, which influences the bonding between them. The relative hydrophilic and hydrophobic properties of adjuvants will impact the wetting of the tablets by the dissolution medium. The influence of CAB-O-SIL M-5P and magnesium stearate in theophylline tablets containing 20% drug, 75% anhydrous lactose and 4% starch 1500 on the dissolution of theophylline is shown in Figure 5. Tablets of three different hardness levels were prepared and the release properties, as shown in Figure 6, were studied in 900 ml of purified water at 37°C and agitated at 50 rpm in the U.S.P. Method II apparatus. The release profiles for theophylline tablets containing the magnesium stearate were significantly lower at all time periods when compared with the tablets containing the fumed silica.

The slow release from the tablets containing the magnesium stearate was due to the more hydrophobic properties of this material, when compared to the more hydrophilic properties of the CAB-O-SIL M-5P. The CAB-O-SIL M-5P containing tablets were harder and less friable. The inclusion of a suitable disintegrating agent

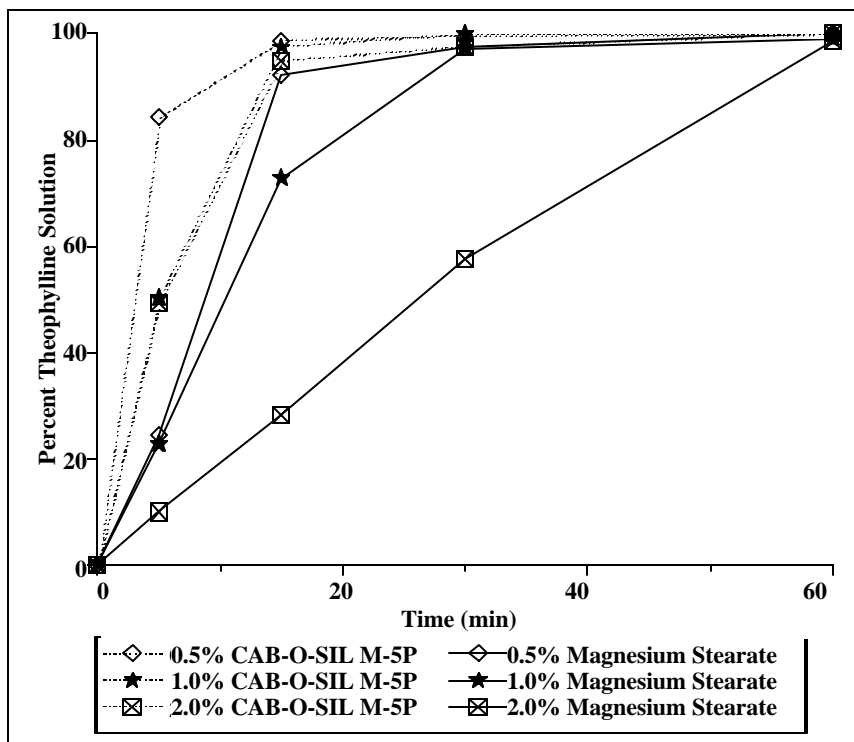


Figure 5

Influence of glidant concentration on the dissolution rate of theophylline from tablets (hardness = 11 kg) in purified water maintained at 37°C using the U.S.P. paddle method (n = 6)

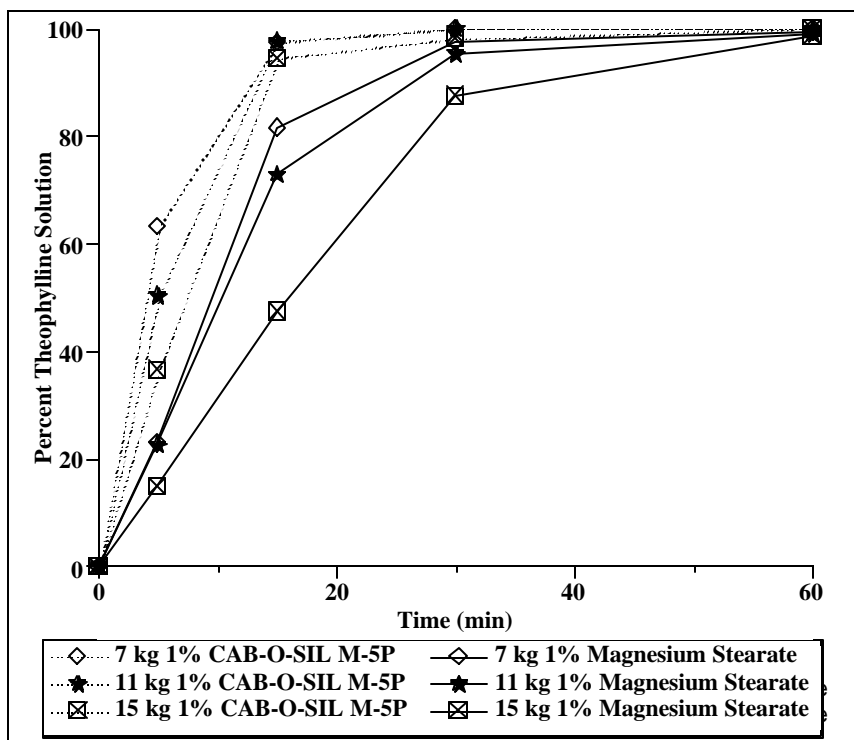


Figure 6

The influence of tablet hardness on the dissolution rate of theophylline from tablets containing 1% CAB-O-SIL M-5P or 1% magnesium stearate in purified water maintained at 37°C using the U.S.P. paddle method (n = 6)

will allow the formulating scientist to optimize not only the mechanical properties of the tablet but also the dissolution profiles of the drug.

Summary

The inclusion of CAB-O-SIL® M-5P in tablet formulations will improve tablet properties including **hardness**, **weight uniformity** and **drug content uniformity**. Reports in the literature have demonstrated that this hydrophilic glidant will contribute to the **tensile strength** of tablets in the normal range of use, 0.1–1% by weight. For most applications, a concentration of 0.5% CAB-O-SIL M-5P appears to be optimal. For hygroscopic material or granulations that exhibit poor flow due to static charge problems, the level of CAB-O-SIL M-5P may need to be increased to 1%. Due to its hydrophilic chemical structure, CAB-O-SIL M-5P will act as a **scavenger of moisture** and help stabilize drugs that require an acidic pH for **optimal stability**. The use of CAB-O-SIL M-5P can overcome hydrolytic degradation in the presence of magnesium stearate for drugs such as aspirin. Gore and Banker reported that colloidal fumed silicas are well known for their large surface areas and highly polar silanol surfaces which favors **water vapor adsorption**.⁸ Solid state stabilization of drugs has been studied by numerous authors. El-Shattawy and co-workers investigated the stability of ampicillin,⁹ erythromycin¹⁰

and cephalexin¹¹ in the presence of several commonly used tablet excipient materials. These studies using differential scanning calorimetry demonstrated that CAB-O-SIL® M-5P was found to be **compatible** with all three antibiotics.

CAB-O-SIL M-5P has been widely used as a **thickening agent** and **stabilizer** in liquid and semisolid formulations.

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