eye on excipients

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This edition of Eye on Excipients discusses direct-compression tableting and describes the benefits and limitations of two direct-compression lubricants.

To form a durable compact in a direct-compression tableting process, you must physically compress, under relatively high pressure, a homogenized blend of powders, including any active pharmaceutical ingredients (APIs) and any excipients necessary to the tablet's function or suitable manufacture. The term "compaction" describes the process of forming a solid tablet out of powder, while the term "compression" describes the powder's reduction in volume during compaction.

The typical direct-compression tableting process consists of the following unit operations: screening, weighing, blending, lubricant blending, and compaction, followed by testing to ensure the tablet's robustness and intended functionality. The process is easy to explain conceptually, but in practice it can be difficult to manufacture robust tablets that provide for all intended functionalities.

In addition to the API(s) tablet manufacturers employ numerous excipients to help give the tablets the desired qualities. Excipients include but aren't limited to diluents, dry binders, sustained-release ingredients, glidants, anti-adherents, pH modifiers, disintegrants, colors, sweeteners, flavors, delayed-release ingredients, preservatives, dissolution adjuvants, and lubricants.

In practice, these ingredients can either contribute to or inhibit the formation of the physical bonding that occurs during the compaction event. Those excipients that contribute to physical bonding during compaction increase tablet hardness, while those ingredients that inhibit physical bonding during compaction reduce tablet hardness. Pharmaceutical manufacturers nearly universally recognize tablet lubricants as reducing the amount of bonding that occurs during compaction, which can lead to a loss in overall tablet hardness, thereby reducing tablet robustness.

Tablet compaction

The compaction portion of the direct-compression unit operation consists of a homogeneous powder blend being gravity-fed into a feed frame or fluidized feeder located on the tablet press' die table. This powder is aspirated into the die cavity when the die and lower punch pass below the feed frame and the punch is drawn downward along the fill cam.

The height of the weight-adjustment ramp determines the amount of powder the press will draw into the die, and therefore, the tablet weight. The aspirated powder contained in the die and resting on top of the lower punch proceeds along the tablet press toward the precompression roll. If engaged, the precompression roll reduces the volume of the powder in the die by applying a relatively light compression that typically expels air from the powder blend.

Subsequently, the powder inside the die travels to the main compression roll, which places a relatively large amount of pressure on the powder blend. This large-magnitude pressure results in significant compression—volume reduction—and significant compaction—bond formation—and forms a durable tablet within the die. Once formed, the tablet travels to the ejection cam, which elevates the lower punch along an angle and ejects the tablet from the die so it can be collected.

Tablet lubricants

A critical excipient during the ejection process is the lubricant. In fact, for the majority of tableting blends, if no lubricant is included, the tablet press will eventually seize due to material building up on the die walls. Also, without a lubricant in the blend, the tablet would undergo extremely high ejection forces due to friction between the tablet and the die wall. High-pressure ejection can harm the press and damage the tablet by weakening or destroying the bonding that occurred during compaction.

While lubricants are necessary, they can negatively impact tablet functionality and durability. Lubricants are hydrophobic and tend to prolong disintegration and dissolution times and inhibit bonding between other ingredients during compaction. This is particularly true

for magnesium stearate, which is the most widely used tablet lubricant due to its efficiency in reducing ejection force and maintaining clean punch surfaces. Compounding these issues, magnesium stearate is a surface-acting lubricant, which means that it lubricates by spreading over the particle surfaces of other tablet ingredients, which can inhibit bonding and repel the water required for tablet disintegration and dissolution.

In contrast, a less widely used tablet lubricant, hydrogenated vegetable oil Type I (HVO), functions in the free fraction, which means it doesn't spread over ingredient particle surfaces during blending. This reduces its inhibition of bonding and disintegration and dissolution, yet its presence at the die wall and punch surfaces still decreases ejection force and helps keep the tooling free of material buildup.

HVO isn't as effective in keeping punch surfaces clean during compaction as magnesium stearate, but you can use it alone as a lubricant when other tablet-blend components don't require surface lubrication.

HVO's real benefit comes when used in conjunction with magnesium stearate. This combination allows you to reduce the amount of magnesium stearate in a blend by adding HVO, which can improve tablet durability, disintegration, and dissolution. In addition, the compaction mechanism of HVO increases tablet hardness, independent of increases in tablet hardness due to its nonspreading lubrication behavior. These qualities make HVO a very rare breed of excipient: a lubricant that is also a dry binder.

Tablet dry binders

Typically, you can classify tablet-blend components into three categories by their compaction mechanisms: brittle fracture, elastic recovery, or plastic deformation. In practice, excipients can exhibit more than one compaction mechanism, but it's common for one mechanism to be dominant.

Excipients that compact by brittle fracture tend to crumble under compression pressure into smaller units, exposing new surfaces for compaction. Excipients that exhibit elastic recovery tend to reduce in volume under compression but recover or bounce back upon removal of the compression pressure. This tends to reduce tablet durability, as this recovery typically results in a loss of bonding energy and can break bonds that have formed during the compaction cycle. In contrast, plastically deforming materials yield to compression pressure and readily reduce in volume without recovery after the compression pressure is removed. Plastically deforming excipients act as glue for the tablet, generally increasing tablet hardness and often reducing tablet friability.

HVO is highly plastically deforming and can actually increase tablet hardness as much as or more than industry-standard dry binders, such as copovidone and hydroxypropyl cellulose, while simultaneously providing free-fraction lubricating properties that those excipients don't exhibit. *T&C*

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