early as possible; compaction issues such as tablet hardness or friability can often be alleviated simply by switching to a more appropriate grade of the same material.[10,13] In addition, apparently equivalent materials sourced from different manufacturers can also differ in their properties and it is therefore essential that excipients obtained from alternative suppliers are evaluated before any changes are adopted.[10,12]

It is also important that potential polymorphic changes during processes such as compaction or wet granulation are monitored as the properties of some excipients such as mannitol may change drastically as a result of polymorphic changes occurring during processes such as wet granulation.[16]

Excipients to enhance the lubrication of oral solid dosage forms

Most tablet formulations require the addition of a lubricant (generally added in powder form) to reduce friction at the interface between the powder or granule and the metal surfaces of the die wall during tablet formation and ejection. The addition of a lubricant can also prevent sticking of tablets to the punch face, reduce wear to tablet or capsule tooling, and improve flow and filling properties. Lubricants are often added to capsule blends to reduce adhesion to metal surfaces and reduce the force required to eject the formed capsule powder 'plug' into the capsule shell.[9] Lubricants are usually added at the end of the blending process, but where a dry granulation step is required, a proportion of the lubricant is added prior to granulation to prevent sticking to the rollers.

There are two basic mechanisms for the action of lubricants: either by the formation of a continuous 'liquid film', which separates the tablet and powder surfaces, or by means of 'boundary lubrication', where lubricant particles form a continuous or noncontinuous resistant layer on the metal surfaces or the powder or granules. Boundary lubrication is more common in pharmaceutical dosage forms.

A wide range of materials have found employment as lubricants in pharmaceutical formulation as shown in Table II.[17,18]

Table II: Classes of Materials used as Lubricants in Pharmaceutical Solid Dosage forms.

Chemical Class	Examples	Typical levels used
Metallic salts of fatty acids	Magnesium stearate; aluminium, calcium and sodium stearates	0.5–1.0%
Fatty acids, hydrocarbons and fatty alcohols	Stearic acid; palmitic acid; stearyl alcohol	2.5%
Fatty acid esters	Glyceryl behenate; glyceryl monostearate	2.0–4.0%
Polymers	Polyethylene glycols; polytetrafluoroethylene	1.0–4.0%
Others	Hydrogenated castor oil	0.5–2.0%
	Hydrogenated vegetable oil	0.5–2.0%
	Sodium stearyl fumarate	0.5–1.0%

Magnesium stearate, which works as a boundary lubricant, is the material most commonly used in both tablet and capsule formulations. Magnesium stearate possesses a number of appropriate physical properties including a small particle size, high surface area and melting point, and a low affinity for tooling and die surfaces, which result in low coefficients of friction and low shear stresses.[19] However, the hydrophobic nature of magnesium stearate, together with its low shear strength, mean that excessive blending may lead to the generation of a 'waterproofing' layer over powder particles, which can inhibit the wetting and dissolution of the eventual dosage form. This magnesium stearate layer also inhibits bond formation during tablet compression; hence overblending can also lead to reduced tablet strength. Special attention should therefore be given to the amount of blending experienced by formulations containing magnesium stearate, not only during blend preparation but also whilst the powder passes through the various hoppers, feed tubes and other surfaces of the processing equipment.

Other stearic acid salts have also been used, however these all have the same potential for adverse effects on tablet hardness and wettability.[17] Fatty acids, hydrocarbons, and fatty alcohols are less effective lubricants than magnesium stearate but do not carry the same risk of overlubrication. Stearic acid is the most commonly used material in this category and is typically added at levels of 2.5%. The hydrophilic nature of sodium stearyl fumarate means that even though it is a boundary lubricant, its use does not attract the same risk to wettability as that of magnesium stearate and it can be used as a replacement where dissolution or tablet hardness effects are a concern.[19] Glyceryl behenate, glyceryl stearate and hydrogenated vegetable oil are examples of liquid film lubricants which function by melting under pressure and are generally added at levels of 2.0–4.0%; of these, glyceryl behenate is the most commonly encountered. Other materials, such as colloidal silicon dioxide, starches, and talc, have also been shown to improve the lubrication of oral solid dosage forms.[18]

Excipients to enhance the disintegration of oral solid dosage forms

Disintegration, whereby a tablet or capsule breaks down into granules or aggregates is the first step in the dissolution of an immediate release formulation. The solubility and particle size of the API will naturally exert a large influence over drug dissolution, but excipients can also exert either a positive or negative effect by virtue of their solubility, wetting or wicking ability. Water soluble, hydrophilic excipients such as lactose or mannitol will naturally assist in wetting and dissolution. Conversely, dibasic calcium phosphate dihydrate, which is insoluble, nevertheless has a very low contact angle and will promote rapid fluid penetration into the dosage form.[11] MCC is also insoluble but has a very high intraparticle porosity, which promotes fluid penetration by means of capillary action; this and the disruption of hydrogen bonds as a result of wetting promote swelling and tablet disintegration.[12] Wetting can also be promoted by the inclusion of low levels (typically $\leq$1%) of solid surface active agents or surfactants at the blending stage. Careful attention should be paid to the regulatory acceptability of these materials and there is some evidence that sodium lauryl sulfate may hinder the dissolution from capsules in acidic media and reduce tablet hardness.[20]

To ensure effective disintegration of solid dosage forms in solution, it is usually necessary to add an excipient specifically designed to act as a disintegrant. Maize starch has a long history as a disintegrant due to its ability to promote water uptake but its prominence, particularly in tablets, has been largely superseded by the advent of the 'superdisintegrants'. These materials, which are generally added at levels up to approximately 8%, fall into one of three main types: modified starches such as sodium starch glycolate, crospovidones e.g. *Polyplasdone XL*, or modified celluloses such as croscarmellose sodium and low-substituted hydroxypropylcellulose (L-HPC). Superdisintegrants draw water into the tablet by capillary action then swell to force the tablet apart by exerting internal pressure.[21] This mode of action means that in the case of capsules, where the powder fill is only lightly compressed, it may be necessary to increase the level of disintegrant used.

The water uptake and swelling capacity of disintegrants containing ionisable materials have been shown to be reduced in acidic solution. However, crospovidone is nonionic and so its mode of action may be less affected by the pH of the dissolution medium.[22] The efficacy of a disintegrant should be assessed in the context of the complete formulation, as the solubility of other