The Effect of Core Design and Formulation on the **Quality of Film Coated Tablets**

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The Effect of Core Design and Formulation on the **Quality of Film Coated Tablets**

This article examines the importance of core design and formulation on the quality of a film coated tablet.

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Tablets are by far the most popular dosage form when administering drugs to patients, and a large proportion of the tablets produced around the world are film coated. Coating is applied for a variety of reasons such as aesthetic appearance; identification and branding; taste or odour masking; enhanced mechanical strength; and protection from moisture, light and/or air.

With the current awareness of health, safety and environmental problems, aqueous film coating is a process that is routinely employed in the preparation of pharmaceutical solid dosage forms. The success of this process is determined by three factors: formulation of the coating system, coating process parameters and tablet core. During the last 20 years, there has been significant research into coating formulations and processes. In focussing on these areas, less attention has been paid to issues that relate to the preparation of a suitable tablet or substrate. This article will highlight the importance of core design and formulation on the quality of a film coated tablet

Tablet Design

The benefits of film coating more than justify the exposure of the product to the rigour of the coating process, during which the tablets (and the applied coating) are constantly subjected to mechanical stress along with conditions of elevated temperature and humidity. Therefore, cores must be designed using more stringent criteria compared with uncoated dosage forms to guarantee a product robust enough to withstand the additional stress imparted by the film coating process. The design of such a substrate has to be considered in terms of:

- The ability of the core to withstand the mechanical stress of the process.
- Maximized adhesion of the coating to the tablet surface, especially when a logo is present.
- A film coat with uniform thickness.

Tablet shape. Tablet shape is a very important factor for successful film coating. There are many examples where an inappropriate core design has been implicated in coated tablet quality problems.

Unfortunately, the lack of published information documenting these situations means that newcomers to film coating rarely have access to this experience.

Figure 1 shows the surface hardness across the crown of differently shaped tablets.[1] Flat-faced and shallow concave tablets have relatively high overall surface hardness, but tend to be brittle at the edges. The deep concave and ball-shaped tablets have good mixing characteristics, but offer the lowest levels of mechanical strength, particularly at the crown.

Flat-, shallow/deep concave-, ball/caplet-shaped tablets are not the best choice for film coating. Figure 2 illustrates areas on the tablet that have the highest erosion potential. Therefore, normal concave is the preferred shape for film coating.

During critical stages of the drying process, usually immediately after deposition of the coating onto the tablet surface, coating systems become extremely viscous and adhesive. As a result, if tablets exhibit large areas of relative 'flatness' on their surfaces, it is possible for them to become bonded together. This situation is prevalent when attempting to coat flat-faced or caplet-shaped tablets (Figure 3). Placing even a very subtle amount of curvature on an otherwise flat surface can minimize twinning problems.

Wilson and Crossman studied film uniformity on tablets of varying shape (capsule, large oval, small oval and round). For each shape, film thickness was measured on the 'face', 'edge' and 'end' (Figure 4).[2] The authors found a significant film thickness difference depending on the area of the tablet surface that was measured. In all cases, the face showed greater thickness than the edge or the end of the core. However, for the round tablet, there was a similarity in film thickness between the face and the end. For all shapes, film on the edges had the lowest thickness compared with the face and the end of the tablet. For an aesthetic or colour coating this may not be a serious issue. The low film thickness on the edges and the ends may however cause serious problems if a modified release or functional coating is applied. In those cases, the round shape would be preferred to reduce the chance of premature film failure.

Tablets with a logo. For tablets with a logo, the design and placement are very important. Figure 5a shows a tablet with an erosion area between the letters in the engraving. The tablet had excellent mechanical strength and friability. However, erosion occurred during the film coating process. Looking at a side view of the uncoated core, a very narrow area was found between the letters, which had higher prominence than the main face of the tablet surface. The tooling manufacturer was contacted and a new design for the tablet was developed that had a broader flatter logo engraving (Figure 5b). This modification to the punch faces eliminated the weak areas on the tablet surface that were prone to attrition. With the new tooling design, the erosion problem was solved.

The design of a logo for film coated tablets has more restrictions than for uncoated tablets. The angle and depth of cut into the tablet surface must allow for the uniform deposition of coating material throughout the engraving. If the cut

Figure 1 Indentation hardness profiles for tablets of different shape.

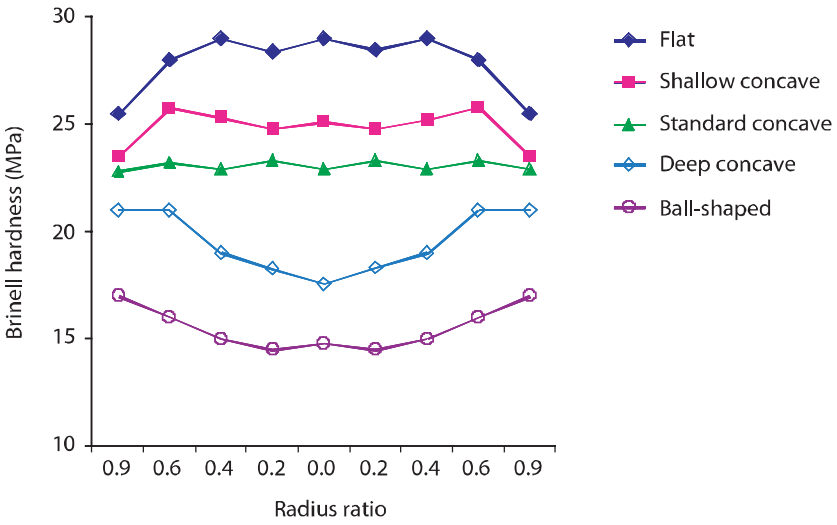
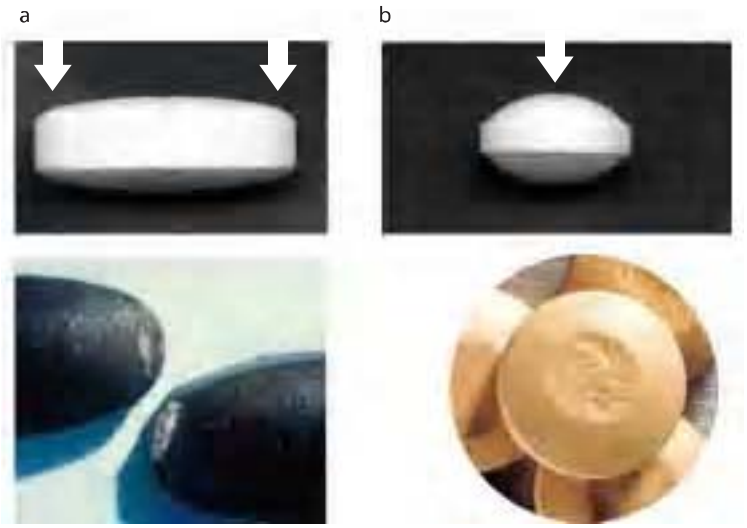


Figure 2 Areas most prone to surface erosion for (a) flat, shallow concave, caplet-shaped; and (b) deep concave tablets.



is too narrow, the applied film may 'bridge' over the logo and compromise the clarity.[3] Therefore, cores destined to receive a coating will have lettering that is less severely angled, wider and shallower than the lettering on uncoated tablets.

There are also restrictions on the maximum area for logo placement depending on the shape and curvature of the tablet surface. The usable area for logo placement becomes much smaller as the surface curvature increases. After establishing the maximum identification area, the next step is to locate the required logo within the confined area. Inappropriate location of the identification (i.e. in a potentially soft zone of the tablet crown) may increase erosion problems. All this information should be taken into account when designing punches for tablets with engraved identification.

The presence or absence of a logo is particularly important in the case of tablets with functional coatings. Enteric-coated tablets are considered to be some of the most complex products to develop because of concerns over film uniformity and potential defects.[4] This is why, traditionally, in most cases logos are avoided and printing is used.

Down *et al.* reported drug dissolution failure caused by pinhole defects in the enteric coating.[5] These defects were observed primarily in the engraved logos on the tablet faces. The problem was resolved by switching to plain-faced cores. However, a recent study by Cunningham *et al.* demonstrated that careful selection of tablet shape, logo design and placement would result in a robust enteric coating.[6]

Tablet Formulation

The formulation of a robust tablet has to be considered in terms of:

- The ability of the core to withstand the mechanical stress of the process.
- Maximized adhesion of the coating to the tablet surface, especially when a logo is present.
- A smooth film coat with uniform thickness.
- The stability of the final coated dosage form on storage.

Tablet mechanical strength and friability. The tablets being coated and the applied coating are constantly subjected to mechanical stress. Tablet breakage and surface erosion are typically seen when the mechanical strength and friability of the tablet core are inadequate. The problem can worsen during scale-up because of the increased weight of tablets charged into the coating pan. This situation may occur after product approval, because the use of ever-increasing pan sizes is not uncommon as product sales increase. Therefore, any product that is performing poorly with respect to mechanical strength on the laboratory scale should not even be exposed to the scale-up process.

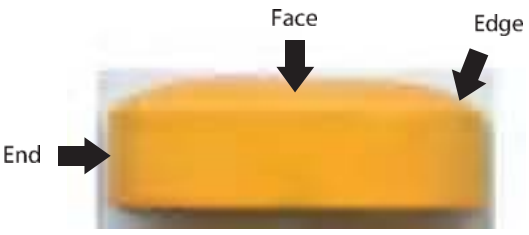
It is extremely difficult to create generalized guidelines defining the physical attributes of a robust tablet that is acceptable for use in a coating process because so much depends on the materials that are being used. Tablets with relatively low breaking force values should be dealt with much more carefully if they are to be coated, particularly during scale-up. Large tablets, such as multivitamin cores, may need to have greater mechanical strength values compared with smaller tablets.

A measure of equal or perhaps greater importance in terms of tablet robustness is friability. This test more accurately reflects the stresses that tablets will encounter when tumbling in a coating pan. Tablets to be film coated should have a maximum friability value of 0.3% and preferably less than 0.1%. This guideline should be adhered to regardless of tablet size or shape.

Drug and excipient particle characteristics can also have a significant affect on the success of film coating. Figure 6 demonstrates a situation where tablet chipping occurred during the coating process because of the presence of large drug crystals. This chipping resulted in small areas of the coating being very thin compared with the rest of the tablet. Variations in coating thickness may present a serious problem when

Figure 3 Twinning during the coating process for (a) flat-faced and (b) caplet-shaped tablets.

Figure 4 Measurement points of film thickness across the tablet surfaces (n=5).



the properties of the film are dependent on its thinnest part, particularly in the case of modified drug release coatings. In this particular scenario, the coating problem was eliminated using an active substance with a smaller particle size. This change resulted in a more uniform core (Figure 6d) capable of withstanding the mechanical stresses of the coating process.

Adhesion of film coating to the tablet core. Good adhesion between a polymeric film and a tablet is a fundamental requirement to guarantee a good bond between the coating and surface of the core as the tablets tumble in the coating pan, and to maintain the clarity of logos. For the formation of an adequate and adhesive film coat, the atomized droplets have to spread completely over the surface of the core — and to a certain degree penetrate into a substrate. Some of the materials used in tablet formulations, however, may interfere with the intermolecular bonding at the film-substrate interface and hinder adhesion of the film to the core.

Lubricants are added to tablet formulations to minimize both die-wall friction and punch adhesion. Both of these requirements necessitate that the lubricants function at the tablet surface, precisely where they are counterproductive in the adhesion process considering the inherent hydrophobicity of lubricants, such as metal stearates.

No excipient used in such small quantities can have as detrimental effect on tablet quality than magnesium stearate. Magnesium stearate, although a very effective lubricant, can reduce the mechanical strength of the cores, decrease film adhesion and slow drug dissolution. Therefore, the quantity of magnesium stearate used in a tablet formulation should be minimized. Self-lubricating products such as Starch 1500 can also be used to reduce the need for significant lubricant addition.

Interaction with moisture during coating and storage. During the spraying phase of the film coating process and subsequent storage, tablets may greatly interact with moisture.[7,8] The water penetration into the core depends on a complex set of interacting factors related to the coating process, the formulation of the coating liquid and the tablet.[9,10]

Most pharmaceutical solid dosage formulations contain disintegrants. Modern disintegrants, often referred to as superdisintegrants, act by rapid

Figure 5 Erosion on the surface of the tablet with a logo.

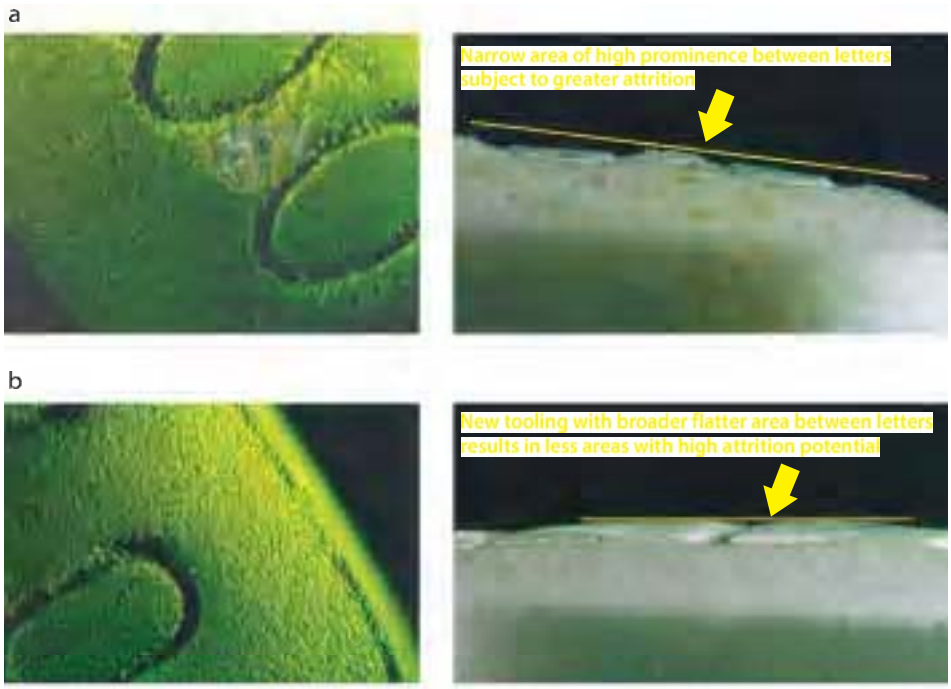
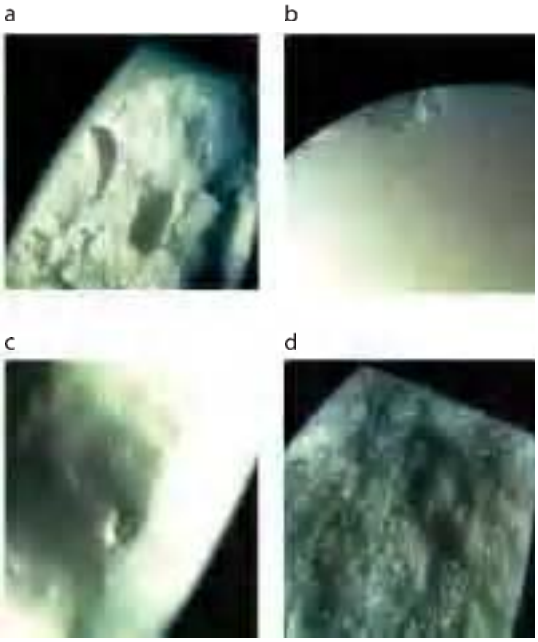


Figure 6 Effect of drug particle size on quality of aqueous enteric film coating (a - fracture surface of the tablet showing large crystals; b - chipping during the coating process; c - resulting film coating defect; d - fracture surface of the tablet containing active substance with smaller particle size).



uptake of water followed by rapid and, for some, enormous swelling up to 300 times excipient volume.[11,12] Inclusion of a high level of superdisintegrants in tablet formulations can affect the physical appearance of the final coated dosage form, such as the smoothness of the film. Superdisintegrant particles compressed into the surface of the tablet may get activated prematurely on contact with droplets of aqueous film coating solution resulting in very fast and excessive water penetration into the core and uneven surface of the coated product (Figure 7).

Water penetration into the tablet core can lead to potential storage problems with formulations that contain moisture-sensitive materials. That is why the choice of disintegrant type in such formulations can have a significant affect on coated product stability. While some materials such as pregelatinized starch can improve the stability of such dosage forms, superdisintegrants can have detrimental affect. Cunningham *et al.* showed that enteric coated acetylsalicylic acid tablets containing Starch 1500 as a filler-disintegrant had the best appearance (Figure 8), drug dissolution and the least increase in free salicylic acid (FSA) on storage.[13] Superdisintegrant (sodium starch glycolate or croscarmellose sodium) inclusion into tablet formulation resulted in a substantial increase in FSA levels. The study showed that the use of the right disintegrant (Starch 1500) provided the necessary dissolution characteristics to the formulation, allowed a dessicant to be excluded from the final packaging and was responsible for the exceptional stability results in this moisture sensitive application. It was also found that in some film coated tablets, use of superdisintegrants should be minimized or avoided.

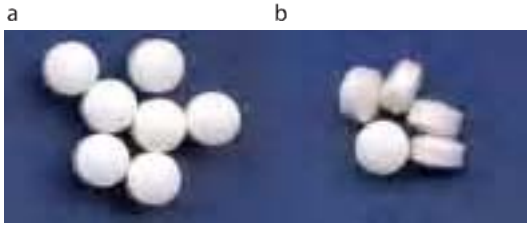
Conclusion

Many of the ingredients chosen in initial tablet formulation development can have a significant impact on aqueous film coating quality. They may affect the physical, mechanical, adhesive, drug-release and stability properties of the coated dosage form.

Decisions as to the ultimate appearance of the tablet are often left until later stages of development and can impact coating quality. To ensure success in the film coating process, formulation together with the design of the tablet should be considered early in the development.

Figure 7 Surface of a film coated tablet containing a high level of a superdisintegrant.

Figure 8 Appearance of coated acetylsalicylic acid tablets after 3 months storage at 40 °C/75% RH (a - formulation with Starch 1500; b - formulation with a superdisintegrant).



References

1. M.E. Aulton, *Pharm. Acta. Helv.* **56**(4–5), 133–136 (1981).
2. K.E. Wilson and E. Crossman, *Drug Dev. Ind. Pharm.* **23**(12), 1239–1243 (1997).
3. L.L. Young (Ed.), Tableting Specification Manual (American Pharmaceutical Association, Washington DC, USA, 2003) pp 54–61.
4. M.P. Jordan, J. Taylor and P.J. Hadfield, Contributed paper, AAPS National Meeting (Denever, CO, USA) 2001.
5. G.R.B. Down *et al.*, *Drug Dev. Ind. Pharm.* **19**(20), 2743–2749 (1993).
6. C.R. Cunningham, B. Korchok and F. Nuneviller, Contributed paper, CRS Annual Meeting (Newport Beach, CA, USA) 2004.
7. E. Okutgen *et al.*, *Drug Dev. Ind. Pharm.* **17**(14), 2005–2016 (1991).
8. N. Poukavoos and G.E. Peck, *Pharm. Res.* **10**(9), 1363–1370 (1993).
9. D. Faroongsang and G.E. Peck, *Drug Dev. Ind. Pharm.* **20**(10), 1777–1794 (1994).
10. A.M. Twitchell, J.E. Hogan and M.E. Aulton, *STP Pharma. Sci.* **5**, 190–195 (1995).
11. R. Thibert and B.C. Hancock, *J. Pharm. Sci.* **85**(Nov), 1255–1258 (1996).
12. A.H. Kibbe (Ed.), Handbook of Pharmaceutical Excipients (Pharmaceutical Press, London, UK, 2000) pp 501–504.
13. C.R. Cunningham, B.K. Kinsey and L.K. Scattergood, *Pharm. Technol. Eur.* **13**(5), 44–53 (2001). ■

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