

# Inventive tableting technology

## Partnership and innovation are redefining the relationship between pharmaceutical manufacturers and excipient suppliers

Pharmaceutical companies are radically adapting their businesses to survive, having realised they need to market drugs with increasing precision, addressing specialist treatment niches, establishing clear points of differentiation and taking much closer notice of end-user preference factors such as appearance, ease of consumption and novel convenience functionality. Accordingly, pharmaceutical industry customers are seeking not excipient suppliers but functional partners prepared to share the burden of managing technical development, regulatory approval and quality assurance within tight cost restrictions.

Here we discuss a tableting system concept developed by Sheffield Pharmaceutical Ingredients, which exemplifies how innovative excipient technologies are playing a key role in the marketing and acceptance of new pharmaceutical products.

This tableting system provides a simple way to create custom fast-dissolving tablet formulations using a free-flowing lactose-based functional powder for direct compression. Customers only need to add the desired active and a flavour (or a taste-masked active), plus lubricant (magnesium stearate), then form into tablets using standard direct compression techniques.

### Orally dissolving tablets

The tableting system concept embraces orally dissolving tablets (ODT), plus two other options for hard

tablets with fast dissolution. Here we will present an overview of the physicochemical properties claimed for the range, and the benefits that arise as a consequence.

The distinction between ODT and fast dissolution is based on the US Food & Drug Administration (FDA) guidance that ODTs should exhibit an in vitro disintegration time of approximately 30 seconds or less, when based on the United States Pharmacopeia (USP) disintegration test method or alternative.

ODTs provide several different layers of benefit for the customers of excipient manufacturers, and their end users in turn. Firstly, because they do not need to be swallowed with fluids (and indeed

are very easy to take), ODTs are an ideal delivery system for people who can't or won't swallow conventional tablets.

Secondly, they are easier to manufacture, with an obvious positive effect on cost. A preformulated ODT excipient medium requires only minimal processing, meaning that there are fewer raw materials to buy and test. ODT ingredients are already resident in the relevant monograph and the overall product is itemised in Drug Master Files, thus speeding up regulatory processes. And, crucially, a pharmaceutical manufacturer can take advantage of ODT characteristics without needing to enter into any formal partnerships or licences.

Figure 1

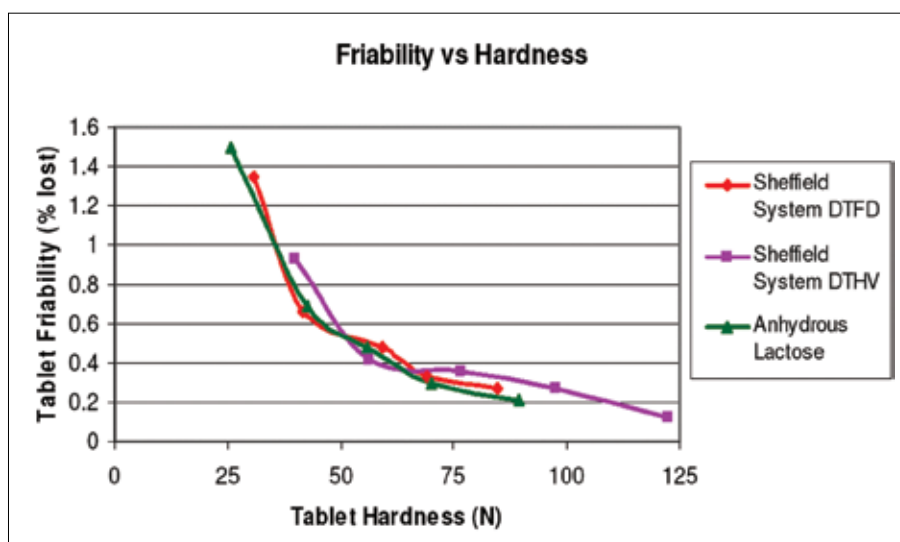


Figure 2

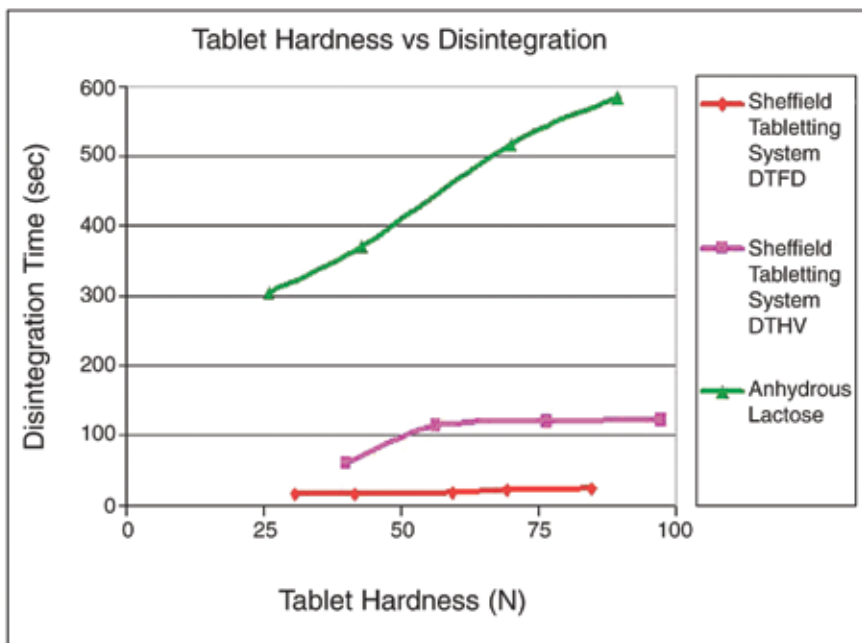
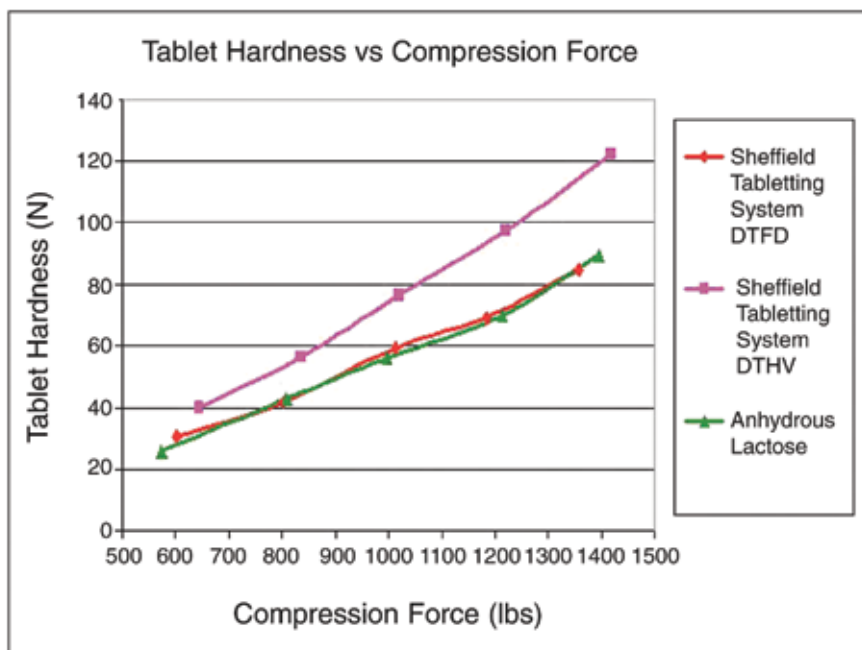


Figure 3



Thirdly, using this tableting system, ODTs can be made with superior hardness and friability.

Here we examine the results of an investigation into the physicochemical characteristics of the ODT tableting

system, showing how ODT hardness varies with disintegration time, and with friability.

Figure 1 shows that ODTs manufactured using this tableting system are consistently fast to dissolve – faster than starch or microcrystalline cellulose (MCC). This means the ODT formulation can also be used for tablets where dissolution is an issue using typical excipients such as MCC or lactose.

Figure 2 indicates greater hardness than most current ODTs, exhibiting sufficiently low friability for packaging in bottles rather than blister packs, achieving a significant cost benefit for manufacturers.

#### Different tableting systems

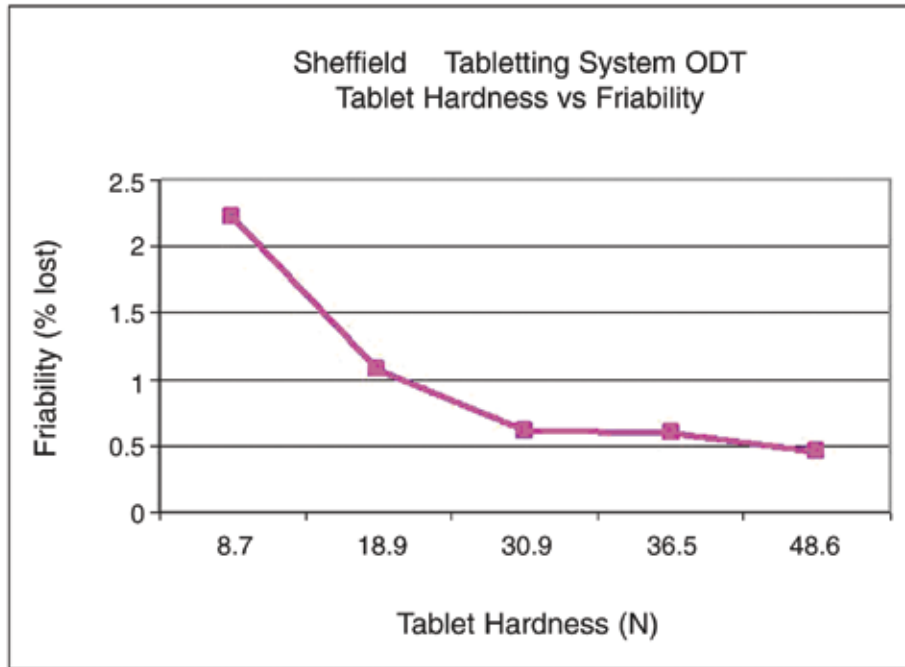
Of course, ODT is not the preferred option for all actives, so different tableting systems are used for tablets that require a combination of hard tablets and fast (i.e. less than 30 seconds) disintegration. Here we have established that by using specially processed lactose it is possible to achieve hardness and friability similar to that of pure lactose at a price similar to MCC, but with a faster disintegration rate.

By adjusting the formulation of the tableting system it is possible to achieve fast disintegration and standard tablet hardness in a standard-flow process (a formulation coded DTFD, 'Fast Disintegration'); or achieve faster-than-standard disintegration and harder tablets in a faster-flow process (a formulation coded DTHV, 'High Velocity').

Figure 3 shows the results of a comparison between tablet hardness and compression force for the two tableting systems described above, compared with anhydrous lactose. There is a visible increase in hardness per compression force with the DTHV option.

Figure 4 shows the results of a comparison between tablet hardness and disintegration time for the same three substances. Here the decreased disintegration time compared with anhydrous lactose is readily apparent.

Figure 4



**Orally dissolving tablets manufactured using this tableting system are consistently fast to dissolve – faster than starch or microcrystalline cellulose**

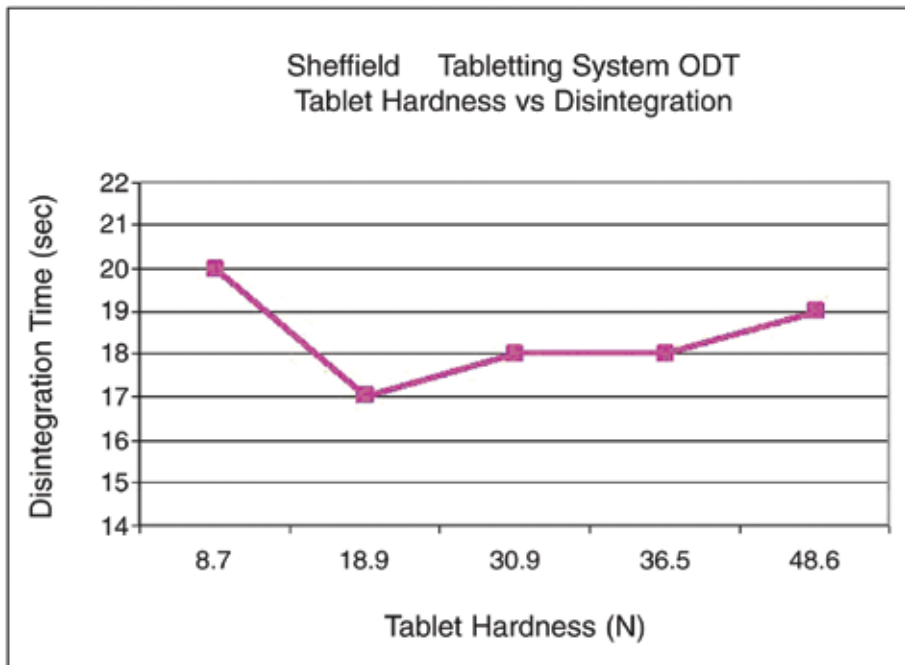


Figure 5 plots the outcome of a comparison between friability and hardness, indicating the DTHV formulation’s distinctive profile.

Pharmaceutical companies are embracing the market transformation in order to remain viable businesses. The winners will be those who approach innovation with a collaborative mindset, and a real commitment to form deep and lasting partnerships of complementary competence.

Accordingly, excipient makers such as Sheffield Pharmaceutical Ingredients are now rising to this challenge, providing innovative new products backed by cGMP manufacturing and global scale regulatory, technical and application expertise. At CPhI Worldwide 2008, the company is due to unveil a revolutionary new fast disintegrating system that mitigates problems with meeting dissolution time issues. ■

Figure 5: Hans Huttinga is the Strategic Marketing Director (Pharma Ingredients) for Kerry Bioscience - Sheffield Pharma Ingredients

This article was written by Hans Huttinga of Sheffield Pharmaceutical Ingredients – part of the international Kerry group