Fast-disintegrating tablet (FDT) technology is one of the recent innovative technologies in pharmaceutical formulations, and the FDT formulation has become a fast-growing segment in oral drug delivery systems. FDTs can be administered easily without water, although taking water makes oral administration even easier. They are suitable for children, the elderly and anyone who has a difficulty in swallowing conventional solid dosage forms. The FDT formulation combines advantages of both solid and liquid dosage forms, such as the easy handling and low production cost of solid dosage forms and the easy administration and no risk of suffocation of liquid formulations. Application of FDT technology can be extended to patients requiring daily medication. Moreover, the technology can give a new dosage-form strategy as a life-cycle management tool for drugs near the end of their patent life.

While there are many advantages, FDT technology has some limitations too. Upon introduction on the tongue, these tablets dissolve or disintegrate quickly with a limited amount of saliva for easy administration. However, it is challenging to keep the tablet mechanically strong while maintaining the fast-disintegrating properties. Balancing the fast disintegration and the high mechanical strength of the tablet is critical to the successful development of formulations. Moreover, disintegration in the mouth can limit the number of drugs that can be incorporated into the FDT formulations, because many drugs are unpleasant in taste. After an FDT disintegrates or dissolves in the saliva, the drug in the tablet remains in the oral cavity for a while until swallowed. Therefore, if the drug has an unfavourable taste, the taste should be masked, which may increase the cost.

In addition to high mechanical strength, fast disintegration and pleasant taste, FDTs should leave no or minimal residue in the mouth, allowing high drug-loading (more than 100mg), and be portable without any friability problems. They should also be resistant to temperature change and high humidity. However, most of these hurdles have been overcome by improved FDT technologies. As a result, FDT formulations have been gaining popularity not only in the pharmaceutical industry, but also in the nutrition industry.

The popularity and usefulness of the initial formulation resulted in the development of several fast-disintegrating technologies. Recently, a new fast-disintegrating technology called Frosta® was developed for making FDTs. The Frosta technology combines the major advantages of fast disintegration of freeze-dried formulation and the high mechanical strength of compressed tablets. Moreover, the technology utilises a conventional wet granulation process and tablet press for cost-effective production of the tablets with desirable properties. The Frosta technology is based on compression of highly plastic granules at low pressures to prepare FDTs. The highly plastic granules are composed of three components: a plastic material, a water-penetration-enhancer and a wet binder. A plastic material and a water-penetration-enhancer can be the same material. Each of the three components plays an important role in obtaining tablets with high strength and fast disintegration time. The key benefits of the Frosta technology are:

- fast disintegration in the mouth – between 5 and 50 seconds, depending on the tablet size;
- low manufacturing cost – the same as making conventional tablets;
- one-step granulation processing;
- strong mechanical property with friability less than 1%; and
- multitablet packaging, with dozens of tablets in one bottle.

For optimum tablet properties, the three components were used to prepare highly plastic granules that could be compressed at low pressures and yet maintain the porous structure required for fast absorption of water into the tablet core. Any granulation method can be used to prepare highly plastic granules.

Tablet excipients with porous structure can have more plastic deformation than non-porous counterparts when compressed under the same conditions. Moreover, when the same material is used for making FDTs, the mechanical strength of tablets is increased when porous granules are used. For example, Maltrin QD® M580 and Maltrin® M180 (Grain Processing Corp., Muscatine, Indiana) are maltodextrin and corn syrup solids with the same DE (dextrose equivalent) value, which is 18. The density is the only difference. Maltrin QD M580 is a porous material with the packed density of 0.40g/cc, while Maltrin M180 is a nonporous material with the packed density of 0.61g/cc. Low density of Maltrin QD M580 with a highly porous structure can be prepared by specially treating Maltrin M180 so...
that the Maltrin M180 particles are agglomerated. When granules were prepared using the two Maltrins with mannitol, the tablet hardness of Maltrin QD M580 and Maltrin M180 were 65.2N and 7.3N, respectively. Due to its porous structure, the Maltrin QD M580 granules created more plastic deformation than the Maltrin M180 granules when compressed under the same conditions.

The high mechanical strength of tablets made from the porous Maltrin QD M580 granules was expected, as it had already been shown that when microsponges – which are porous polymeric microspheres – and a drug are mixed, the mixture shows higher compressibility due to the plastic deformation of the sponge-like structure of the microsponges. When the mechanical properties of low-crystalline powdered celluloses were evaluated, the materials started plastic deformation at relatively low compression pressures, while the total volume reduction was comparable to microcrystalline celluloses and powdered celluloses. Granules with large pores showed low compression energy loss. They are also more prone to particle rearrangement, plastic deformation and brittle fracture upon compression, resulting in the increased tablet mechanical strength.

Two major components of the highly plastic granules are a plastic material and a water-penetration-enhancer. In general, the proportion of the two components needs to be adjusted to obtain the optimal tablet properties. If a large portion of a water-penetration-enhancer is dissolved during the granulation process, the granules would lose their plasticity resulting in the low mechanical strength of the tablets. For example, when various ratios of the Mannogem™ EZ Spray (mannitol, SPI Pharma Inc., New Castle, Delaware) and Maltrin QD M580 were mixed and granulated using the same amount of a wet binder, the tablet hardness as well as the tablet disintegration time increased as the proportion of Mannogem EZ Spray was increased. The optimal proportion of the two components needs to be investigated for the desirable mechanical strength and disintegration time.

Simply compressing the mixture of a plastic material and a water-penetration-enhancer did not produce tablets with a desirable mechanical strength. It was necessary to add a binder during the granulation process to achieve a good bonding effect between the particles for achieving high mechanical strength. Moreover, the type and concentration of the binder in solution had to be adjusted to produce granules with desirable physical properties.

There are a couple of important considerations of the formulation in the three-component system. The plastic material in the Frosta tablets can be water-soluble or water-dispersible, and can also be porous. Plastic deformation of the materials can improve the inter-particle bonding necessary for better mechanical strength of the tablet. As mentioned above, if a plastic material is polymeric, it may build a viscous layer on the tablet surface upon contact with water. The viscous layer may prevent water penetration into the tablet matrix, causing slow disintegration. One way of preventing such a problem is to mix the plastic material with a water-penetration-enhancer at a certain ratio, and compress them at a low pressure. This will produce plastic deformation of the materials, creating intimate contact among the particles. In this process, the plastic particles can be separated from each other by water-penetration-enhancing particles, which may prevent the formation of the viscous layer on the tablet surface.

Although the plastic materials can make close contacts to increase the chance of bonding by compression, the formation of adequate bonding among the granules at a low compression pressure requires a suitable binder. The binder here can also prevent segregation of the porous materials and the water-penetration-enhancers during mixing and granulation. If the binder is in a liquid or semi-solid state, it should not significantly destroy the porous structure of the materials. One method of avoiding this is to apply higher concentrations of the binder to reduce the water activity. Another way is to allow only a short contact time with the porous structure when making granules using relatively low concentrations of the binder, so that the porous structure would not be disrupted by the binder solution.

The Frosta tablets are mechanically strong with friability less than 1%, and are relatively stable in an open-air environment. They are robust enough to be packaged in multitablet vials. When tested in vitro, Frosta tablets absorbed water very quickly and disintegrated instantly upon contact with water, forming a paste for easy swallowing. Depending on the size, the Frosta tablets can disintegrate in less than 10 seconds after placing them in the oral cavity for easy swallowing. Scanning electron microscopy of the inner structure of a Frosta tablet showed the presence of a lot of pores between the granules throughout the table matrix. It is these pores that increase the absorption of water by capillary force. Upon contact with the saliva or

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