Overview

Pharmaceutical firms often desire to deliver crystalline and solubilized forms of compounds in once- or twice-daily dosing regimens to maximize therapeutic effect and patient compliance. To meet this need, Bend Research has developed osmotic tablet technologies that release soluble and insoluble drugs in predictable, reliable, and stable ways. Bend Research also has experience with, and welcomes, projects that require customized, nonconventional “optimized for pharmacology” release profiles.

Bend Research uses proven techniques and has significant experience in formulating and scaling osmotic tablet formulations from batches of fewer than 10 tablets up to the 250-kg production scale. It also has in-house capability to manufacture supplies under current Good Manufacturing Practice (cGMP) conditions for Phase 1 through Phase 3 clinical studies.

Two of our patented osmotic-tablet platform technologies are:

Asymmetric-Membrane Technology (AMT)

- A single-layer tablet with an insoluble, asymmetric microporous membrane produced by controlled-release separation.
- Applicable drug substance and dose: water soluble, low to high dose.

Swellable-Core Technology (SCT)

- A bi-layer tablet with an insoluble, semipermeable coating and a laser-drilled delivery orifice.
- Applicable drug substance and dose: water soluble, poorly water soluble, or bioavailability-enhanced forms (e.g., spray-dried dispersions [SDDs]); low-to-moderate doses.

Technology Description

SCT and AMT are osmotic/hydrostatic pressure-driven dosage forms that provide steady-state zero-order drug release. Release is typically independent of gastrointestinal pH and agitation. These characteristics minimize patient-to-patient variability and maximize in vitro/in vivo correlations compared with oral controlled-release dosage forms. A wide range of steady-state release rates is possible. In addition, modifications to the platform technologies such as immediate, delayed, and custom release profiles—as well as fixed-dose combination therapies—can be designed into the finished dosage form. Lastly, due to the physical and chemical stability of the polymer membranes, dissolution performance does not change with time, so osmotic tablets can be packaged in conventional bottles and blisters.

SCT Tablets

SCT tablets (Figure 2 on page 2) are bi-layer tablets coated with an insoluble, dense, semipermeable coating and have a laser-drilled hole. The two layers are a sweller layer and an API-containing layer. The sweller layer contains hydrophilic swelling polymer(s) and other tablet excipients. Following ingestion, the sweller layer imbibes water and swells to generate hydrostatic pressure that extrudes, or pumps, the solution/suspension contents of the drug layer through the hole in the coating on the drug-layer side. The release rate is primarily controlled by the rate of water permeation through the coating. However, the osmotic, swelling, and viscosity properties of the tablet-core sweller and active layers also contribute to the release rate and are important in ensuring that the entire active layer is delivered from the tablet.
Other tablet configurations are also possible. For example, the same or a different API can be coated onto the osmotic core for immediate or modified-release, providing a wide range of final drug-product “fit for purpose” characteristics.

SCT tablets are manufactured using conventional bi-layer tableting, film-coating, and laser-drilling. The tablet sweller layer is typically a direct-compression formulation. The active layer, depending on the API properties and dose, may be formulated by direct compression, wet granulation, or dry granulation. The membrane is formed by solvent film-coating in a conventional pan coater and the delivery orifice is created on the drug-layer side of the tablet with a laser drill, using either a batch array or continuous tablet feeding. Bend Research designs and builds in-house batch and continuous laser drill units for development and cGMP use, as well as for use at client locations.

**AMT Tablets**

AMT tablets (Figure 3) are single-layer tablets film-coated with a porous, semipermeable membrane. Soluble tablet-core ingredients, including the API, generate an osmotic pressure gradient across the coating. As water volume increases within the tablet, hydrostatic pressure develops and forces drug solution out through the microporous coating. The release rate is controlled by the water permeability of the coating and the osmotic pressure of tablet core. Coating porosity is achieved using a well-controlled, proprietary Bend Research phase-separation process dictated primarily by the polymers and co-solvent system.

High-porosity AMT coatings can permit higher water fluxes, shorter lag times and faster release than SCT systems. Importantly, the interconnected pores serve as the delivery medium so AMT tablets do not require laser-drilled orifices. AMT tablets are manufactured using conventional tableting and film-coating technologies. The tablet core is compressed, depending on API properties, using direct-compression, wet-granulation, or dry-granulation techniques. The semipermeable membrane polymers are dissolved in solvent and film-coated using conventional pan coaters.