

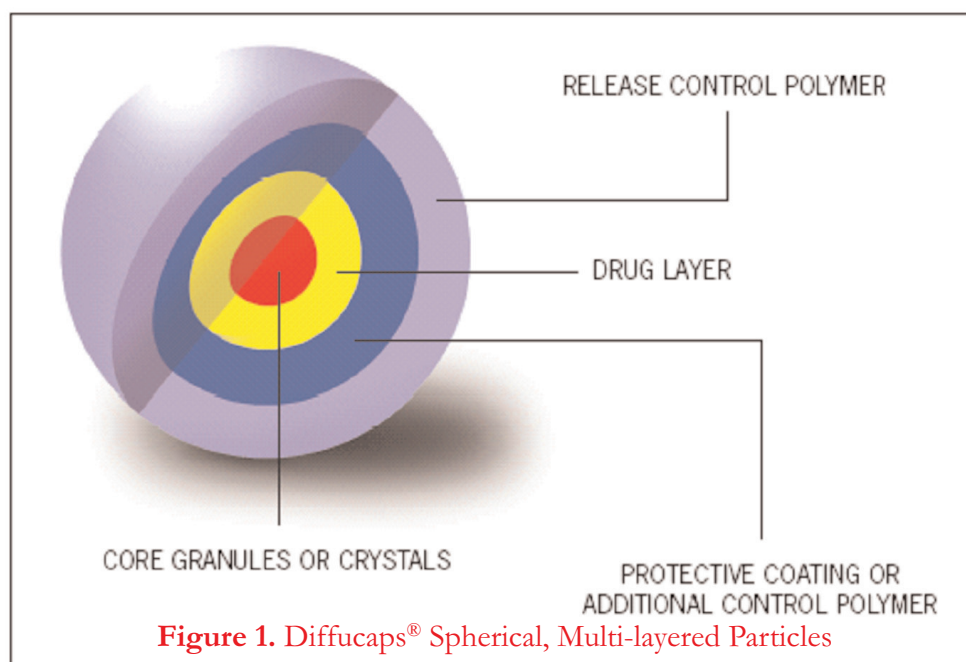
Optimizing Oral Drug Delivery with Multiparticulate Technology

by Troy M. Harmon, MS, MBA, VP of Business Development, Eurand, Inc.

Multiparticulate drug dosage forms are composed of small beads, each small bead further composed of many layers. Some layers contain drug substance; others are rate-controlling polymers. With Eurand's **Diffucaps®** multiparticulate system, customized drug release profiles are created by first layering active drug onto an inert core (such as a cellulose sphere), then applying one or more rate-controlling, functional polymers, to produce spherical, multi-layered particles (**Figure 1**). The drug layering process can be conducted either from aqueous or solvent based drug solutions.

Multiple Release Profiles

Many release profiles can be achieved using this approach—including sustained release, time-delayed release, and pulsatile release of active pharmaceutical ingredients for absorption throughout the GI tract. Time-delayed release of the drug as either a burst or sustained release profile can be achieved over a period of 1 to 12 hours, with a lag time of 4 to 10 hours. The duration of drug release following the lag-time depends on the composition and thickness of the polymer barrier and the lag-time coating itself. The multiparticulate system provides optimal release profiles for either single drugs or for a combination of drugs.



Multiple Dosage Forms & Advantages

Eurand's technology also allows for a variety of finished dosage forms. The finished dosage form may be a modified-release capsule, a standard (conventional) tablet or an orally disintegrating tablet (ODT). Two or more bead populations can be readily combined into a dosage form, permitting easy adjustment of pharmacokinetic profile and/or creation of multiple strengths of a drug product. In addition, the beads, which are typically ≤ 1 mm in diameter, exit the stomach in a more consistent fashion than larger tablets, decreasing pharmacokinetic variability. Eurand has also developed formulation technology that combines the customized drug release offered by Diffucaps with technologies that enhance the solubility of insoluble drugs in the gastrointestinal tract; this provides a degree of delivery control that goes beyond that of single technology systems.

Pulsatile Drug Delivery

Eurand's timed, pulsatile delivery system is capable of providing one or more rapid release pulses at predetermined lag times, such as when chronotherapy is required, and at specific sites, such as for absorption along the GI tract. These capabilities can help optimize efficacy and/or minimize side-effects of a drug substance. For example, Eurand has created a circadian rhythm release (CRR) dosage form for a cardiovascular drug, propranolol hydrochloride, with a four-hour delay in release after oral administration. Administered at bedtime, propranolol is released after the initial delay such that maximum plasma level occurs in the early morning hours, when the patient is most at risk.

More Technology for Controlling Drug Release

The Diffucaps[®] multiparticulate system for customized drug release is one of Eurand's four technologies for controlling drug release. Other technologies include:

- **Diffutab[®]** technology for sustained release profiles and targeted delivery of pharmaceutical products. This technology incorporates a blend of hydrophilic polymers that control drug release via diffusion through, and erosion of, a matrix tablet. The Diffutab technology is particularly useful for the development of high dosage products and is an effective way to develop sustained release, once-a-day dosage forms.
- **Orbexa[®]** technology is a multiparticulate system that enables high drug loading and provides a formulation choice for products that require granulation. This technology produces beads that are of controlled size and density - and suitable for formulation as controlled release multiparticulates - using granulation, spheronization and extrusion techniques. The resultant beads can be coated with functional polymer membranes for additional release rate control and may be filled into capsules or provided in sachet form. This process allows for high drug concentrations within each bead. The technology is suited for use with sensitive drugs such as proteins.
- **Eurand Minitabs[®]** technology combines the simplicity of tablet formulation with the sophisticated drug release control offered by multiparticulate drug forms. Eurand Minitabs are tiny, approximately 2 mm in diameter, cylindrical tablets. Functional membranes may be applied to the tablets to further control release rate. Eurand Minitabs offer high drug loading, a wide range of release rate designs, and fine tuning of these release rates. Capsules containing the Eurand Minitabs can be opened and the contents used as a "sprinkle" formulation.

About the Author

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About Eurand

Eurand is a specialty pharmaceutical company that develops enhanced pharmaceutical and biopharmaceutical products based on its proprietary drug formulation technologies. Eurand has had four products approved by the FDA since 2000 and has a pipeline of product candidates in development for itself and its collaboration partners. Eurand's technology platforms include bioavailability enhancement of poorly soluble drugs, customized release, taste-making/fast-dissolving formulations and drug conjugation. Eurand is a global company with facilities in the USA and Europe. For more information, visit www.eurand.com.