How to Select the Right Polymers for Your Modified Release Tablet or Capsule

Modified release (MR) formulations present unique complications around excipient selection. When choosing polymers to enable long-lasting drug delivery, formulators have a wealth of options. However, from the wide range of possibilities, certain options stand out in performance, predictability, and ease of manufacture.

"Formulation errors can lead to difficulties down the road of a product's life cycle. Selecting the desired dosage form and dissolution release profile will help you decide which polymers to use to achieve your desired objective. Following best practices will help ensure a robust formulation and make the development and manufacturing processes easier."

Richard Sidewell, Ph.D., Vice President and Chief Scientific Officer, Recro®

Dissolution Profile

An informed decision starts by understanding the desired dissolution profile and dosage form. Then, the pharmacology, physicochemical properties, pharmacokinetics, and the intended therapeutic benefit of the drug will direct the choice of dissolution drug release profile. Options include first- or zero-order sustained release, enteric formulations, and multiphasic delayed or extended formulations.

Once you decide the desired dissolution behavior, a skilled formulator can help decide on the optimal dosage form, tablet or capsule, and how best to achieve the target drug release profile.

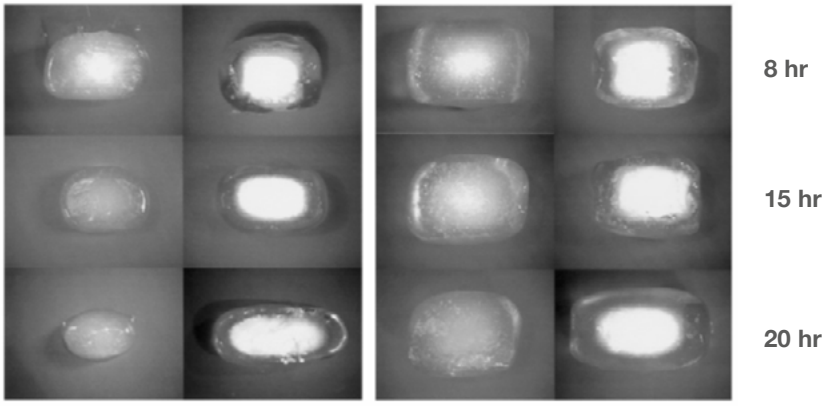
Polymers by MR Dosage Form

The most common MR dosage forms include hydrophilic matrix tablets and multiparticulate reservoir systems.

Hydrophilic Matrix

Commonly used for sustained release (SR) dosage forms, matrix tablets offer a wide range of clinical, technical, and commercial benefits. These stable, robust systems offer a wide range of achievable release profiles for a wide range of API behaviors.

Polymers for hydrophilic matrices should be soluble across a wide range of pH and exhibit a low risk of chemical interaction with the drug. Optimal particle size, good flow, and compressibility are also factors to consider.



Polymer properties impact hydration and swelling behaviors of polymers for matrix tablet formulation.

Image courtesy of Colorcon.

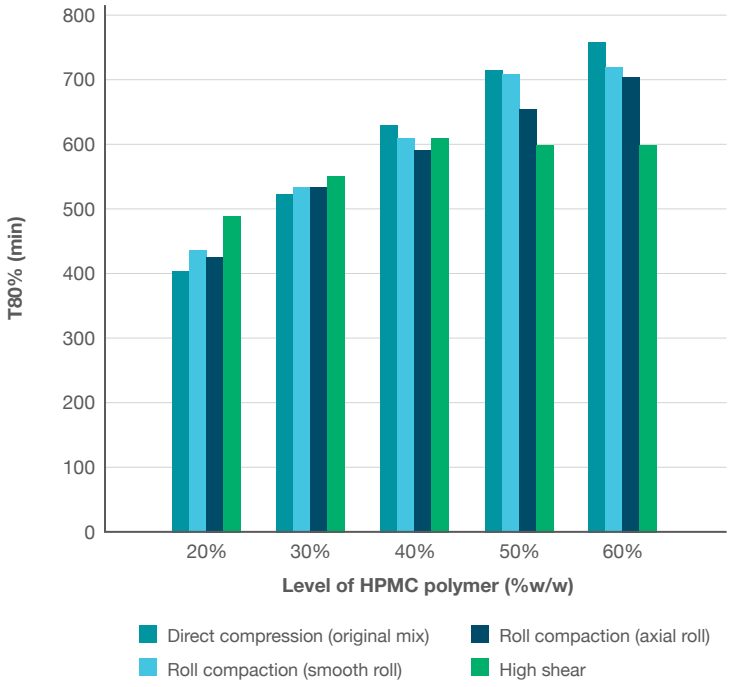
To further refine polymer selection, choose a polymer that hydrates quickly and forms and maintains a tight gel structure. Hypromellose (HPMC), K-chemistry, exhibits these qualities. Hypromellose is very widely used in hydrophilic matrix tablets and is, in our opinion, the best place to start your formulation development.

"Make sure your release is controlled by chemistry and material, not by process. The formulation should be robust enough to overcome variations seen in the manufacturing process."

Charles Vesey, R.Ph., M.S., Formulation Technologies Manager, Colorcon, Inc.

The polymer chemistry and molecular weight (or viscosity grade) are the key parameters in selecting the polymer. However, the formulation should also contain specific types of excipients that can play a key role.

The most important excipients for a hydrophilic matrix tablet formulation are the fillers. Plastic, brittle, soluble, and insoluble fillers should be included. Lactose monohydrate and microcrystalline cellulose together fulfill all four of these roles, providing formulation levers to optimize both manufacturability and the dissolution drug release profile. From a best practices point of view, aim for 30% polymer load, with the bulk of the remainder consisting of drug and fillers. Using more or less than about 30% polymer may increase the variability of the dissolution drug release and make the formulation performance more dependent on processing conditions.



Effect of manufacturing method and polymer concentration on T80 values. The manufacturing method exhibits the least impact on T80 levels at the 30% polymer level.
Image courtesy of Dupont Nutrition and Biosciences.
Sheskey, P.J., Hendren, J., "The effects of roll compaction equipment variables, granulation technique, and HPMC polymer level on a controlled release matrix model drug formulation," Pharm. Technol., 23(3), 90-106 (1999)

Reservoir Systems/Coated Multiparticulates

Multiparticulate (MP) systems consist of pellets coated with a drug and overcoated with different polymers. They allow for tailoring the dissolution drug release and can spread out in the gastrointestinal tract, sometimes reducing gastric irritation or food effect.

Polymer selection is based primarily on functional requirements. Polymers for coating should lend themselves to formulating into a sprayable solution or suspension that dries into a strong and flexible film with good adhesion. The solubility and permeability of the polymer and pH-independence or dependence also influence polymer choice.

Sustained-release multiparticulate capsules often use pH-independent polymers like ethylcellulose or the polymethacrylate family of polymers, while delayed release dosage forms more frequently use pH-dependent polymers such as methacrylic acid copolymers.

Similar to hydrophilic matrix tablets, there are certain formulation best practices to follow. The choice of polymer is only the first step. Excipients, like pore formers, plasticizers and anti-adherents can also affect dissolution drug release.

The goal is to control the drug release primarily via the choice of polymer and pore former, using a coating level that provides a film thickness near 30-50 microns. Lower film thickness can lead to dissolution variability, making the formulation susceptible to minor changes in substrate particle size or surface morphology, while higher thicknesses may lead to incomplete terminal release.

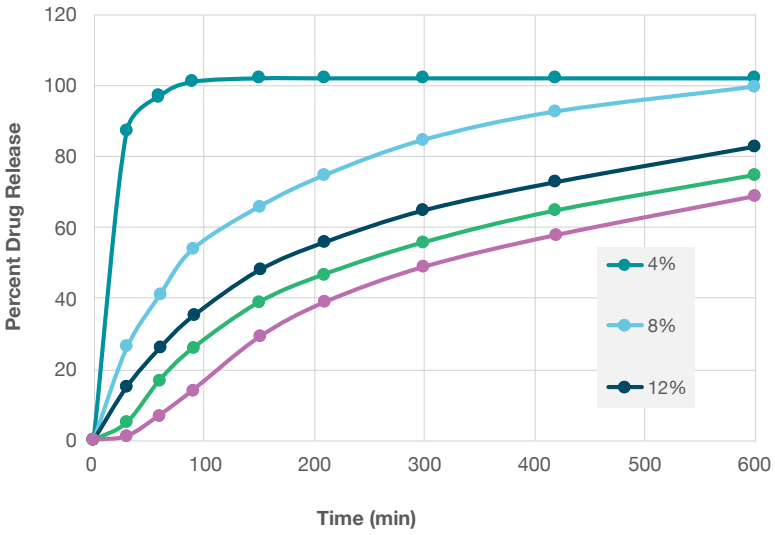


Image courtesy of Colorcon.

Comparative Study of Theoretical Versus Actual Weight Gain for a Surelease® Barrier Membrane on Coated Pellets, Colorcon, AAPS, 2004

Conclusion

Consider drug substance properties, clinical performance needs, and dosage form when selecting polymers. An understanding of how polymer characteristics influence performance will help you refine polymer selection. By choosing well and employing formulation best practices, drug developers can lower the possibility of manufacturing issues and performance variability later in the product's life cycle.

View recorded webinar: How to Select the Right Polymers for Your Modified Release Tablet or Capsule