Customized release profiles using EUDRAGIT® polymers

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Functional EUDRAGIT® polymers offer a wide variety of formulation options, which allow formulation design tailored to specific therapeutic requirements or the API characteristics. By combining different polymer types or applying several coating layers, almost every desired release profile can be achieved. The presentation introduces selected examples:

1. Gastro-intestinal targeting by polymer mixtures

Multiparticulates coated with a mixture of pH-dependent poly(meth)acrylate polymers result in specialized formulations with adjustable dissolution profiles, as shown in Figure 1 and can be of use when targeting a specific region within the GI tract.

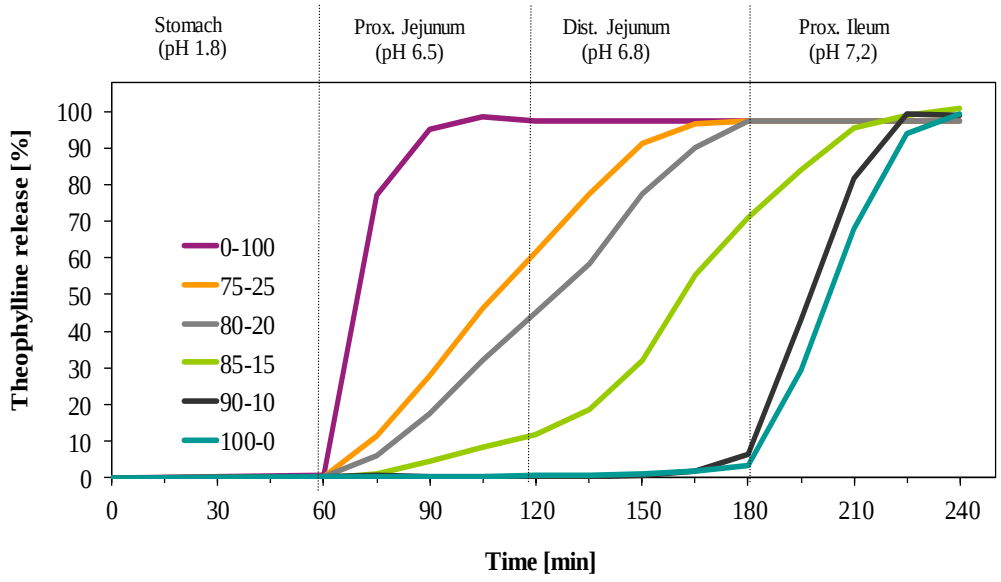

Figure 1: Mixtures of EUDRAGIT® FS 30 D and EUDRAGIT® L 30 D-55 to influence dissolution pH of theophylline granules

2. Enhanced drug release after stomach transit

Considerable value to solid oral dosage form development is added by the application of specialized modified-release systems that aim for an increased therapeutic index as well as improved patient compliance. For instance, the design

of a formulation that accelerates the release of the active pharmaceutical ingredient within the small intestine or colon is especially preferred for drugs that show a very narrow adsorption window and/or require a rapid onset of action. In collaboration with the University College London, Evonik has developed a double-layer technology marketed under the brand name Duocoat®. It consists of two anionic EUDRAGIT® coating layers and can be applied on both monolithic and multiparticulate dosage forms. In vivo studies in humans confirmed the up to three times faster disintegration of the system compared to conventional coated tablets. Variations in the EUDRAGIT® polymer type used lead to a specific GI targeting characterized by a rapid action onset and stress the high versatility of EUDRAGIT® in oral solid formulation development.

3. How to mimic OROS® release kinetics through multiparticulates coated with EUDRAGIT ® polymers

Controlled drug delivery has gained importance within the pharmaceutical development, improving patient compliance with prescribed dosing regimens. A promising and advanced technology to reduce the effects of food intake or GI motility is the osmotic controlled-release oral delivery system (OROS). It consists of a rigid tablet with a semi-permeable outer membrane and at least one laser drilled hole. The functional mechanism is described as water absorption through the semi-permeable, rate-controlling membrane into the core as a result of the osmotic activity gradient established across the membrane by the osmotic excipients. The drug is continuously expelled from the core through the orifices as the tablet travels along the gastrointestinal tract. However, challenges such as the complex manufacturing process call for alternatives with similar release characteristics but easier manufacturing technologies.

In collaboration with Midas Pharma GmbH, Evonik has developed paliperidone coated multiparticulates mimicking the drug release of Invega®. A conventional drug layering and coating process using mixtures of pH-dependent and pH-independent EUDRAGIT® polymers along with suitable excipients proved the feasibility to achieve a pH-independent drug release pattern similar to Invega®. Alcohol-resistance in up to 40% ethanol was further proven. The example confirms the feasibility to achieve advanced drug release patterns with conventional coating strategies and sets path for the oral formulation development of challenging actives.