Pharmaceutical Dissolution Testing

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Physiological Parameters Relevant to Dissolution Testing: Hydrodynamic Considerations

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HYDRODYNAMICS AND DISSOLUTION

Dissolution

Why Is Hydrodynamics Relevant to Dissolution Testing?

Release-related bioavailability problems have been encountered in the pharmaceutical development of formulations for a number of quite different chemical entities, including ciclosporin, digoxin, griseofulvin, and itraconazole, to name but a few. A thorough knowledge of hydrodynamics is useful in

the course of dissolution method development and formulation development, as well as for the pharmaceutical industry's quality needs, e.g., batch-to-batch control. Occasionally, quality control specifications are not met due to "minor" variations involving hydrodynamics, such as the use of different volumes, or modified stirring devices or sampling procedures. The development of drug formulations is facilitated by the choice of an appropriate dissolution apparatus based on insight into its specific hydrodynamic performance. Using the right test might make it easier, for instance, to isolate the impact of different excipients and process parameters on drug release at an early stage of pharmaceutical formulation development. Furthermore, a sound knowledge of in vivo hydrodynamics may help to better understand and possibly to improve forecasting of in vivo dissolution and absorption of biopharmaceutical classification system (BCS) II compounds. Although gastrointestinal (GI) fluids are well-characterized and biorelevant dissolution media [e.g., Fasted State Simulated Intestinal Fluid (FaSSIF) and Fed State Simulated Intestinal Fluid (FeSSIF)] have been developed to simulate various states in the GI tract, knowledge of hydrodynamics appears to be relatively scant both in vitro and in vivo. This chapter gives a brief introduction of the basic hydrodynamics relevant to in vitro dissolution testing, including the convective diffusion theory. This section is followed by hydrodynamic considerations of in vitro dissolution testing and hydrodynamic problems inherent to in vivo bioavailability of solid oral dosage forms.

The Dissolution Process

Dissolution can be described as a mass transfer process. Although mass transfer processes commonly are under the combined influence of both thermodynamics and hydrodynamics, usually one of these prevails in terms of the overall dissolution process (1–3). Hydrodynamics is predominant for the overall dissolution rate if the mass transfer process is *mainly* controlled by convection and/or diffusion, as is usually the case for poorly soluble substances. This is of great

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