

# Preface

The ideal drug delivery system has been depicted as “getting the right amount of drug to the right place at the right time.” It is now widely accepted that making drug available “immediately” following oral administration does not provide such idealized delivery in many cases. Consequently strategies, materials, and technologies have evolved to control delivery by delaying, slowing, pulsing, or delivering to a specific region of the gastrointestinal tract. The introductory chapter in this book traces the history and evolution of the concepts and achievements that has brought the discipline to where it is today.

Despite the advent of many useful release-modifying polymers and technologies, one of the greatest barriers to providing an appropriate release profile (and associated plasma presence) is the gastrointestinal tract. Knowing and understanding its structure, tissues, mechanics, and functions, and the limitations (and possibilities) that these present in attaining a target plasma profile is a prerequisite for successful dosage form design. Chapter 2 provides such perspectives.

Proving efficacy and safety for a novel molecule is currently so difficult, time consuming, and expensive that industrial R&D-based organizations are under pressure to “hurry” a drug to market when it is shown to be effective and safe. More nuanced effects may only become apparent after widespread use, prompting dosage form redesign. Hence, most current controlled release oral dosage forms are “second-generation” products. Whether shortcomings in “first-generation” (mostly “immediate release”) products have contributed to “failures” in development cannot be stated but, conceivably, greater focus on a broader range of delivery options in phase 1 or phase 2 clinical trials, possibly allied with the use of relevant biomarkers, may offer hope that attrition can be reduced and performance optimized. Such possibilities are discussed from an industrial R&D perspective in Chapter 3.

It is clearly unrealistic (and expensive) to trial each and every delivery and formulation concept or system in human subjects. In vitro and animal studies are also valuable, both during exploratory and quality-monitoring phases. The range, predictive capabilities, and limitations of such models are presented and discussed in two chapters in this book.

The mechanisms by which release of drug from the dosage form is controlled can profoundly impact location, rate, and profile of release, and as a consequence,

the plasma profile following absorption. Such behaviors can be influenced by release-modifying polymers or mixtures thereof, the presence of other materials and geometric (shape and size) factors. This is a wide subject area that is reflected in several chapters devoted to such topics.

Manufacturing technologies are immensely important for imparting reliability and consistency to dosage form performance. Quality of the release modifiers is also crucial. Many, being polymeric, may contain residues that could destabilize the drug (or other excipients). Hence, consistency of quality is an important consideration. It is heartening therefore that high-quality information on such phenomena is being generated and published by excipient providers to guide the formulation or manufacturing technologist on material performance. Chapters on polymers for matrices, capsules for controlled release, and multiparticulates in this book emanate from such sources and can provide useful guidance when considering “quality-by-design-based programs.”

Fatty acids, fatty alcohols, and waxes that do not melt at body temperature are sometimes used to form insoluble matrices (possibly in combination with other materials) to slow release from dosage forms. Their capability for self-assembly in GI tract-like milieu is now evincing much interest, particularly with insoluble drugs, as controlled release platforms for the future. Hence, they merit a chapter on the topic, provided by probably the foremost group operating in this area (Monash University, Melbourne).

Regional delivery and control of drugs usually concern delivery to and absorption from the small intestine. On occasion, however, delivery in a controlled manner via the buccal cavity may be advantageous, in terms of onset of action or avoidance of hepatic metabolism. It is appropriate therefore that such “point of entry” (to the GI tract) delivery be allocated a chapter.

One of the “holy grails” for prolonging drug absorption (and consequent plasma presence) concerns retention of the dosage unit in the gastric region, drug being released gradually for absorption further along the GI tract. Gastroretentive strategies, devices, and performance are accordingly considered in a chapter.

Finally, drug delivery at “the other end” of the GI tract, both for local action and systemic absorption, must not be disregarded, particularly as lack of enzymatic activity in the colon makes it a tempting location for delivering peptides or other macromolecular entities. Hence, a chapter on colonic delivery is included.

These chapters have, as far as is possible, been formatted so that they can largely “stand alone.” However, some repetition is inevitable as materials and mechanisms may be common to more than one strategy. Furthermore, the editors would like to stress that satisfactorily controlling drug release requires a “holistic” approach. Knowledge of the drug, the release-controlling agents, the mode and site for delivery, as well as the absorptive processes associated with oral delivery need to be factored into the dosage form design strategy for getting the correct amount of drug “to the right place at the right time.” It is hoped therefore that insights contained in this volume provide the research scientist, formulation specialist, and manufacturing technologist with such broad-based information for dosage form design, manufacture, and control.

<http://www.springer.com/978-1-4614-1003-4>

Controlled Release in Oral Drug Delivery

Wilson, C.G.; Crowley, P.J. (Eds.)

2011, XIV, 414 p., Hardcover

ISBN: 978-1-4614-1003-4