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Multiparticulate Drug Delivery

Formulation, Processing and Manufacturing

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I dedicate this book to my parents who despite their lack of formal education, inspired me to learn and share my learning, even though it meant that we did not see each other for many years; to my lovely wife, Angela; and sons, Jonathan and Anthony, for their support and inspiration to always do my best.

Preface

Multiparticulate drug delivery systems are widely used in the pharmaceutical industry due to their formulation flexibility for the manufacturers and clinical benefits that they offer to the patients. Although the introduction and use of this platform technology dates back to 1950s (under the concept of Spansules by SmithKline and French), there is still a significant level of interest to leverage multiparticulates for achieving various release profiles and for special age groups like pediatric and elderly patients. Multiparticulate systems are developed in a wide range of sizes, i.e., as small as 150 μm or as large as 2–3 mm in diameter and offer superior clinical and technical advantages over many other specialized drug delivery technologies. Due to their multiplicity of units and small sizes, they exhibit reduced risk of dose dumping, spread along the gastro-intestinal tract (GIT), when taken orally, and therefore, offer specific biopharmaceutics advantages over the larger single units. Their transit time through different segments of the GIT is more predictable, reducing inter- and intra-subject variability. Multiparticulates possess large surface area for drug release and when dispersed along the gut, maximize drug absorption without possible local irritation in the GIT.

There is a widespread availability of machinery suitable for the development and manufacture of multiparticulates in the pharmaceutical industry, which is another driving factor for popularity of this drug delivery technology. Most pharmaceutical companies have small- to large-scale fluid bed technology with various setup options to handle multiparticulates and, therefore, enable development of desired formulations using various design approaches with polymers in aqueous or solvent-based systems. In addition, there is a wealth of knowledge and know-how around this technology in the literature, among suppliers of raw materials, polymers, and machine manufacturers serving formulation scientists achieve their desired formulation design and finish drug products. This book is an accumulation of experiences, thoughts, and best practices offered by leading experts from academia, users, and manufacturers. It is complementary to *Multiparticulate Oral Drug Delivery*, a book edited by Isaac Ghebre-Sellassie and published by Marcel Dekker, Inc. in 1994, with a view to update some of the content and add recent advances related to the

technology. This book is intended for scientists who are new or already familiar with the multiparticulate technology, whether in the academia or in the industry. It is based on science and practice which provides the readers with knowledge of various choices available to formulate, scale-up, and test the quality and performance of multiparticulates.

The manufacture of inert starter seeds, mainly based on sugar spheres and their functionally related characteristics, has been discussed in Chap. 2. These starter seeds are then used for drug layering and further processing based on target release profiles. Alternative methods for the development and manufacture of multiparticulates such as extrusion-spheronization, mini-tabs, and microencapsulation where drug is included in the core of the multiparticulates are discussed in Chaps. 3, 5, and 6, respectively. Majority of processing of multiparticulates are carried out using a fluid bed machine, and the late David Jones, who was the undisputed subject matter expert in this area, described the fundamentals of fluid bed technology with special emphasis on process robustness and scale-up in Chap. 4. Polymers are generally used to coat the drug bearing multiparticulates in order to modulate the release of the drug. The most commonly used functional polymers for these purposes: poly(meth)acrylate copolymers and ethylcellulose have been described, with specific case studies for their unique applications, in Chaps. 10 and 11, respectively. In most cases, multiparticulates are filled into hard shell capsules as described in Chap. 13 or on occasions, they are compressed into tablets. In recent years, there has been a major interest in special applications of multiparticulates for fixed dose combinations and pediatric formulations, and Chaps. 7 and 9 cover these important topics. Chapters 8, 12, and 14 discuss at length the characterization of multiparticulates. While Chap. 12 describes various ways for in-line characterization of multiparticulates, Chap. 8 discusses the dissolution testing of the final formulation and how to relate these data to *in vivo* performance (Chap. 14).

I would like to express my special thanks to all contributors who allocated their time and effort to prepare their respective chapters, review the others, and help me bring this book to completion.

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