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These books were intended to fulfill the need to provide in one place a concise summary of the making and filling of capsules, and of developing formulations for capsules. We are honored to have the opportunity to join the efforts of these prior editors in providing an updated discussion and description of capsule formulation and filling technology and the role of capsules in drug delivery. We are especially honored that Fridrun Podczeck, Brian E. Jones, and J. Michael Newton, editors and/or authors of chapters of those earlier books, have also contributed to this book.Advances in Capsule Formulation Development and TechnologyAmong solid dosage forms, the capsule is second only to the compressed tablet in a frequency of utilization for drug delivery, and the hard shell capsule continues to be the more frequently used form. Because hard shell capsules are often perceived as “simpler” than other oral dosage forms, they are frequently the first dosage form administered to humans and sometimes the final marketed dosage form. Even when the marketed product is to be a tablet, firms may sometimes make a tablet formulation and initially fill it in hard shell capsules to facilitate clinical testing. During the past 15 years or so, there have been several interesting and important advances in capsule formulation science and technology, including (1) alternative (to gelatin) shell compositions and enhanced shell function such as enteric capsules, (2) unique drug delivery systems, (3) using capsules to manage poorly soluble drugs, (4) filling small doses of drugs into capsules without excipients, (5) capsule filling machine simulation, and (6) application of artificial intelligence and other modeling methods in support of formulation development and Quality by Design (QbD).An Introduction to Two-Piece Hard Capsules and Their Marketing BenefitsTwo-piece hard capsules are a well-established dosage form that provides solutions to many of today’s drug delivery and nutraceutical formulation challenges.1 Widely used in the pharmaceutical and nutritional industry for more than a century, two-piece capsules are still a recognized and trusted dosage form.2 When viewed as an empty container, they are highly flexible and amenable to many fill material types including powders, granulations, pellets, minitablets, semisolids, and liquids.3 Uses for two-piece capsules are equally flexible, including immediate release, sustained release, enteric release, clinical blinding, inhalation therapy, and vaccines.4,5 While the majority of hard capsules are composed of gelatin, hydroxypropylmethylcellulose (HPMC) has emerged as a naturally-sourced, lower water content alternative offering further flexibility to the formulator.Modern drug discovery has yielded insoluble and complex molecules that challenge the pharmaceutical formulator to develop an orally available dosage form while meeting aggressive timelines. Likewise, the nutraceutical formulator is under even more aggressive development timelines and is usually constrained by the inability to use traditional formulation aids such as binders, flow aids, and disintegrants. For both formulators, the hard capsule typically offers a quicker and simpler developmental path than tablets, resulting in a faster time to market and considerable cost advantages.Hard capsules are available in a wide range of sizes to meet most requirements. Colorants and printing options improve product identification and product branding, aid in anti-counterfeiting, and help improve patient compliance. 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Pharmaceutical drug delivery embraces a range of delivery carriers and constructs that have dimensions ranging from several nanometers (nanotechnology) to numerous millimeters (conventional dosage forms, i.e., pellets, tablets, and capsules). Such delivery systems spawn a whole array of assemblies for delivery of highly potent active drugs through different routes of administrations to numerous sites and targets in the human or animal body to treat disease conditions. Such delivery types and carrier systems, with their relative sizes together with some molecules and bacterial cells, are shown in Figure 12.1. Invented more than 160 years ago, the capsule today is second only to the compressed tablet among solid dosage in frequency of utilization for drug delivery, and its utilization is growing. According to one estimate,* approximately 10–15% of FDA-approved drugs in 2014 were capsule formulations, about double that in 2007. 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