1.2 The Preformulation Focus

While the nature of drugs has changed rapidly, the science of preformulation remains traditional—to deliver, we must first know what we are delivering. The drugs developed today fall into three main categories: small molecules, large molecules, and botanical extracts. The preformulation work required for each category is quite different from the others. The classic small-molecule chemistry involves the measurement of solubility, pK_a, crystallinity, polymorphism, and so on. For large molecules, particularly proteins and peptides, often, the 3D structure or even interaction with formulation components requiring a four-dimensional (4D) evaluation of drugs in solution must be studied. Botanical extracts, the oldest class of drugs, are now the newest category for the preformulation scientist, as the regulatory authorities such as the U.S. FDA and the European Medicines Agency (EMA) have established guidelines for their approval. For botanical drugs (often called phytomedicines in Europe), the fingerprinting methods using thin-layer chromatography (TLC), infrared (IR), or mass spectrometry (MS) are more relevant.

The preformulation of botanical drugs presents a different set of understanding; the uncertainty of the chemical or biological structures involved, the use of extracts that are difficult to characterize, and the variability of the cultivar involved, all offer many scientific challenges. However, these challenges also offer many new opportunities for bringing in new science that will allow us to better understand how drugs work.

1.3 Development Phases

The development of NAEs undergoes a lengthy and expensive cycle that varies greatly depending on the type of drug developed. What follows is a typical development cycle.

1.3.1 Stage 1: Lead Finding or Establishing Directions (1–2 Years)

These are studies to understand how alteration of a biological function or mechanism would create a therapeutically useful entity or process. The strategic research of a particular company is usually guided by factors such as its inherent research competence and expertise, therapeutic areas of unmet medical need, and market potential. Market potential is the strongest motivation, and as a result, companies invest heavily in specific therapy areas. It is not difficult to label companies as cardiovascular, anticancer, endocrine, or other such focused companies. It takes years, often decades, to pool the scientific and clinical expertise that would provide the combination of elements necessary for efficient new discoveries. However, in recent years, many large companies have begun to look outside for new drug leads; smaller research companies have often proven more efficient. Outsourcing of research, even at the level of research lead compounds, is now a common place, and companies such as Abbott Laboratories have developed an expertise in securing new drugs from the outside vendors. The in-house expertise development is limited not only to scientific expertise to provide a specific direction but also at times to a specific type of product, such as biological drugs versus the small molecules, innovative drug delivery systems versus the traditional systems, and so on.