program required by the EMA is one such example. It is important to recognize that it is during this phase of studies that drugs are recalled. The most recent example of the recall of the cyclooxygenase (COX)-2 selective inhibitor medication Vioxx (generic drug name is rofecoxib) (Merck) in September 2004 shows the importance of this phase of study. Although the studies of phases I–III are expensive to conduct, a failed phase IV study can bankrupt companies.

Given the statistical reality that only one of the 5000 lead compounds reaches the market, the amortized cost over the entire development program has exceeded the billion-dollar mark for each new approval; however, for the molecule in question, it may range from $100 million to $300 million, depending on the complexity of the testing involved.

According to pharmaceutical research-based manufacturers (PhRMa), the representative body of the research-based pharmaceutical companies, in 2017, 20 top PhRMa member companies invested an estimated $100 billion in research to develop new treatments for diseases.

1.4 Phytomedicines

The search for and the exploitation of natural products and properties have been the mainstays of the biotechnology industries. However, natural product search and discovery are not synonymous with drug discovery. But, if we examine how novel natural product chemotypes along with interesting structures and biological activities continue to be reported, this becomes the mainstay of drug discovery, as it has been in the therapeutic areas, such as neurodegenerative disease, cardiovascular disease, most solid tumors, and immune-inflammatory diseases. Today, well over half of the drugs are either directly derived from biological sources or have been produced as a result of biodiversity evaluation. Antibiotics remain the largest sellers of all drugs. Significantly, however, the reported discovery of microbial metabolites with nonantibiotic activities has increased progressively over the past 30 years and now exceeds that of antibiotic compounds.

One prerequisite of natural product discovery that remains paramount is the range and novelty of molecular diversity. This diversity surpasses that of combinatorial chemical libraries and consequently provides unique lead compounds for drug and other developments. Newly discovered bioactive products do not usually become drugs per se but may enter a chemical transformation program in which the bioactivity and pharmacodynamic properties are modified to suit particular therapeutic needs. In recent years, most regulatory authorities worldwide have carved out a path to approve natural products, without having to identify the exact active ingredients of their specifications. The use of markers is suggested, and greater emphasis is placed on characterization of extracts. This means a greater involvement of the preformulation group in drug discovery for natural or botanical products. Recent efforts to harmonize standards are evident from the monographs developed by the American Herbal Pharmacopoeia. Another major effort is the European Scientific Cooperative on Phytotherapy (ESCOP). It was founded in June 1989 as an umbrella organization representing national phytotherapy associations across Europe, especially in their discussions with European medicine regulators. Since 1996, it has been a company in the United Kingdom. Its goals are to advance the scientific status