

1 INTRODUCTION

By definition, the word *natural* is an adjective referring to something that is present in or produced by nature and not artificial or man-made. When the word *natural* is used in verbiage or written, many times it is assumed that the definition is something good or pure. However, many effective poisons are natural products [145]. The term *natural products* today is quite commonly understood to refer to herbs, herbal concoctions, dietary supplements, traditional Chinese medicine, or alternative medicine [72]. That will not be the case in this chapter. The information presented here will be restricted to the discovery and development of modern drugs that have been isolated or derived from natural sources. While in some cases, such discovery and development may have been based on herbs, folklore, or traditional or alternative medicine, the research and discovery of, along with the development of, herbal remedies or dietary supplements typically present different challenges with different goals [93, 152]. So while the stories of herbs and drugs are very much intertwined, it needs to be fully appreciated that the use of herbs as natural product therapy is different than the use of herbs as a platform for drug discovery and further development.

2 HISTORY AND BACKGROUND OF THE USE OF NATURAL PRODUCTS AS THERAPEUTIC AGENTS

Natural products are generally either of prebiotic origin or originate from microbes, plants, or animal sources [115, 116]. As chemicals, natural products include such classes of compounds as terpenoids, polyketides, amino acids, peptides, proteins, carbohydrates, lipids, nucleic acid bases, ribonucleic acid (RNA), deoxyribonucleic acid (DNA), and so forth. Natural products are not just accidents or products of convenience of nature. More than likely they are a natural expression of the increase in complexity of organisms [76]. Interest in natural sources to provide treatments for pain, palliatives, or curatives for a variety of maladies or recreational use reaches back to the earliest points of history.

Nature has provided many things for humankind over the years, including the tools for the first attempts at therapeutic intervention [115, 116]. Neanderthal remains have been found to contain the remnants of medicinal herbs [72]. The *Nei Ching* is one of the earliest health science anthologies ever produced and dates back to the thirtieth century BC [115, 116]. Some of the first records on the use of natural products in medicine were written in cuneiform in Mesopotamia on clay tablets and date to approximately 2600 BC [29, 30, 115, 116]. Indeed, many of these agents continue to exist in one form or another to this day as treatments for inflammation, influenza, coughing, and parasitic infestation. Chinese herb guides document the use of herbaceous plants as far back in time as 2000 BC [72]. In fact, *The Chinese Materia Medica* has been