leads generated from chemical libraries and considers what role natural products could play here.

Keywords
Diversity-oriented synthesis • Drug discovery • Fragment-based drug discovery • Natural products • Privileged structures • Unexplored natural product sources

1 Introduction

For thousands of years, man has found sources in nature to treat his ailments. With the emergence of early civilizations and the development of written language, soon the first efforts were made to record medical practices. Of course, many of the described remedies were heavily influenced by religious practices or superstition and were ineffective, but some are still used today, such as morphine (**1**) as analgesic from the *Papaver somniferum* plant (first described by the Mesopotamians) and artemisinin (**2**) as anti-malaria agent from the *Artemisia annua* plant (first described in Chinese traditional medicine) (Fig. 1).

The emergence of organic chemistry in the nineteenth century enabled the synthesis, extraction, and modification of natural products to improve their usefulness as medicines. Added to that, increased interest in microbiology led to the realization that many diseases are caused by pathogens.

While the first compounds developed to combat these pathogens were synthetic compounds (e.g., the sulphonamides by G. Domagk), the serendipitous discovery of penicillin from *Penicillium chrysogenum* by Fleming in 1928 gave a large boost to natural product research. Not long after the successful introduction of penicillin, many more classes of antibiotics from natural sources were discovered as well as other compounds with useful bioactivities such as immunosuppression (cyclosporin A), cytotoxicity (taxol), and cholesterol lowering (lovastatin). These compounds had a major impact on healthcare and therefore contributed to a considerable increase in life expectancy and quality of life during the second half of the twentieth century in the western world. Thanks to these success stories, interest in natural product research was at an all-time high.

However, the development of high-throughput screening (HTS), combinatorial chemistry, and fragment-based screening led to a decreased interest in natural

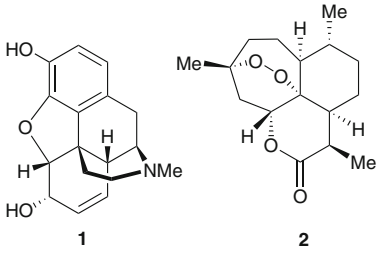

Fig. 1 Structures of morphine (**1**) and artemisinin (**2**)