

Short Commentary

The Total Synthesis of Naturally Occurring Compounds in the Development of New Drugs for the Diseases Treatment

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Commentary

Science is in continuous development to provide the higher life quality to the human beings as well as alive species over earth. Several efforts had been carried out to address common and hard health problematics form different ways. The development of new drugs-based diseases treatment is one of the powerful tools in medicine, providing relief to a certain suffering. In this sense, the nature contains an excellent pool of chemical nucleus available with demonstrated activity against an specific issue which is the result of the innate evolutive development [1]. These chemical compounds (secondary metabolites) represents one of the most plausible, razonable and excellent starting points of research looking for new drugs in the treatment of diseases [2]. The aforementioned compounds could come from different “natural sources” like plants, fungi and marine sponges among the most representatives [3]. Specifically these natural secondary metabolites are called “Naturally Occurring Compounds” or simply “Natural Compounds”.

The natural compounds has been topic of continuos interest for the organic-synthetic chemist. Because their molecular ar-

chitecture so often represents a synthetic chemical challenge, and also the preliminary biological activity found it inspire them to test them [4]. Strong expectations around their preparation such as obtaining enough amount of compound for preclinical evaluation and the opportunity to prepare “analogues” which can be pharmacologically superior to the natural found them, are all the time in the chemist mind. These two points, the scalability [5] and the opportunity to generate molecular diversity [6] represent the main impact of the total synthesis of naturally occurring compounds in the development of new drugs for the deseases treatment. In such a way that starting from natural compounds it has been possible to develop several pharmacological treatments at industrial scale, which has allowed it to be available around the world. Here in is described few of the most representative examples in which the total synthesis of natural compounds resulted in approved pharmaceutical treatments.

Analgesic and Anti-inflammatory Treatments

One of the more famous analgesic and anti-inflammatory compounds, the aspirin 2, was obtained from natural compound salicin 1 isolated form the bark of *Salix alba* tree [7]. It is currently worldwide used as primary treatment in dosages for children (100 mg) and/or for adult (500 mg) (Figure 1). Aspirin represents one of the oldest and succesful treatments continuously in the market.

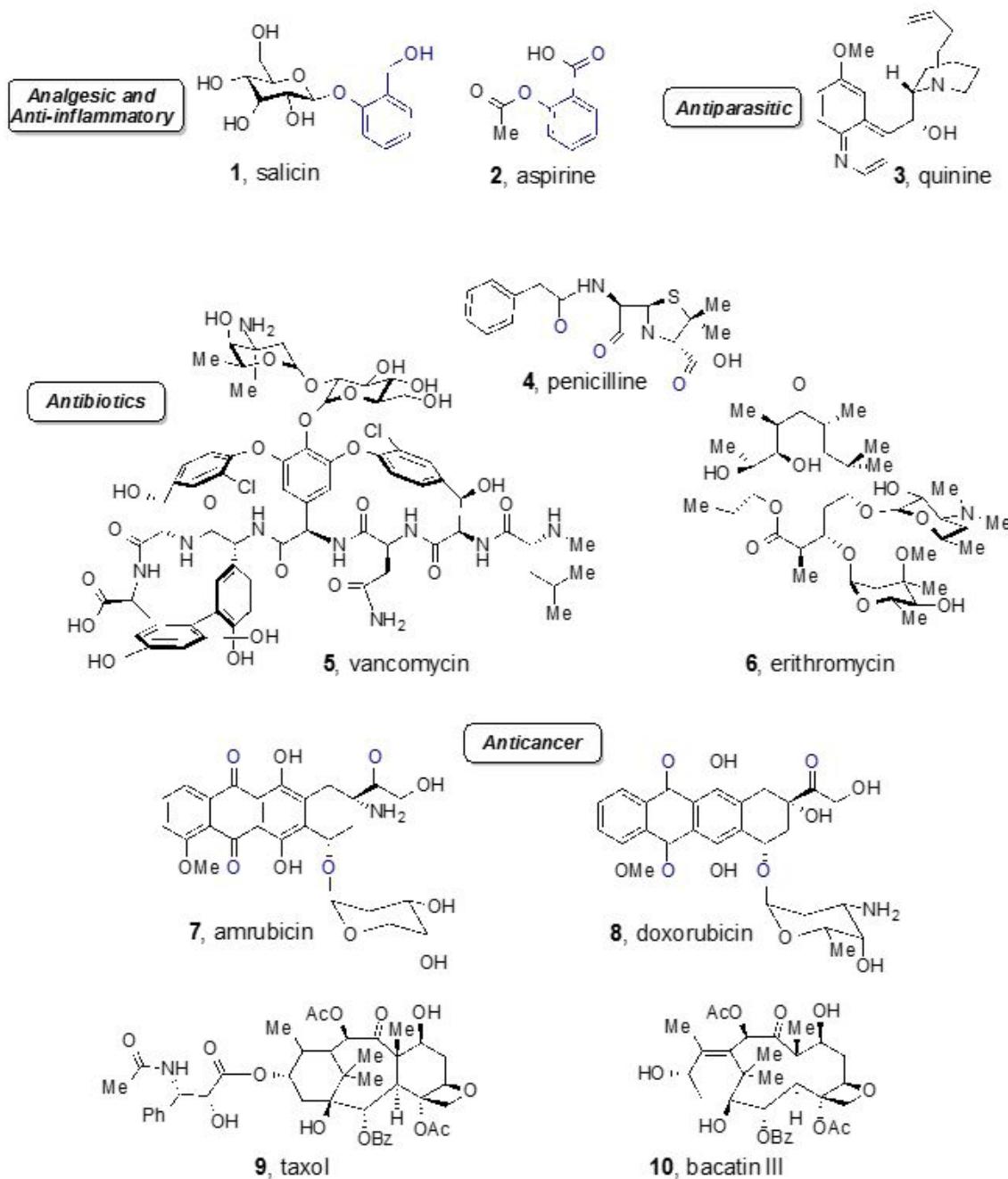


Figure 1: Some naturally occurring compounds which became into approved drugs for the treatment of different diseases.

Antiparasitic Treatments

The potent antimalarial quinine **3**, is a natural compound obtained from the bark of the *Cinchona* sp. tree. This was broadly used against *Plasmodium falciparum*, becoming as the election treatment in the strongest cases of malaria, mainly in Africa [7] (Figure 1). The use of quinine becomes a powerful tool in the treatment of this parasitosis when the resistance to chloroquine was found. However, now a days its administration is just recommended if artemisinin or artesuante derivatives are not available.

Antibacterial Treatments

Impossible not to mention the serendipitous discovery in 1929 by Alexander Fleming of penicillin **4** [8]. This is one of the most important contribution into the bactericidal drugs. The industrialization of penicillin started with the antibiotics age and were the following generations like cephalosporins whose structures were based upon naturally occurring penicillin. Now day penicillin is a first stage treatment in bacterial infections (Figure 1). On the other hand, the advanced and more difficult cases of bacterial infections are successfully addressed with the glycopeptide-lactamic antibiotic vancomycin **5** as well as the glycopeptide-lactonic antibiotic erythromycin **6**. These two tremendously efficacious macrolides have been used as treatment in cases of bacterial resistance [9, 10]. Both were naturally synthesized by *Amycolatopsis orientalis* and *Saccharopolyspora erythraea* respectively (Figure 1).

Anticancer Treatments

Amrubicin **7**, is another singular example of natural compound which led to doxorubicin (Adriamycin®) **8** after minor chemical modifications. Although both of them are synthesized by *Streptomyces* sp. and they were used as approved drug for different cancer diseases, doxorubicin is broadly more used. Its effectiveness in the treatment of acute leukemia, lung and thyroid cancer, bone sarcomas as well as the Hodgkins and non-Hodgkins lymphoma has been fully demonstrated [9]. This drug constitutes one of the more helpful treatments coming from a natural product (Figure 1). On the other hand the natural compound taxol (Paclitaxel®) **9**, was initially extracted from the *Taxus brevifolia* bark. The nucleus is highly efficient in the ovarian, breast, lung, cervical and pancreatic cancer treatment. Additionally has been found excellent activity in the Kaposi sarcoma. The biosynthetic precursor of taxol in the *Taxus* tree is the baccatin III **10**, which constitutes an excellent nucleus for taxol derivatization [11] (Figure 1).

These ten natural compounds are only few of the more representative examples of naturally occurring compounds which became successful treatments in very different health areas. Moreover is absolutely important to highlight the fact that total

synthesis has an enormous impact in the development of new alternatives to address a particular or general illness. Since it allows us to scale up the natural amount of compound provided by nature and take over to the industrial process. Additionally the total synthesis give us the opportunity to synthesized chemically relevant analogs, and getting a derivative with higher pharmacological activity.

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