Editorial

"Alkaloids in Nature: Synthesis, Isolation and Pharmacological Applications" Part 2

It is quite known that the nitrogenous compounds isolated or synthesized in nature have been used by their different therapeutic and medicinal properties around the world, nevertheless, not all the well-known compounds have been tested in many of the current diseases that affect to our society. Indeed, many alkaloids isolated from sponges, crustaceans, for instance, possess very innovative and interesting chemical moieties for the development of new drugs. In general the alkaloids that we have mentioned in the previous Issue (Part 1) are a small but very revealing family of terrestrial and marine alkaloids that important authors have mentioned by means of reviews or research works.

In this sense, the logical contribution of this wide family of nitrogenous compounds of an unusual structural diversity as well as of its biological activity will be framed in some alkaloids that will be emphasized by new authors and their lines of research in this PART 2. Firstly, we will emphasize some reports of the phenanthroindolizidine alkaloids and pharmacological applications [1], or some interesting syntheses of these compounds, featuring an unusual amidyl radical 5-exo/5-exo cyclization/rearrangement cascade of a xanthate precursor [2].

Another interesting alkaloid family mentioned in this issue are the marine ascidians, marine invertebrate filter feeders, that belongs to a promising resource for bioactive compounds. Thus, a recent report including to 2 species of marine ascidians, *Aplidium elegans* and *Ciona edwardsii*, collected in Mediterranean area, led to isolation of a series of alkyl sulfates including 3 new molecules. In order to know effects on the growth of 2 cell lines, J774A.1 (BALB/c murine macrophages) and C6 (rat glioma) in vitro, such compounds were tested and show a selectivity onto J774A.1 cells [3].

Finally, some examples that will be mentioned later on are the marine bromopyrrole alkaloids. Certain examples with chalcone, isoxazole and flavone structural features have been synthesized and evaluated for *in vitro* anticancer activity by MTT assay against five human cancer cell lines with interesting pharmacological data [4].

All reports of these compounds and their natural sources will be described with several therapeutic applications, taking into account the benefits and projections of a wide and heterogeneous family of alkaloids. However, we want to highlight an important contribution of the description of synthetic and natural drugs in the medicinal chemistry. Thus, by using the words of Dr. Henning Steinhagen [5], "*the global pharmaceutical industry has been in a widely proclaimed productivity and identity crisis. Megamergers, massive layoffs in the research & development sector and heavily increasing outsourcing seem to be the prime responses in the hope for a cure. Prior to that, especially the quantitative approach —"the numbers game"—* to drug discovery had largely failed in the delivery of novel, breakthrough, disease-modifying rather than only symptom-relieving medicines". Dr. Steinhagen used these words in a review to a medicinal chemistry book. The book in question entitles "The Evolution of Drug Discovery: From Traditional Medicines to Modern Drugs" [6].

In order to continue with our special issue *"Alkaloids in nature: synthesis, isolation and pharmacological applications"* Part 2, we have again collected important contributions in the field of the alkaloids of different chemical frameworks, some extent to novelty synthetic ways, and unusual pharmacological applications, that they will contribute to understand the interest for these drugs used in several therapeutic treatment and with minor side effects known at the present.

This special issue contains 9 articles between mini-review, review and research articles. In addition, wherever appropriate, illustrations, flow charts or tables for easier and straightforward understanding of the contents are presented.

The first article of this special issue mentions the phenanthroindolizidine alkaloids as a well-known class of compounds due to their interesting biological activities, especially anticancer ones. Represented by more than 60 substances, they are mainly isolated from plants of the Moraceae and Asclepiadaceae families. The second article of Prof. Derosa shows us in particular to berberine as a quaternary ammonium salt from the protoberberine group of isoquinoline alkaloids with anti-lipogenic and hypoglycemic effects. The next article presents an intensive research effort during the last 25 years affording an impressive number of alkaloids isolated from marine ascidians, which remain unique among marine invertebrates in that they overwhelmingly produce this kind of metabolites. The four research article from Prof. Miyairi is based in a short review focuses on recent achievements in the field of asymmetric carbon-nitrogen atom bond formation reactions using cinchona alkaloids and their derivatives. The next article to mention the ability of 7*H*-naphtho[1,2,3-*de*]quinolin-7-one derivatives in the treatment of behavioral disorders as psychosis.

The sixth contribution by Cebey *et al*. describes the antidepressant effects of oxoisoaporphines by using as pattern control the *trans*-resveratrol and through a Forced Swimming Test (FST). The seventh contribution of Prof. Kittakoop is referred to alkaloid scaffolds in drugs, particularly those recently approved in 2012; it also covers the scaffolds in leads and drug candidates which are in clinical trials and preclinical pipeline. The eighth contribution mentions to bromopyrrole alkaloids that constitute a family of exclusively marine alkaloids and represent a fascinating example of the large variety of compounds formed by marine sponges which exhibit different biological activities such as antifeedent, anti-biofilm, anticancer, antiinflammatory,

antimicrobial, immunomodulatory, analgesic, antiserotonergic, antiangiogenic, antihistaminic, chitinase inhibitor and actimyosin ATPase activator. Finally, Prof. Larsson to mention in his contribution to the colchicine and related phenethylisoquinoline alkaloids from the family Colchicaceae.

This second part of the review of alkaloids isolated and synthesized by different methods shows an extent contribution in the scope of the medicinal chemistry, and the possibilities of direct applications in the treatment of diseases as diverse as mood behavioral, anticancer, parasitology, etc. Our contribution in the field of natural products is absolutely highlighted and diverse, including pharmacological data and experimental procedure of some chemical frameworks of alkaloids most relevant at the present. We hope this issue in its two parts will be a guide of knowledge of the alkaline compounds present in many drugs used either as common salts or in supramolecular systems as drug delivery.

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