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Editorial

Special Issue on "The Design, Synthesis and Biological Evaluation of Compounds with Medicinal Value"

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1. Introduction

During the last few decades, in industrialized countries a significant increase in infectious, cardiovascular, inflammatory and neurodegenerative diseases was registered, as well as different forms of cancer, diabetes, and so on [1–4]. Among them, microbial infections and cancer are still the major causes of death among the world population due to the increased drug resistance phenomena. For these reasons, there is an urgent need to design and synthesize new antimicrobial agents, particularly active against Gram (-) pathogens, that could be used to fight drug resistance. Along with them, there is the need of new antineoplastic drugs with higher selectivity on tumoral cells, which are able to overcome cancer cell resistance with moderate side effects.

Recently, some delivery systems have been proved particularly effective as antimicrobial and anticancer carriers due to the targeted drug delivery at the action sites, reduced drug-resistance and side effects, and the increased therapeutic index.

In this scenario, the Special Issue "*The design, synthesis and biological evaluation of compounds with medicinal value*", which includes the 13 latest original papers, will allow us to deepen and develop innovative research regarding the above mentioned relevant topics.

2. Promising Scaffolds in Medicinal Chemistry

The study of privileged scaffolds in medicinal chemistry supplies scientists with a solid start in the search for new and improved therapeutic molecules. In this Special Issue, in which 39 papers were submitted and 13 of them were published, some interesting and promising scaffolds with antimicrobial, antitumor, and antioxidant properties and with the ability to act on various cellular targets are reported.

In particular, three papers focus on the antimicrobial properties of new synthesized compounds. In the first one, Rastija V. et al. [5] reported a series of 4,5–dihydro-1*H*-pyrazole derivatives that have been tested for their antibacterial properties towards four bacterial strains: *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis* and *Staphylococcus aureus*. Among them, 5-(2-chlorophenyl)-3-(4-fluorophenyl)-4,5–dihydro-1*H*-pyrazole-1-carbaldehyde has been shown to be a strong inhibitor of the monophenolase activity of mushroom tyrosinases. For the prediction of the activity for phosphodiesterase inhibition, docking studies have also been performed.

The second paper, authored by Spina C. et al. [6], concerns the metal complexes that have recently been considered with success for many applications in medicinal chemistry [7–11].

Particularly, silver complexes were employed as antimicrobial agents [12], and, recently, novel silver compounds in higher oxidation states, Ag(II) and Ag(III), have emerged as desirable alternatives to existing forms of antimicrobial agents. In this context, Spina C. et al. present a facile and one-pot strategy for the preparation of a higher oxidation state silver-silica gel, Ag_7NO_{11}:SiO_2, framework based on the direct oxidation of silver nitrate from an oxidizing alkali silicate aqueous solution. The corresponding characterization, thermal

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stability, aqueous degradation, and antimicrobial efficacy of the Ag_7NO_{11}:SiO_2 framework have also been evaluated [6].

Urease is a therapeutic target associated with several important diseases and health problems [13,14].

Ali M. et al. in the paper "Enamine Barbiturates and Thiobarbiturates as a New Class of Bacterial Urease Inhibitors" [15], exploiting the privileged structure assigned to the (thio)barbiturate (pyrimidine) scaffold, tested the capacity of two (thio)barbiturate-based compound collections to inhibit bacterial urease.

Various compounds have, in fact, been reported to be potential candidates for the treatment of certain clinical conditions caused by bacterial ureases [16].

Therefore, in this third paper [15], several compounds endowed with higher activity than acetohydroxamic acid, used as a standard tested compound, have been reported. Thanks to the conformational and docking studies, energetically low-lying conformers and the binding mechanism of these new pyrimidine derivatives have been identified as urease inhibitors.

Cancer is a high-incidence and life-threatening disease. Nowadays, high-income countries (HIC) continue to have the highest incidence for lung, colorectal, breast, and prostate cancer, although some low- and middle-income countries (LMIC) now count among those with the highest rates [17,18].

One of the major challenges for relieving its burden is to develop highly effective drugs with few/no side effects on normal mammalian cells [19–21].

In this area, three other papers focus on the anticancer activity of heterocyclic molecules.

In particular, in the first article [22], a series of novel N-benzylisatin-aryl-hydrazones was designed, synthesized and evaluated for antimicrobial and antiproliferative activities with SAR and ADME studies, aiming to develop anticancer drugs with no antimicrobial, yet high antiproliferative activities. These synthesized hydrazones, indeed, revealed no effects on any of the strains of bacteria and fungi up to 100-µg/disc concentration. However, four compounds showed two-to-four fold antiproliferative activity over Gefitinib [22].

The imidazole ring is an important scaffold in medicinal chemistry, as several derivatives have shown a wide array of biological activities [23–25]. A second paper [26] reports a series of 2,4,5-triphenyl imidazole derivatives for their activities as antiproliferative, antioxidant, AChE, and XO inhibitor compounds, designed in order to find new leads with these biological profiles. To confirm the in vitro evaluations, molecular docking and in silico analysis of their ADME properties were made. These studies allowed the selection of the best candidates and set the path for studies on new drug families [26].

Another paper, authored by Islam M. S. et al., [27] reported the synthesis of highly functionalized spirooxindoles analogues, via a single step, multicomponent, one-pot reaction, which is a very versatile method in medicinal chemistry [28].

These compounds were then tested in vitro for their antiproliferative effects against three cancer cell lines, namely, HepG2 (liver cancer), MCF-7 (breast cancer), and HCT-116 (colon cancer). A spirooxindole of the series exhibited broad activity against this panel of cell lines when compared to *cis*platin. Modeling studies, including shape similarity, lipophilicity scores, and physicochemical parameters were calculated [27].

Another paper [29], in the area of the drug delivery systems, concerns the development of a sol–gel-based coating used as an entrapping polymeric cross-linked network for an N-palmitoyl-ethanolamine (PEA) derivative, 2-methyl-pentadecanoic acid (4-nitro-phenyl)-amide or N-palmitoyl-(4-nitro-phenyl)-amine (PNPA), with anti-inflammatory and antioxidant properties.

Finally, Iacopetta D. et al. [30], in the context of supercritical fluid technology and as an innovative method to extract nutraceuticals from natural matrices, reported the extraction of nutraceuticals as polyphenolic compounds from plant matrices, such as the cactus pear, able to prevent and treat several chronic-degenerative diseases.

3. Nutraceuticals: A New Challenge for Medicinal Chemistry

In recent years, there is a growing interest in nutraceuticals for their health promoting or disease-preventing effects. Various nutrient, herbal and dietary supplements able to act against various disease conditions and thus promote quality of life are studied and reported in the literature [31–35].

In the Special Issue "*The Design, Synthesis, and Biological Evaluation of Compounds with Medicinal Value*", three reviews have been published in this area: one concerning the health-promoting properties of pomegranate and its bioactive compounds against principal human pathologies [36], another one that deepened the beneficial effects of β-Caryophyllene, a natural bicyclic sesquiterpene [37], and the last one that systematically analyzed the effects of Tinospora cordifolia-derived phytocomponents on cancer [38].

4. Others

In the Special Issue, other interesting topics have been developed.

Surgical site infection (SSI) is a frequent complication of surgical procedures. Ceresoli M. et al. [39] have critically analyzed the role of triclosan-coated sutures (TCS) on SSI prevention in abdominal surgery. A cost analysis to provide a more comprehensive representation of the value of this technology in clinical practice has also been reported.

Sender-Janeczek et al. [40] have reported new local drug delivery with antibiotics in the nonsurgical treatment of periodontitis. The effectiveness of the activity of the piperacillin and tazobactam combination in the form of an intrapocket-administered chemotherapy has been assessed.

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