Editorial

Current Developments in Organochalcogens Chemistry

J. B. Teixeira da Rocha

After the discovery of dozens of selenoproteins in living species and the clinical applications of 2-phenyl-1,2-benzisoselenazol-3(2*H*)-one (ebselen) in neuro-pathologies, the interest in organochalcogen chemistry has significantly bloomed [1]. By searching online database (Scopus/PubMed), more than 600 and 1500 research articles can be accessed for diphenyl diselenide (the janus-faced compound) and ebselen respectively, which provides an in-depth insight about their diverse pharmacological and toxicological potencies. Mechanistically, the biological role of sulfur and selenium (in living tissues) can be attributed to their functional groups, *i.e.* sulfhydryl (-SH) and selenohydryl (-SeH) groups. The –SH and SeH are soft nucleophiles that can catalyze redox reactions. In the same vein, the synthesis of new organochalcogens has been extensively stimulated by the intention of imitating selenoproteins; particularly, the antioxidant enzyme glutathione peroxidase (GPx). Consequently, an infinity of organic compounds of selenium and tellurium that can mimic the reactions of GPx has been observed in the last 30-40 years. However, the pharmacology and toxicology of such Gpx-like compounds have been tested only in a few number of cases.

Here in this volume "Current Developments in Organochalcogens Chemistry", we provide a general picture of the use of the three chalcogens (S, Se and Te) in chemistry and biochemistry [2-10]. It will become evident that much more research is needed about the chemistry and the potential pharmacological use of these agents to treat human pathologies. Furthermore, there are still gaps or connectivity in our knowledge about these versatile elements. Basic research about the synthesis, theoretical, chemical and biochemical behavior of novel chalcogenides will certainly increase our understanding about their possible technological or therapeutic applications.

Here in this special issue, the versatility of organochalcogens as electrophiles reagents can be seen in the excellent reviews of Santi and collaborators [9] and Potapov and collaborators [6]. In accordance with the versatility of chalcogens, Drabowicz [3] gives an overview of the synthesis of chiral hypervalent derivatives of sulfur, selenium and tellurium, including some with potential biological activity (for instance, via degradation of peroxide). Regarding the biological application of inorganic and organochalcogens, we are reaching to a bottleneck and it is clear now that we will need more rational *in silico* approaches to the synthesis of new compounds directed to interact with specific biological targets. The use of bioinspiration principle in organochalcogens synthesis has offered promising agents to the pharmacologists. For instance, here in this volume, Arai and Iwaoka [2] give us an extraordinary example of some bio-inspired tetrahydroselenophene derivatives, with very interesting biological properties. Regarding the synthesis of bioactive organoselenium compounds, Braga and collaborators [8] offer the readers a comprehensive review about the 5-membered heterocycles containing selenium and emphasize the importance of developing new members of this class of biologically active compounds.

Taken together, it is clear that more toxicological and pharmacological studies are required in the organochalcogen field; however, the number of compounds to be tested *in vitro* and *in vivo* is immeasurably great. Thus, to solve this conundrum of what compounds should be tested biologically, we will need detailed new *in silico* computational studies. The task is not simple, but as can be read in the interesting review of Wolters and Orian [10], computational tools can be used to guide the synthesis of new compounds with high probability of finding a target both in terms of reactivity, energetic and specificity of interaction. Though computational methods cannot predict the exact behavior of a chemical inside the complex biological environment, they certainly will give to the chemists and molecular pharmacologists cues that will guide the synthesis of more efficient agents than those synthesized on empirical grounds.

In fact, the question of the narrow window between the pharmacological and toxicological properties of organochalcogens can be seen in the review of Puntel and collaborators [7] about the toxicity of simple diaryldichalcogenides and ebselen in isolated mitochondria. This is particularly intriguing in view of the recent studies showing the mitochondrial protective effects of diphenyl diselenide in rodents and mammalian cells [11-14]. Regarding the use of redox active sulfur compounds in pharmacology, the review of Jacobs and collaborators [4] gives us a concise and impressive picture about the emerging field of polysulfides and polysulfanes. They elegantly indicate that the chemistry, biochemistry and pharmacology of inorganic and organic sulfur compounds need to be studied in much more detail. In fact, this is somewhat paradoxical, because sulfur has much broader roles in life than selenium, but sulfur has been less explored as redox active compounds than selenium. In short, the interest in the chemistry of chalcogens has a long history, but the exploitation of chalcogens as technological or pharmacological agents is still incipient. Thus, international efforts are needed to discuss and propose alternative and rational pathways to be followed to further develop the field of chalcogens.

These efforts are expected to bring organochalgogens into the technological and therapeutic arsenals available to help humankind. In addition to the traditional *International Conference on the Chemistry of Selenium and Tellurium* that is going to its 13th edition in Japan at Gifu (23rd-27th May 2016), other important examples of collaborative efforts to accelerate the development of the field of organochalcogens can be found around the world [see for instance, the activities of the *Se-S Red Cat Network* at http://sesredcat.jimdo.com/wses/]. However, much more efforts have to be done to impel this promising field of

1875-5348/16 $58.00+.00

chemistry. We modestly hope that this volume stimulates the discussion about the necessity of developing rational and hierarchic approaches, guided by *in silico* methods, to propose the synthesis of new active organochalcogens. New computational methods to deal with the complexity of cellular environment are also highly needed. Similarly, the development of through put *in vitro* technique to test the potential toxicity and biochemical efficiency of organochalcogens are is highly needed.

To conclude, I would like to thank the assistant editor of this special issue, Dr. Waseem Hassan for his dedication, hard work and admirable work ethics.

We also thank all the authors who contributed to this special issue, Miss Abeerah Hashim, the editorial manager, and Prof. Dr. Atta-ur-Rahman, the editor-in-chief of the journal.

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