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Editorial
Special Issue: Biotechnological and medical relevance of ureases



The fact that most enzymes are proteins was demonstrated by the Nobel Prize Laureate James Batcheller Sumner in a work done with urease from *Canavalia ensiformis* (jack bean) extracts. Urease, the first enzyme to be crystallized, has been implicated in nitrogen losses in agriculture when urea is used as fertilizer. The urease activity can also be detrimental to urea-fed ruminant and non-ruminant animals by increasing ammonia in gastrointestinal tract and affecting negatively nutrient absorption and animal growth performance. The occurrence of some microorganism-triggered diseases has been attributed to ureases. This special issue brings compilations on biotechnological aspects of ureases in agricultural, livestock, medical and engineering settings, and highlights the progress on the development of urease inhibitors of pharmacological interests.

The first article introduces the general facets of ureases. In their article, Karine Kappaun et al. provide details on the biochemistry and structure of some ureases from plants, bacteria and fungi. The mechanism by which ureases catalyze urea hydrolysis and the biological roles of such ureolytic activity are discussed. The relatively recently disclosed nature of non-enzymatic proprieties of ureases is also addressed by them showing how versatile ureases are.

Heitor Cantarella et al. present the state-of-the art with respect to the performance in field of *N*-(butyl) thiophosphoric triamide (NBPT), a urease inhibitor most widely used in agriculture. Authors describe conditions that increase urease activity in soils, the NBPT-driven mechanism of enzyme inhibition and the contribution of this inhibitor to building up nitrogen (N) reserves in soil. The ability of NBPT to prevent N losses from soil and its effect on seed germination and plant metabolism are explored together with NBPT stability, longevity, and efficacy. Next, Luzia V. Modolo et al. report the advances, since 2005, in the search for urease inhibitors (other than NBPT) of agricultural interest. The collection points out the potential of (di)substituted thioureas, benzothiazoles, coumarin derivatives, phenolic aldehyde derivatives, phosphoramidates, quinones and silver nanoparticles investigated by an *in vitro* approach using urease purified from jack bean. Examples of *N*-substituted thioureas, benzothiazoles, quinones, phenolic aldehyde derivatives and phosphoramidates in addition to hydroquinone and oxidized charcoal are provided from studies based on the inhibition of soil ureases. On the other hand, few organic substances (hydroquinone and phosphoramidates) and ammonium thiosulfate, B, Cu, S and/or Zn were investigated in plant-soil systems. The extent of mitigation of greenhouse gases production from urea is widely discussed for some urease inhibitors. Moving to livestock production, Amlan K. Patra and Jörg R. Aschenbacha list several bacteria of gastrointestinal tract of farm animals that exhibit urease activity and the factors known to affect the activity of this enzyme in livestock animals. The implication of urease in urea metabolism in the rumen is vastly debated. Authors also gathered several reports on the use of urease inhibitors to control ammonia production in the gastrointestinal tract of animals either from *in vitro* or *in vivo* assays.

David Y. Graham and Muhammad Miftahussurur overview clinical tests based on urease to diagnose *Helicobacter pylori* infections. Detailed information is given on rapid urease (RUT) and urea breath (UBT) tests. Authors make a comparison among the available methods and comment on the best one both for detection of active *H. pylori* infection and confirmation of cure after therapy.

In the next article Barbara Krajewska describes how urease activity can be exploited in $CaCO_3$ mineralization. The process offers enormous innovative potential in multiple engineering fields as an eco-friendly and benign technique to be used for remediation, cementation and deposition in field applications *in situ*, e.g. in the strengthening and consolidation of soil/sand, the protection and restoration of stone and concrete structures, conservation of stone cultural heritage materials, cleaning waste- and groundwater of toxic metals, and plugging geological formations for the enhancement of oil recovery and geologic CO_2 sequestration.

The last three articles deal with the most relevant urease inhibitors of pharmacological interests. Yuri F. Rego et al. describe several systematic screening studies for the inhibitory activity of several rationally designed organic compounds. Considerations on structure–activity relationship are also presented. According to the authors, the information on the inhibitory activity of differ-

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ent classes of compounds can be useful to guide the development of new urease inhibitors that may be used in future in molecular therapy against pathogenic bacteria. By contrast, Paweł Kafarski and Michał Talma describe the most recent discoveries of some potent urease inhibitors (from natural sources and synthetic ones). Particularly, these authors detail modeling and crystallographic studies that were done to better understand how these inhibitors interact with urease enzymes. Finally, the review by Ângelo de Fátima et al. report the most significant examples of Schiff bases and related metal complexes that exhibit antiurease properties. Copper(II) is the most widely studied metal and showed the best urease inhibitory effect. In addition, the number of reports disclosing the effects of Schiff bases and/or their metal complexes on purified urease from *Canavalia ensiformis* has increased; however, the effects of such substances on urease from *H. pylori* require further investigation. The authors state that the studies done with Schiff bases and/or their metal complexes have been shown to be a useful source of effective anti-ureolytic agents with a potential to treat diseases caused by urease-dependent pathogenic microorganisms.

In this special issue, we bring together information on ureases from several perspectives to continually inspire scientists who work in this area and encourage young scientists to engage in researches related to the fascinating universe of ureases. Finally, we want to express our gratitude to all contributors who embraced the project and anonymous reviewers for their time to make this special issue a reality.

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