

27 May 2019, at 11:30

in Aula I of the Department of Chemical Sciences (DiSC)

Prof. João B. T. Rocha
(Universidade Federal de Santa Maria, Brasil)

will give a workshop on :

“Ebselen and diphenyl diselenide as modulators of methylmercury toxicity”

Abstract:

Selenium is essential to the life of many animals but not for fungi and plants. The physiological chemistry of selenium is performed by the selenol group of selenocysteine found in a few seleno-proteins. Given the antioxidant role of some selenoenzymes (e.g., glutathione peroxidase or GPx and thioredoxin reductase or TrxR isoforms), the interest in synthetic organoselenium compounds increased after the use of ebselen in clinical trials. Ebselen is a safe and approved pharmacological agent for use in humans. However, the efficacy of ebselen has systematically failed in clinical trials. In 1956, diphenyl diselenide was tested in a small clinical trial, but it did not have beneficial effects in a leukemia patient. In contrast, selenocystine had pharmacological effects against leukemia but severe toxic side-effects. Despite this, the synthesis and empirical pharmacological in vivo evaluation of hundreds of selenium compounds are still common. The exact molecular mechanisms involved in the antioxidant properties of ebselen and diselenide are unknown but can be mediated by the limited formation of selenol intermediates and via modulation of antioxidant responsive elements (AREs). Electrophilic forms of Hg (E+Hg) have a strong affinity for thiolate and selenolate groups. So, after the metabolism of ebselen and diphenyl diselenide to their selenol intermediates, they could hypothetically form stable complexes with E+Hg forms. Accordingly, we have reported neuroprotective effects of ebselen and diphenyl diselenide in different in vitro and in vivo models of exposure to (MeHg+). Consequently, we suggest that ebselen should be tested in human volunteers to determine whether or not it will decrease the blood burden and increase the urinary excretion of Hg. However, the studies about the safety of diphenyl diselenide in humans are still minimal to justify its use in volunteers. Furthermore, the indiscriminate use of organoselenium compounds in living vertebrates has to be discouraged, because they violate international norms about the use of animals in pre-clinical research. Alternative toxicological in vitro and in silico tests have to be performed to avoid violations of the ethical use of vertebrates in research.

Prof. Leonard Jan Prins

Prof. Laura Orian