MMSL Military Medical Science Letters Since 1925

Mil. Med. Sci. Lett. (Voj. Zdrav. Listy) 2018, 87(supplementum 1)
ISSN 2571-113X (Online)

MEETING ABSTRACTS

SYNTHESIS OF NERVE AGENTS' SURROGATES FROM DIALKYL ALKYLPHOSPHONATES FOR ANTIDOTE SCREENING AND TOXICOLOGICAL STUDIES

Samir F. de A. Cavalcante [1,2,3], Leandro B. Bernardo [1], Kamil Kuča [2], Alessandro B. C. Simas [3]
Presenting Author: Samir F. de A. Cavalcante

[1] Instituto de Defesa Química, Biológica, Radiológica e Nuclear – IDQBRN, Exército Brasileiro, Centro Tecnológico do Exército, Avenida das Américas 28705, Área 4 – IDQBRN, Guaratiba, Rio de Janeiro, 23020-470, Brazil.
[2] Department of Chemistry, Faculty of Science, University of Hradec Kralové, Rokitanskeho, 62, 50003, Hradec Kralové, Czech Republic.
[3] Instituto de Pesquisas de Produtos Naturais – IPPN, Universidade Federal do Rio de Janeiro, Centro de Ciências da Saúde, Bloco H, Cidade Universitária, Rio de Janeiro, 21941-902, Brazil.

Abstract: Nerve Agents are toxic organophosphorus compounds which inhibit cholinesterases, pivotal enzyme in Parasympathetic Neurotransmission. As they are Schedule 1 compounds in accordance to Chemical Weapons Convention, strict controls are applied and some research groups may have their work hampered due to requirements for synthesis and manipulation. Nerve Agents' surrogates have emerged as affordable substitutes for more realistic approach for development of antidotes and biochemical and toxicity studies, as they are structurally related to Nerve Agents and considered as CWC Schedule 2 compounds, yielding similar enzyme adducts. As Laboratório de Análises Químicas – LAQ (ISO 17025) at IDQBRN have been participated in OPCW Proficiency Tests, striven to obtain the "OPCW Designated Laboratory" status, we have synthesized different dialkyl alkylphosphonates for verification purposes. Therefore, we have proposed synthesis of surrogates for our research on Medicinal Chemistry using them as starting materials. They have proven to be very useful compounds in our research and our syntheses have delivered good yields and purity of final compounds.

Keywords: Nerve Agents' Surrogates; Chemical Weapons Convention; Cholinesterases; Drug Screening; Dialkyl Alkylphosphonates

Acknowledgement

S.F.A.C. would like to thank OPCW for research grant (L/ICA/ICB/201062/15) and Brazilian Army and University of Hradec Kralové for travel grant.

References

1. Meek, E. C.; Chambers, H. W.; Coban A.; Funck, K. E.; Pringle, R. B.; Ross, M. K.; Chambers, J. E. Synthesis and I*n Vitro* and *In Vivo* Inhibition Potencies of Highly Relevant Nerve Agent Surrogates. *Toxicol. Sci*. **2012**, *126*, 525, doi: 10.1093/toxsci/kfs013.
2. Coban, A.; Carr, L. R.; Chambers, H. W.; Willeford, K. E.; Chambers, J. E. Comparison of inhibition kinetics of several organophosphates, including some nerve agent surrogates, using human erythrocyte and rat and mouse brain acetylcholinesterase. *Toxicol. Lett*. **2016**, *248*, 39, doi: 10.1016/j.toxlet.2016.03.002.
3. Cavalcante, S. F. A.; de Paula, R. L.; Kitagawa, D. A. S.; Barcellos, M. C.; Simas, A. B. C.; Granjeiro, J. M. Synthesis of reference compounds related to Chemical Weapons Convention for verification and drug development purposes – a Brazilian endeavour. *Journal of Physics: Conference Series* **2018**, *975*, 012020, doi: 10.1088/1742-6596/975/1/012020.