Collaborations Pharmaceuticals, Inc. Provides New Insights Into Metabolism of Chemical Warfare Nerve Agents In Humans

Collaborations Pharmaceuticals and Battelle published a new paper which provides new insights on the in vitro metabolism of four chemical warfare nerve agents.

Collaborations Pharmaceuticals logo

RALEIGH, NC, UNITED STATES, January 15, 2025 /EINPresswire.com/ -- Many pesticides and Chemical Warfare Nerve Agents (CWNA) act as inhibitors of the enzyme acetylcholinesterase and upon their exposure can ultimately lead to severe toxicity and death in humans. The metabolism of CWNA in humans is poorly understood. As there is a limited understanding of the metabolism of CWNAs in humans both in terms of what metabolites are formed and their respective toxicity, there are severe restrictions in how they can be treated.

An ongoing Defense Threat Reduction Agency (DTRA) funded collaboration between researchers from Collaborations Pharmaceuticals, Inc (CPI) and Battelle has recently led to a published paper entitled "Metabolic Characterization of Sarin, Cyclosarin and Novichoks (A-230, A-232) In Human Liver Microsomes" which has provided new insights on the metabolism of these chemical weapons which may have broader importance.

“We have used a common in vitro method which incubates these chemicals with human liver microsomes and then uses sensitive HPLC-MS analytical approaches to understand how these CWNA are broken down,”said Dr. Sean Ekins, CEO of Collaborations Pharmaceuticals, Inc. “The results of this work could contribute to the understanding of which enzymes are involved and how they are removed from the human body or whether they linger.”

The study showed that the rank order of metabolic stability was sarin < cyclosarin < Novichok A-

230 < Novichok A-232. All four compounds showed the enzyme paraoxonoase is partially responsible for this metabolism. These findings illustrate distinct differences in clearance for each CWNA as compared to those previously observed with another molecule, namely VX, for which there was no observation of a role for paraoxonoase.

“This work could be extended to look at other enzymes to fill in the additional gaps of which additional enzymes may also have a role, as well as focusing in on those that could then lead to potential treatments for each CWNA,” Ekins said. “Importantly, our data suggests that no single small molecule is likely to be fully effective as a treatment for all CWNAs due to the apparent role of several different enzymes in the metabolism.”

About this work
Thomas R. Lane, David Koebel, Eric Lucas, Sean Cleary, Robert Moyer and Sean Ekins. Metabolic Characterization of Sarin, Cyclosarin and Novichoks (A-230, A-232) In Human Liver Microsomes
https://pubs.acs.org/doi/full/10.1021/acs.chemrestox.4c00538

This work was funded by DTRA grant # HDTRA11910020

About Battelle

Every day, the people of Battelle apply science and technology to solving what matters most. At major technology centers and national laboratories around the world, Battelle conducts research and development, designs and manufactures products, and delivers critical services for government and commercial customers. Headquartered in Columbus, Ohio since its founding in 1929, Battelle serves the national security, health and life sciences, and energy and environmental industries. For more information, visit www.battelle.org.

Sean Ekins
Collaborations Pharmaceuticals, Inc.
+1 215-687-1320
email us here
