Re-Purposing Drugs as Countermeasures for Chemical Weapon Toxicities: Interactive Pharmacology Training

Lauren M Aleksunes, Joshua P Gray, Jaclynn Meshanni, Jeffrey D Laskin, Debra L Laskin

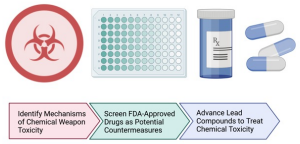
Department of Pharmacology and Toxicology, School of Pharmacy; Environmental and Occupational Health Sciences Institute, Rutgers University, Piscataway, NJ; US Coast Guard Academy, New London, CT

RUTGERS Environmental and Occupational Health Sciences Institute | EOHSI

COUNTER ACT Countermeasures Against Chemical Threats

Abstract

The risk of a terrorist attack in the U.S. has created challenges on how to effectively treat toxicities that result from exposure to chemical weapons. To address this concern, the U.S. has organized a trans-agency initiative across academia, government, and industry to develop and approve drugs to treat tissue injury resulting from exposure to chemical threat agents. We sought to develop and evaluate an interactive educational session that provides hands-on instruction on how to re-purpose FDA approved drugs as therapeutics to treat toxicity from exposure to chemical weapons. As part of the Rutgers Summer Undergraduate Research Fellowship, 23 undergraduate students participated in a two-hour session that included: 1) an overview of chemical weapon toxicities, 2) primer on pharmacology principles, and 3) an interactive session where teams of students were provided lists of FDA approved drugs to evaluate potential mechanisms of action and suitability as countermeasures for 4 chemical weapon case scenarios. The interactive session culminated in a competition for the best grant 'sales pitch'. Pre- and post-program self-assessments using 5-point Likert rating scales were conducted during the session using Poll Everywhere. From this interactive training, students improved their understanding of 1) the ability of chemical weapons to cause long-term toxicities (means: pre-2.2; post-4.1, p<0.0001), 2) impact of route of administration and exposure scenario on drug efficacy (means: pre-2.6; post-4.3, p<0.0001), and 3) re-purposing FDA-approved drugs to treat exposure to chemical weapons (means: pre-1.7; post-4.0, p<0.0001). Seventy six percent of participants were 'very likely' or ' extremely likely' to recommend this activity to other students. Taken together, use of an interactive training exercise can provide students new insights into drug development for chemical weapon toxicities.



Training Session Overview

- Overview of the NIH CounterACT Program and Chemical Weapon Toxicities
- Lecture on Drug Delivery and Pharmacokinetics
- Interactive Team-Based Case Studies to Re-Purpose FDA-Approved Drugs as Countermeasures in Zoom Breakout Rooms
- Competition of Teams Pitching their Repurposed Drugs

Interactive Training Overview

Each team was assigned a list of 10 FDA approved drugs to review (mechanism of action, route of administration, safety profile, etc.)

Part 1: Each team was assigned a case study scenario which included the chemical weapon exposure scenario, known pathological changes, clinical symptoms and mechanisms of toxicity.

- *Breakout 1: Identify 5 properties desired in a therapy to treat the toxicity associated with the chemical weapon in the case study.*
- *Breakout 2: After hearing properties from other teams, points were assigned to each property according to its importance in treating chemical weapon toxicity.*

Part 2: Moderator presents an example rubric to evaluate the utility of potential therapies researched during the pre-work.

- *Breakout 1: Teams apply their rubric to three of the FDA-approved drugs from the pre-work in order to identify the most promising intervention.*
- *Breakout 2: Prepare a 3-minute grant sales pitch that highlights the promise of their top candidate drug for re-purposing to treat chemical weapon toxicity.*

Part 3: In the main Zoom room, each team presented their therapeutic intervention and the audience including other participants, SURF leadership, and invited speakers voted on the best 'sales pitch'. Gift cards were provided to the top team.

4 Chemical Weapon Case Scenarios

Phosgene Oxime Dermal Toxicity

Exposure Scenario: Soldier & Civilian Exposure

Tetramethylenedisulfotetramine Neurotoxicity

Exposure Scenario: Seizures

Parathion Neurotoxicity

Exposure Scenario: Disposed Cylinder Found in Lake

Chlorine Pulmonary Toxicity

Exposure Scenario: Laboratory Accident at Home

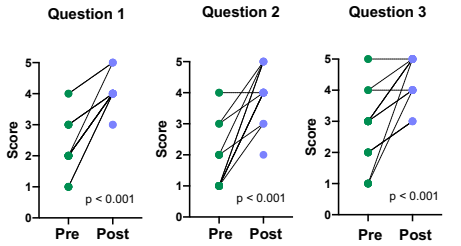
Create Your Drug Scoring Rubric

What properties should a good therapy have?

	Property	Total # of Points for This Property (1-8)
#1		
#2		
#3		
#4		
#5		
	Total Possible Points for Good Therapy: * *Note: Not all properties should be equally weighted*	**20**

Example Template Provided to Participants

Assessment



Question 1: How would you rate your understanding of how chemical weapons cause long-term toxicities?

Question 2: How would you rate your understanding of how to re-purpose FDA approved drugs for a new therapeutic indication?

Question 3: How would you rate your understanding of how route of administration and exposure scenarios affect the usefulness of a drug?

Figure 1. Pre- and Post-Lesson Self-Assessment of Participant Knowledge. Students were asked three polling questions at the start and the end of the didactic and interactive sessions. Responses were converted to a 5-point Likert scale: 1 none, 2 slight, 3 somewhat, 4 moderate, 5 high. Students had approximately 1 minute to answer each question. Pre-Lesson: N=21-23 respondents. Post-Lesson: N=17-19 respondents.

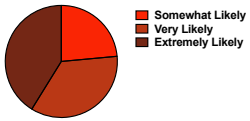


Figure 2. Post-Assessment of Activity. Students were asked the likelihood they would recommend this activity to their colleagues (scale: extremely likely, very likely, somewhat likely, not very likely, not at all). N=17 respondents.

Main Takeaway

An interactive training exercise can provide undergraduate students new insights into drug development for chemical weapon toxicities.

Acknowledgments

This work was supported by NIEHS P30ES005022, R25ES020721, T32ES007148, NIAMS U54AR055073, NINDS NS108956 and NCATS UL1TR003017 and the ASPET SURF and SOT Intern Programs.

For More Information: https://surf.rutgers.edu