

## USC School of Pharmacy

### **RXRS 304: Mysterious Deaths: Toxicology, Poisons, Literature and History**

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**Course Weight:** 4 Units (course meets 3 hours per week, one hour outside education)

**Days/Time/Location:** Friday 2:00- 4:50 VKC 201

**Course catalogue description (25 words or less):** Poisons as described in classical literature where they helped shape, modify or change history. Presented in the context of pharmacological/toxicological principles of drug action.

#### **Introduction**

This course introduces the student to pharmacological and toxicological principles as well as biological mechanisms of action in the setting of the use of poisons in literature and history. By the end of the course, the students will understand principles related to hazard and risk assessment, the influence of dose, route and formulation on health outcomes as well as how molecules of different origins have been used for the benefit (medicines) and detriment (poisons) in humans. The course will also introduce the student to the history of forensic analysis and how this field has evolved. Techniques used in modern day forensics to demonstrate evidence of the use of poisons will be presented. Using historical events taken from the literature, scientific principles linked to toxicology and poisonings will be presented in a unique illustrative context.

#### **Objectives**

The course is designed for undergraduates of both scientific and non-scientific majors with an interest in understanding the principles and concepts underlying toxicology, pharmacology and biological mechanisms. Chapters from the required textbook will be supplemented with a

variety of source materials including articles from scientific journals and public websites. Selected cases studies will be critically reviewed and emerging “hot” topics discussed.

**Upon successful completion of this course a student should be able to:**

- Understand and discuss the influence of dose and route on hazard
- Understand and discuss the basic pharmacological and toxicological principles underlying the use of molecules to modify biological processes
- Understand and discuss what determines the toxicity of a molecule
- Know the history of the development of forensic toxicology as a discipline to provide evidence of exposure to poisons
- Have a working knowledge and be able to discuss the mechanism of action and the use of toxicants as poisons throughout history and literature

**Assignments and Grading:**

Class participation:	20 pts (8%)
4 quizzes @ 10 pts each	40 pts (16%)
2 midterm exams @ 40 pts each:	80 pts (32%)
1 written report due on the day of the exam	50 pts (20%)
1 final exam (partially cumulative):	<u>60 pts (24%)</u>
Total:	250 pts.

Class Participation and Attendance (20 pts): On a scale of 10, 0-indicating no participation, 10-indicating best participation. You can therefore increase the probability of getting a higher mark by being proactive in terms of asking (relevant) questions in class and/or contributing to discussions.

Attendance at all classes is expected. Participation will include asking and answering questions and being actively involved in the discussion. It is expected that the students read the assigned papers prior to the lecture and be prepared to discuss background, current understanding, treatments, and gaps in knowledge for the topic in each lecture.

Class Deliverable (written report): The class deliverable will be a 5 page write up from one of the extra class sources of information based on a toxin or poison of choice. On a scale of 50, 0-no deliverable turned in, 50-an excellent synopsis of the extracurricular source of information. It is expected that the students will engaged one of the extracurricular sources of information (one of the cited videos of 45 minutes or longer, reading of one of the recommended or suggested sources, or reading of one of the reviewed pieces of literature [e.g. a book by Agatha Christie]) of a subject of interest.

The midterms (40 points each) will include multiple choice questions, and T/F questions and fill-in the blank or short answer questions.

The final exam (60 points) will be similar format as the midterms. The final exam will be cumulative, but will emphasize material covered after the 2<sup>nd</sup> midterm.

There are no make-up exams. If exceptional circumstances prevent you from attending an exam, your reason for missing it must be accompanied by a written statement from a third party (e.g. a note from a medical doctor).

Notes, books, calculators, electronic dictionaries, regular dictionaries, cell phones or any other aids are not allowed during exams.

Students will be asked to complete an anonymous critical evaluation of the course at its completion.

**Required Text:**

**The Poisoner's Handbook: Murder and the Birth of Forensic Medicine in Jazz Age New York**

Deborah Blum

ISBN-13: 978-0143118824

ISBN-10: 014311882X

Available on Amazon for ~ \$9.00 - \$15.00

**We will supplement the reading with several “MOVIE NIGHTS” where classic movies depicting a famous poisoning event will be screened. We will provide pizza, drinks, popcorn, etc. IT WILL BE FUN. WE will work with the class to find several evenings that will work. One of the MOVIE nights may end up be during class.**

**Course Readings**

*Required Readings (selected, short, easy to read chapters)*

- John Emsley. *Molecules of Murder: Criminal and Classic Cases*. (2008) RCS Publishing, Thomas Graham House, Science Park, Milton Road, Cambridge CB4 0WF, UK
- John Emsley. *The Elements of Murder: A History of Poisons*. (2005) Oxford University Press, Great Clarendon Street, OX2 6DP
- Kathryn Harkup. *A is for Arsenic: The Poisons of Agatha Christie*. (2015) Bloomsbury Sigma, 1385 Broadway, New York, New York 10018.

Although not mandatory, it is strongly suggested that the students purchase these books for this course as it will provide a resource to reinforce and supplement the lectures on the use of poisons throughout literature and history. The students will be able to use identified chapters in the text to support their learning process throughout the semester.

Acocella, J. Murder by Poison. *The New Yorker*, October 14, 2013.

Alizadeh et al. Black henbane and its toxicity – a descriptive review. *Avicenna J of Phytomedicine*, 4:297-311, 2014.

Chidiac, EJ, et al. Mandragora: Anesthetic of the Ancients. *Anesth Analg* 115:1437-41, 2012.

Holzman, RS. The Legacy of Atropos, the Fate Who Cut the Thread of Life. 89:241-249, 1998.

Langman, LJ and BM Kapur. Toxicology: Then and Now, *Clinical Biochemistry* 39:498-510, 2006.

Pearce, DN. Sherlock Holmes, Conan Doyle and cocaine. *Journal of the History of Neurosciences* 3:227-232, 1994.

Rozman KK and J Doull. Paracelsus, Haber and Arndt. *Toxicology* 160:191-196, 2001.

Other course materials including but not limited to the syllabus, supplemental reading assignments and additional handouts will be posted on <http://blackboard.usc.edu/>. Students are encouraged to use the online discussions among students via Blackboard.

### ***Recommended***

Bardell, EB. Literary Reflections of Pharmacy XI: Thallium as "An Untraceable Poison". *Pharmacy in History* 30:188-190, 1988.

Dayon, AD. What killed Socrates? Toxicological considerations and questions. *Postgrad Med J* 85:34-37, 2009.

Hughes, MF et al. Arsenic Exposure and Toxicology: A Historical Perspective. *Toxicological Sciences* 123:3005-332, 2011.

Lee, MR. Solanaceae IV: Atropa belladonna, Deadly Nightshade. *J R Coll Physicians Edinb* 37:77-84, 2007.

Reynolds, T. Hemlock alkaloids from Socrates to poison aloes. *Phytochemistry* 66:1399-1406, 2005.

### **Course Outline**

This course will be in the format of a directed seminar/lecture under the guidance of the instructor for the specific session. During each weekly session the instructor will engage the students with questions and draw comments or interpretations primarily based on the assigned reading. Students are expected to ask questions and participate in an interactive fashion.

### **Course schedule is as follows:**

Week & Date	Topic	Subtopics to be Included	Assigned and Supplemental Reading
<b>Introduction and Background</b>			
Jan 12 DD	Introduction: expectations and goals of this class. General overview of pharmacology and toxicology. How and Why drugs work or don't	<ul style="list-style-type: none"> <li>• Basic principles of hazard vs risk</li> <li>• Basic principles of dose response</li> <li>• Understanding of what determines the toxicity of a molecule</li> </ul>	<p><b>These video's will help give an overview of how drugs and the body interact.</b></p> <p>Basics on Pharmacokinetics: what the body does to a drug  <a href="https://www.youtube.com/watch?v=NKV5iaUVBU">https://www.youtube.com/watch?v=NKV5iaUVBU</a></p> <p>Very brief overview of PD and PK:            Utube:  <a href="https://www.youtube.com/watch?v=to bx537kFal">https://www.youtube.com/watch?v=to bx537kFal</a></p> <p>PK:  <a href="https://www.youtube.com/watch?v=mp93nPUzHqM">https://www.youtube.com/watch?v=mp93nPUzHqM</a> followed by watching:  <b>Clearance:</b>  <a href="https://www.youtube.com/watch?v=hHUFJAsgqkY">https://www.youtube.com/watch?v=hHUFJAsgqkY</a></p>
Jan 19 MEC	Milestones in Forensic Analysis of Poisons	<ul style="list-style-type: none"> <li>• Understand the development of assays to measure poisons</li> <li>• Understand how forensic toxicology has progressed with time to enable determination of cause of death</li> </ul>	Introductory Chapter, Emsley, 2008 Langman and Kapur, 2006 Norris and Gettler, NY Coroner's Office, 1918
Jan 26 MC <b>Quiz 1</b>	History of the Use of Poisons: Overview	<ul style="list-style-type: none"> <li>• Learn about famous individuals that were poisoned</li> <li>• Understand the use of poisons in politics</li> <li>• Understand the role of the pharmacist in compounding and dispensing medicines</li> <li>• Understand how chemicals can be used as both medicines and poisons</li> </ul>	<a href="https://toxlearn.nlm.nih.gov/Module1.htm">https://toxlearn.nlm.nih.gov/Module1.htm</a> The Victorian Pharmacy (trailer) <a href="https://www.youtube.com/watch?v=G-aa671XBs">https://www.youtube.com/watch?v=G-aa671XBs</a>
Feb 2 MC	Hemlock	<ul style="list-style-type: none"> <li>• Learn about the use of hemlock in history and literature</li> <li>• Understand the mechanism by which hemlock works</li> </ul>	Chapter H, Harkup, 2015 Five Little Pigs; Agatha Christie (trailer) <a href="https://www.youtube.com/watch?v=P7lQZ6pk7qc">https://www.youtube.com/watch?v=P7lQZ6pk7qc</a>
<b>Feb 9</b>	<b>MIDTERM 1 Feb 9<sup>th</sup> (first hour)</b>		
		•	
Feb 9 MC	Mercury and Lead	<ul style="list-style-type: none"> <li>• Learn about the medicinal and toxicological aspects of mercury and lead based materials</li> <li>• Understand the mechanism by which these metals affect biology</li> <li>• Understand the concept of methyl mercury accumulation in the food chain</li> </ul>	Chapters 2-4; 12-14, Emsley, 2005 Medical Masquerade: One Man's Experience with Methyl Mercury Poisoning <a href="https://www.youtube.com/watch?feature=player_embedded&amp;v=e2Nsy0c22R8">https://www.youtube.com/watch?feature=player_embedded&amp;v=e2Nsy0c22R8</a>
Feb 16 MEC	Arsenic	<ul style="list-style-type: none"> <li>• Learn about the use of arsenic as a medicine and a poison history and literature</li> <li>• Learn about industrial uses of arsenic</li> </ul>	Chapters 2-4; 12-14, Emsley, 2005 Chapter A, Harkup, 2015 Kinter Lecture Arsenic <a href="https://www.youtube.com/watch?v=eISq">https://www.youtube.com/watch?v=eISq</a>

		<ul style="list-style-type: none"> <li>• Understand the mechanism by which arsenates and arsenite works</li> </ul>	UjkMWFU
Feb 23 MC <b>Quiz 2</b>	Belladonna, Henbane and Mandrake	<ul style="list-style-type: none"> <li>• Understand the historical uses of plant alkaloids</li> <li>• Understand the medicinal uses of materials derived from these plants</li> <li>• Review the use of these plants in literature</li> <li>• Understand the mechanisms of actions of these materials on the nervous system</li> </ul>	Chapter 2, 3, Emsley, 2008; Chapter B, Harkup, 2015 The use of sacred weeds <a href="https://www.youtube.com/watch?v=uLZiKBdMEIc">https://www.youtube.com/watch?v=uLZiKBdMEIc</a>
Mar 2 MC	Cyanide: Nazi Regime, Tylenol, Jonestown Massacre and others	<ul style="list-style-type: none"> <li>• Understand the historical uses of cyanide</li> <li>• Review the use of cyanide in literature</li> <li>• Understand the mechanisms of actions of cyanide</li> </ul>	Chapter 8, Emsley, 2008 Chapter C, Harkup, 2015 Cyanides in Excedrin <a href="https://www.youtube.com/watch?v=0FQrGvAUs18">https://www.youtube.com/watch?v=0FQrGvAUs18</a> Hermann Goring <a href="https://www.youtube.com/watch?v=B6yn2cBsb2A">https://www.youtube.com/watch?v=B6yn2cBsb2A</a>
<b>Mar 9 Midterm 2 first hour</b>			
Mar 9 MEC	Methanol poisoning	<ul style="list-style-type: none"> <li>• Understand the use of methanol in improper alcoholic drink production</li> <li>• Understand the mechanisms of methanol, and how it differs from ethanol toxicity</li> </ul>	Methanol poisoning <a href="https://www.youtube.com/watch?v=PsVwJBSfBAY">https://www.youtube.com/watch?v=PsVwJBSfBAY</a>
March 23 MC	Ricin	<ul style="list-style-type: none"> <li>• Understand the use of ricin in history and literature</li> <li>• Understand the mechanism of action of ricin</li> </ul>	Chapter 1, Emsley, 2008 Chapter R, Harkup, 2015 The Umbrella Assassin <a href="https://www.youtube.com/watch?v=b2Qpwo8Uutis">https://www.youtube.com/watch?v=b2Qpwo8Uutis</a>
Mar 30 MC <b>Quiz 3</b>	Morphine and Morphine Like Compounds	<ul style="list-style-type: none"> <li>• Understand the historical uses of opiates</li> <li>• Review the use of opiates in literature</li> <li>• Understand the medicinal uses of opiates</li> <li>• Understand the mechanisms of actions of opiates</li> </ul>	Chapter 4 Emsley, 2008 Chapter O, Harkup, 2015 How opioids work  Opioid Nation: The Making of an Epidemic <a href="https://www.youtube.com/watch?v=ygqalpOT3Tw">https://www.youtube.com/watch?v=ygqalpOT3Tw</a>
Apr 6 MC	Carbon Monoxide	<ul style="list-style-type: none"> <li>• Understand the toxicity of carbon monoxide</li> <li>• Understand sources of carbon monoxide</li> <li>• Understand the mechanisms of action of carbon monoxide</li> </ul>	Chapter 7, Emsley, 2008 Poisoner's Guide to Communicating Chemistry <a href="https://www.youtube.com/watch?v=QP DwzcppG0o">https://www.youtube.com/watch?v=QP DwzcppG0o</a>
Apr 13 MC	Environmental poisoning	<ul style="list-style-type: none"> <li>• Learn about the history of environmental toxicology</li> <li>• Understand the MOA of major environmental chemicals</li> <li>• Learn about toxic events that affected large numbers/groups of people in the last decades</li> </ul>	Book: Our stolen future; by Theo Colborn, D. Dumanoski, and J.P. Myers <u>Websites:</u> <a href="http://www.environmentalhealthnews.org/">http://www.environmentalhealthnews.org/</a> <a href="http://www.endocrinedisruption.org/">http://www.endocrinedisruption.org/</a> <a href="http://toxnet.nlm.nih.gov/cgi-bin/sis/search">http://toxnet.nlm.nih.gov/cgi-bin/sis/search</a> Movie: a civil action
Apr 20 MEC	Polonium and Thallium	<ul style="list-style-type: none"> <li>• Understand the use of polonium and thallium in history and literature</li> </ul>	Chapter 10, Emsley, 2008 Chapter T, Harkup, 2015

Quiz 4		<ul style="list-style-type: none"> <li>• Understand the mechanism of action of polonium and thallium</li> </ul>	The polonium plot <a href="https://www.youtube.com/watch?v=1FgcFaJEnh8">https://www.youtube.com/watch?v=1FgcFaJEnh8</a>
Apr 27 MC	Botulinum toxin and BOTOX	<ul style="list-style-type: none"> <li>• Understand botulinum toxin effects, potential uses against humans and antitoxin</li> <li>• Learn about the history and cosmetic and therapeutic use of Botox</li> <li>• Learn about the challenges of producing safely a drug with serious toxicity</li> </ul>	<a href="https://www.bloomberg.com/news/features/2017-10-26/inside-fort-botox-where-a-deadly-toxin-yields-2-8-billion-drug">https://www.bloomberg.com/news/features/2017-10-26/inside-fort-botox-where-a-deadly-toxin-yields-2-8-billion-drug</a>
<b>RXRS 304-FINAL Final Exam May 7<sup>th</sup> 2:00 – 4:00 VKC 101</b>			

## Statement on Academic Conduct and Support Systems

### Academic Conduct

Plagiarism – presenting someone else’s ideas as your own, either verbatim or recast in your own words – is a serious academic offense with serious consequences. Please familiarize yourself with the discussion of plagiarism in *SCampus* in Section 11, *Behavior Violating University Standards* <https://scampus.usc.edu/1100-behavior-violating-university-standards-and-appropriate-sanctions>. Other forms of academic dishonesty are equally unacceptable. See additional information in *SCampus* and university policies on scientific misconduct, <http://policy.usc.edu/scientific-misconduct>.

Discrimination, sexual assault, and harassment are not tolerated by the university. You are encouraged to report any incidents to the *Office of Equity and Diversity* <http://equity.usc.edu> or to the *Department of Public Safety* <http://capsnet.usc.edu/department/department-public-safety/online-forms/contact-us>. This is important for the safety of the whole USC community. Another member of the university community – such as a friend, classmate, advisor, or faculty member – can help initiate the report, or can initiate the report on behalf of another person. *The Center for Women and Men* <http://www.usc.edu/student-affairs/cwm/> provides 24/7 confidential support, and the sexual assault resource center webpage <http://sarc.usc.edu> describes reporting options and other resources.

### Support Systems

A number of USC’s schools provide support for students who need help with scholarly writing. Check with your advisor or program staff to find out more. Students whose primary language is not English should check with the *American Language Institute* <http://dornsife.usc.edu/ali>, which sponsors courses and workshops specifically for international graduate students. *The Office of Disability Services and Programs* [http://sait.usc.edu/academicsupport/centerprograms/dsp/home\\_index.html](http://sait.usc.edu/academicsupport/centerprograms/dsp/home_index.html) provides certification for students with disabilities and helps arrange the relevant accommodations. If an officially declared emergency makes travel to campus infeasible, *USC Emergency Information* <http://emergency.usc.edu> will provide safety and other updates, including ways in which instruction will be continued by means of blackboard, teleconferencing, and other technology.

### Emergency Preparedness/Course Continuity:

In case of emergency, and travel to campus is difficult, USC executive leadership will announce an electronic way for instructors to teach students in their residence halls or homes using a combination of Blackboard, teleconferencing, and other technologies. Instructors should be prepared to assign students a "Plan B" project that can be completed at a distance. For additional information about maintaining your classes in an emergency please access:  
<http://cst.usc.edu/services/emergencyprep.html>