Exercise 3

CHEMICAL TOXICITY

Fig. X3-1

The availability of the Internet has made it relatively quick and easy to obtain toxicological information about chemicals. When working with chemicals, it is helpful to have some idea of the relative toxicities of the chemicals. In the case of high toxicity, special precautions may be necessary. Because it is generally not possible to obtain toxicological data for humans (except from terrible accidents), most existing toxicological data has been obtained from the study of rodents. In this exercise, you will search the Internet to obtain LD_{50} (Oral-rat) values of several chemicals and for a few cases, the LD_{LO} for humans. The LD_{50} (Oral-rat) values represent the number of milligrams per kilogram of body weight that will kill half of the rats that orally consume the amount given. The applications of these values to humans is certainly subject to question and undoubtedly sometimes leads to incorrect conclusions but is the best we can generally do. The LD_{50} (Oral-rat) values if available are usually in MSDS (Material Safety Data Sheet) and there are many sites on the Internet that can locate MSDS. One way to locate useful MSDS sites is the ***Organic Chemistry Directory***. Listings of MSDS sites can be found in the first section (Physical Properties) of this Directory.

http://murov.info/orgchem.htm **Bookmark this site for future use**

Another option is to type in the name of the chemical followed by msds in the Google search box. The latter is a hit and miss method and probably the quickest way to locate the desired information is to use one of the sites below. Especially useful for this exercise is the *Chemidplus site*. If you are using an MSDS listing, scroll down to the toxicological heading (usually #11, the second one after physical properties which is another very useful section of the MSDS) which is about 3/4 of the way through the MSDS and look for LD_{50} (Oral-rat) values.

1.Tabulation + MSDS

Acros - http://www.acros.com/portal/alias__Rainbow/lang__en/tabID__21/DesktopDefault.aspx
Aldrich, Sigma - http://www.sigmaaldrich.com/
Alpha Chemical - http://www.alfa.com/alf/laboratory_chemical_suppliers.htm
Fisher - https://new.fishersci.com/wps/portal/HOME
ChemExper Chem. Directory - http://www.chemexper.com/
ChemFinder Web Server - http://chemfinder.cambridgesoft.com/
Chemical Book - http://www.chemicalbook.com/
Chemidplus - http://chem.sis.nlm.nih.gov/chemidplus/
or **http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp**
Chemindex - http://ccinfoweb.ccohs.ca/chemindex/search.html
Chemspider - http://www.chemspider.com/
EMD Chemicals - http://www.emdchemicals.com/corporate/emd_corporate.asp
TCI America - http://www.tciamerica.com/brochure/catalog.html
Wikipedia - http://en.wikipedia.org/wiki/List_of_organic_compounds
http://en.wikipedia.org/wiki/List_of_inorganic_compounds

2. MSDS
Vermont Safety Information Resources, Inc. - http://hazard.com/msds/

References

Blumberg, A. A.; *J. Chem. Educ.*, **1994**, 71 (11), p 912.
Yehudit Judy Dori, Y. D.; Barak, M.; Adir, N. *J. Chem. Educ.*, **2003**, *80 (9)*, p 1084.
Zimpleman, J. M. *J. Chem. Educ.*, **1999**, *76 (12)*, p 1662.
Murov , S. *J. Chem. Educ.*, **2001**, *78 (10)*, p 1429.

Toxicities of Chemicals

1. Use one or more of the sites near the beginning of this ***Exercise*** to find the missing values for the compounds below. From these values, calculate the extrapolated LD_{50} value for a 70 kg rat in units of grams. When available, also record the LD_{50} value for humans. The site **http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp** is suggested for this search.

Compound	formula	LD_{50} (oral-rat) (mg/kg)	LD_{50} for 70 kg rat (g)	LD_{LO} for humans (mg/kg)
glucose	$C_6H_{12}O_6$			na
iodine	I_2			
ethanol	C_2H_6O			
potassium iodide	KI			na
acetaminophen	$C_8H_9NO_2$			
dichloromethane	CH_2Cl_2			
vanillin	$C_8H_8O_3$			na
caffeine	$C_8H_{10}N_4O_2$			
nicotine	$C_{10}H_{14}O_2$			na
arsenic(III) chloride	$AsCl_3$			na
potassium cyanide	KCN			na
warfarin (coumadin)	$C_{19}H_{16}O_4$			(man)
dioxin	$C_{12}H_4Cl_4O_2$			na

[Note: For the following questions, assume that the LD_{50} values for rats can be applied to humans and that an average human weighs 70 kg.]

2. a. The average cup of coffee contains about 100 mg of caffeine. How many cups of coffee could potentially be lethal to half of the drinkers? (Note: This author found that the LD_{50} value for rats is the same as the LD_{LO} for humans. Unexpected and unusual coincidences should be viewed with suspicion and it is possible that one of the values was incorrectly recorded. There are many errors in LD_{50} tabulations presumably because lists have been compiled by non-chemists and differences in labels and chemical names have not been adequately noticed.)

   b. Recognizing that the answer to #2a depends on many assumptions and has a large margin of error, is the very sad and unfortunate story reported at the site below surprising?

   http://the-tech.mit.edu/V118/N56/shorts.56n.html
   http://www.solarnavigator.net/solar_cola/caffeine.htm

3. Assume that a typical glass of beer contains 6% ethyl alcohol and 350 mL. How many beers could potentially be lethal to half of the drinkers?

4. The average cigarette contains about 20 mg of nicotine and the smoking of one cigarette results in the absorption of about 1 mg of nicotine in the bloodstream. To a 70 kg human, how many cigarettes could be lethal if consumed and how many if smoked?

5. During nuclear accidents, people exposed to radiation are sometimes advised to take potassium iodide to dilute the radioactive iodide that has been released and can be incorporated into the thyroid gland.

   a. Does this sound like a wise procedure?

   b. During these episodes, the media often describes the use of iodine as therapy. Explain the problem with this announcement.

   c. Compare iodine's LD_{LO} value for human's with its LD_{50} value for rats and consider a comparison of the two values for other compounds in your table. Consistent with the LD_{LO} for iodine, halogens are considered to be very toxic but the LD_{50} value for rats seems to indicate a low toxicity. Critically evaluate the values.

6. Would you consider vanillin to be a safe food additive? Explain your answer.

7. Hetch Hetchy reservoir in the Sierra Nevada Mountains near Yosemite was formed when the O'Shaughnessy Dam was completed in 1923 on the Tuolomne River to provide a water source and storage for San Francisco.[1] The reservoir holds 360,000 acre feet of water. An acre ft. = 1.23×10^6 L. Terrorist threats are in the news today on a daily basis and one of the many concerns is that our water supplies could be contaminated with a very toxic substance.

   a. To determine whether this is feasible, calculate the amount of potassium cyanide that would have to be dumped into Hetch Hetchy to kill half of the people who drink 230 grams (about 8 oz.) of the water. Assume the density of the reservoir contents is 1.0 g/mL.

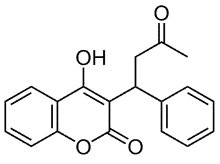
   b. Do you think it would be possible to dump the amount calculated above into the reservoir without being detected? Explain your answer.

   c. Answer the previous question assuming that dioxin is used instead of potassium cyanide. Explain your answer.

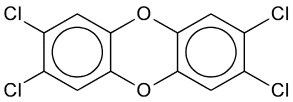
8. The venom of black widows has a rat LD_{50} of approximately 0.002 mg/kg. Assuming a density of 1 g/mL, what volume of venom do black widows and rattlesnakes have to inject to have a 50% chance of killing a human? What are the many assumptions that go into this calculation? Does the amount intuitively seem like a reasonable amount for a spider bite?

[1]The construction of the dam was strongly opposed by environmentalists including the famous naturalist John Muir, the first president of the Sierra Club. John Muir described Hetch Hetchy as "a wonderfully exact counterpart" of Yosemite Valley, and therefore "one of nature's rarest and most precious mountain temples." Despite John Muir's efforts, the dam was built but even today, environmental groups are working to have the dam removed and the valley restored to its natural beauty.

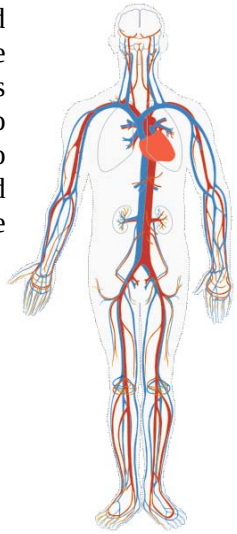
9. Warfarin (also called coumadin) is a commonly used prescription drug used to thin blood. A person on coumadin, must have frequent blood tests to monitor the coumadin concentration. Does the LD_{50} of coumadin explain the need for the frequent testing. Explain your answer.



10. Dioxin is a byproduct in some organic syntheses and is produced in small quantities during some of the processes used to bleach paper. Does LD_{50} justify concern about the use of this chemical. Perform an Internet search on dioxin to determine if there have been any environmental problems caused by dioxin.



11. You have probably heard it said that people with high blood pressure should decrease their consumption of foods high in sodium ion content. One alternative to the use of table salt is the use of potassium chloride. It is possible that at least a part of the cause of blood pressure increase is due to chloride. Explain why it is difficult to perform a controlled study to distinguish between the blood pressure effects of sodium and chloride and perform an Internet search to try to ascertain the best and most recent available evidence on this issue. Is substitution of KCl for NaCl a wise therapy? Examples of possible Internet sites that might be useful are:



http://www.annals.org/cgi/content/abstract/98/5_Part_2/817
http://www.nejm.org/doi/full/10.1056/NEJM199003013220901
http://www.nejm.org/doi/full/10.1056/NEJM198710223171702
http://jn.nutrition.org/content/121/3/330.full.pdf J. L. Greger U. of Wisconsin
http://www.ncbi.nlm.nih.gov/pubmed/15723964
He FJ,Markandu ND, Coltart R, Barron J, MacGregor GA. Source Blood Pressure Unit, St. George's Hospital Medical School, London, United Kingdom.

http://www.ncbi.nlm.nih.gov/pubmed/2706092
http://www.ncbi.nlm.nih.gov/pubmed/1627756
Smith SR, Klotman PE, Svetkey LP. Source Department of Medicine, Duke University Medical Center, Durham, NC 27710.

http://annals.org/article.aspx?articleid=696585
Theodore A. Kotchen, M.D.; University of Kentucky Medical Center, Medicine/Endocrinology, 800 Rose St., Room N503; Lexington, KY 40536.

http://hyper.ahajournals.org/content/17/1_Suppl/I158 M A Boegehold, T A Kotchen
http://hyper.ahajournals.org/content/45/5/849.full