**Homework 6 - Toxicology**

**Questions: Note to instructor: Below is a list of questions that are suitable for a homework assignment. You may select any number of question that you may feel is best suited for your class. This serves a guide and additional questions are welcome.**

1. **What is the difference between a toxin and a toxic agent?**

A **toxin** is a [poisonous](https://en.wikipedia.org/wiki/Poison) substance produced within living cells or organisms. A **toxic agent** is any [toxic](https://en.wikipedia.org/wiki/Toxicity) substance.[[1]](https://en.wikipedia.org/wiki/Toxicant#cite_note-TMT-1) In popular usage, the term is often used to denote substances made by humans or introduced [into the environment by human activity](https://en.wikipedia.org/wiki/Human_impact_on_the_environment), in contrast to [toxins](https://en.wikipedia.org/wiki/Toxin), which are toxicants produced naturally by a living [organism](https://en.wikipedia.org/wiki/Organism).[[2]](https://en.wikipedia.org/wiki/Toxicant#cite_note-2)[[3]](https://en.wikipedia.org/wiki/Toxicant#cite_note-3)[[4]](https://en.wikipedia.org/wiki/Toxicant#cite_note-4) Toxicants are [poisonous](https://en.wikipedia.org/wiki/Poison).

1. **What is the LD50 of caffeine? Is there a beneficial dose for caffeine? And, is there an adverse effect dose (besides the lethal dose)? You may have to do some research to find this information – remember to check your sources and ensure you are gathering information from a credible source.**

compared to 265 mg/kg for caffeine; LD50 (oral, rat) 367.7 mg/kg (SDS)

300-400mg of caffeine can be consumed daily without any adverse effects.

1. Have a look at the following web link: <https://www.caffeineinformer.com/death-by-caffeine>. Calculate how many cups of your favorite caffeinated beverage might give you a lethal effect.
2. **An individual is exposed to a compound one a day for 5 days. On days 1, 2, 3 and 4 they exhibit no physical response, but on the 5th day they show symptoms of a toxicological response. Explain what is going using dose-response curves.**



1. **What is the difference between a NOAEL and LOAEL?**

No-Observed-Adverse-effect and Lowest Observed Adverse Effect Level

**Toxicokinetics Questions: These questions related to the chemical and physical properties of chemicals as they are absorbed, distributed, metabolized, and excreted (ADME) from the body. Chemicals with certain chemical and physical properties will be more readily absorbed and distributed therefore causing a toxic effect. This will help us to think about how we might apply these general rules to the design of molecules that have reduced impact within our bodies.**

1. **How does lipophilicity affect the absorption of a molecule into the body?**

Substances with high lipid solubility readily diffuse through the phospholipid membrane.

Large hydrophobic molecules must diffuse through the lipid portion of the membrane, with the rate of transport correlating with its lipid solubility. In general, highly ionized chemicals have low lipid solubility and do not readily pass through the lipid membrane.

1. **What are the primary chemical and physical properties that will affect whether or not a molecule is absorbed by inhalation?**

Physical form of the agent (gas/vapor or particle), particle size, blood (water) solubility, lipid solubility

In contrast to absorption via the gastrointestinal tract or through the skin, gases and particles, which are water-soluble (and thus blood soluble), will be absorbed more efficiently from the lung alveoli. Very small particles *(<1 µM)* are able to penetrate deep into the alveolar sacs where they can deposit and be absorbed.

Large particles *(>5 µM)* are generally deposited in the nasopharyngeal *(head airways region)* region with little absorption.  Particles 2-5 µM can penetrate into the tracheobronchial region.  Very small particles *(<1 µM)* are able to penetrate deep into the alveolar sacs where they can deposit and be absorbed.

If the agent is absorbed and is also lipid soluble, it can rapidly distribute throughout the body passing through the cell membranes of various organs or into fat depots.  The time to reach equilibrium is even greater for the lipid soluble substances.  Chloroform and ether are examples of lipid-soluble substances with high blood solubility.

1. **Why do chemists prefer to manipulate toxicokinetics parameters rather than toxicodynamics parameters to change the toxicity of the molecule?**

Toxicokinetics (TC) parameters (MW, solubility, volatility, charge and particle size) are much easier to change than toxicodynamics parameters (like receptor binding). TC parameters can be changed relatively easily by a chemical transformation (adding or removing a functional group).



Toxicodynamics parameters often define bioavailability, so how quickly will the chemical be absorbed into the body. Limiting absorption is much better approach from the health standpoint than dealing with the damage once the chemical is inside of the body.