Practice Problems on Pharmaceutical Drugs

1. In the United States, the pharmaceutical-drug approval process is regulated by the FDA. Which organization in Canada performs the same function as the FDA?
   A) Health Canada
   B) Natural Health Products Directorate
   C) Canada Border Services Agency
   D) Canada Revenue Agency
   E) Liquor Control Board of Ontario

   (4 chose this; 2006 final exam)

2. With the assistance of the known, three-dimensional structure of an enzyme, a pharmaceutical company designed a drug that inhibited the enzyme. What is this method of drug discovery referred to as?
   A) Serendipitous discovery
   B) Structure-activity relationship studies
   C) Combinatorial chemistry
   D) High-throughput screening
   E) Structure-guided drug design

3. A pharmaceutical company needs to submit an Investigational New Drug (IND) application to the FDA prior to the start of which phase of drug development?
   A) Clinical trials
   B) Marketing
   C) Shareholder approval
   D) Preclinical Trials
   E) Fundraising
4. Shown below are portions of a news article that appeared on April 8, 2005.

*Pfizer pulling painkiller Bextra from shelves*

WASHINGTON – Pfizer Inc. said Thursday it will pull its arthritis drug Bextra from the market at the request of U.S. regulators. Pfizer said the drug was pulled over U.S. FDA concerns over the risk of potentially fatal skin reactions.

*Health Canada has asked Pfizer to discontinue sales of Bextra. In December, Health Canada warned patients that Bextra carried heart and skin risks and should not be used before or after surgery, or for other purposes that aren’t approved.*

Based on the information presented, which one of statements A – E is correct?

A) Bextra was never intended for use as an arthritis drug.
B) Health Canada encouraged the off-label use of Bextra.
C) The U.S. FDA also regulates drugs in Canada.
D) Bextra was withdrawn due to the data gathered post-approval.
E) None of the above

5. The drug *Gleevec* has been approved for the treatment of leukemia and stomach cancer. However, physicians have also used it to treat kidney, lung, pancreatic, and brain cancers. Based on this information, which one of the following statements is correct?

A) *Gleevec* is an orphan drug.
B) *Gleevec* has no side effects.
C) The physicians were using *Gleevec* off-label.
D) *Gleevec* was developed using high-throughput screening.
E) Phase I, II, and III trials were not needed to approve *Gleevec* for stomach cancer.
6. *Camptothecin*, right, is a natural product that kills leukemia cells. Researchers then synthesized the derivatives below and assessed their ability to kill leukemia cells. This type of experiment is best described as what?

A) Structure-activity relationship study
B) High-throughput screening
C) Structure-guided drug design
D) Isolation from natural sources
E) Total serendipity
7. Which one of the following does NOT constitute an *in vitro* experiment?

A) Testing the ability of a drug to kill a bacterial culture
B) Measuring the rate at which bacteria transport a drug across the cell membrane
C) Determining whether a drug inhibits an isolated enzyme
D) Studying the toxicity of a drug towards a culture of human cells
E) Testing the efficacy of a drug in mice *(in vivo)*

8. Which one of the following hydrogens is the most acidic?

![Chemical structure]

8. Which one of the following hydrogens is the most acidic?

A) H
B) H
C) C
D) D
E) E

9. Sulfanilamide has antibacterial activity, but sulfanilate does not. Why?

![Chemical structures]

A) Sulfanilamide is always neutral and thus is able to enter the cell
B) Sulfanilate ion does not bind to the key bacterial enzyme
C) Only weakly acidic molecules can act as inhibitors for the bacterial enzyme
D) Sulfanilate is rapidly metabolized by bacteria, with loss of sulfate by oxidative cleavage
E) Sulfanilate is unable to cross the bacterial membrane
10. Mammals, unlike bacteria, are not affected by sulfa drugs. Which one of the following statements most correctly explains this behaviour?

A) Mammals are unable to synthesize folic acid so sulfa drugs cannot interfere
B) Sulfa drugs block the synthesis of folic acid, a cofactor which bacteria need while humans do not
C) Mammalian enzymes do not bind sulfa drugs
D) Sulfa drugs cannot enter mammalian cells
E) Sulfa drugs are hydrolyzed to harmless materials by mammalian cells

11. Protonsil was the first drug found to cure septicemia. Which one of the following statements is NOT correct?

A) Protonsil is an azo dye
B) Consumption of Protonsil leads to inhibition of the enzyme needed by bacteria to synthesize folic acid
C) Protonsil exists in both an ionized and neutral form in solution
D) Protonsil must be oxidized in vivo before it becomes active
E) Protonsil must be reduced in vivo before it becomes active
12. Which one of the following is expected to be the worst sulfa drug?

- **A)** \[
\text{NH}_2 \quad \text{SO}_2^- \quad \text{N}
\]
- **B)** \[
\text{NH}_2 \quad \text{SO}_2^- \quad \text{NH}
\]
- **C)** \[
\text{SO}_2^- \quad \text{NH}
\]
- **D)** \[
\text{SO}_2^- \quad \text{NH}
\]
- **E)** \[
\text{SO}_2^- \quad \text{NH}
\]

13. Most sulfa drugs in current use have a heterocyclic ring attached to nitrogen. Which one of these statements correctly describes the purpose of this ring?

- **A)** To improve the solubility of the drug in the blood
- **B)** To provide extra binding interactions to the bacterial enzyme and thus enhance activity
- **C)** To increase the nucleophilicity of the sulfonamide to give more rapid reaction
- **D)** To slow down hydrolysis of the sulfonamide so the drug will be longer acting
- **E)** To adjust the pKa of the drug to the optimum range
14. During the biosynthesis of folic acid from glutamic acid, \(p\)-aminobenzoate, and the pteridine derivative, two coupling reactions took place. Which two carbon and/or nitrogen atoms acted as nucleophiles during the biosynthesis?

A) 1 and 5
B) 2 and 4
C) 3 and 5
D) 2 and 5
E) 3 and 4

15. In the first step of the biosynthesis of folic acid by bacteria, \(p\)-aminobenzoic acid is linked to a pteridine derivative. This reaction requires ATP, why?

A) ATP protects the carboxylate group by phosphorylation.
B) ATP phosphorylates the alcohol, making it a good leaving group.
C) ATP phosphorlylates the amino group, making it a better electrophile.
D) ATP holds \(p\)-aminobenzoic acid and the pteridine in the proper position required for reaction to occur.
E) ATP phosphorylates the alcohol, making it a better nucleophile.
16. The structure of sulfasalazine, a drug that is used to treat rheumatoid arthritis, is shown below. Sulfasalazine is a prodrug which undergoes reduction in the liver to its active form. Which one of A-E represents the products of sulfasalazine reduction?

A) II and V  
B) II and III  
C) IV, V, and VI  
D) I and III  
E) I and II