

PHAR 332 SPRING 2007  
FUNDAMENTALS OF DRUG ACTION II  
EXAM 4 - FINAL EXAM

SEAT NUMBER

YOUR NAME \_\_\_\_\_.

WRITE YOUR NAME ON THE **SECOND PAGE** IN THE INDICATED PLACE AS WELL.

**DIRECTIONS**

Sit in the assigned seat. This is a two-hour exam, worth 250 points. The exam is closed-book; no aids are permitted.. The exam must be written **in ink**. If you use a pencil, we will not regrade the exam. Answer all questions completely and accurately. Use the proper number of significant figures, and the correct scientific units, where needed. In the essay questions, use good English; your score will reflect your use of proper English as well as the scientific content of your answer. The exam has 13 (thirteen) pages total; check your exam to make sure it is complete.

***Warning! Cheating on an exam may result in failing the exam, dismissal from the course, and/or other penalties!***

We reserve the right to photocopy your exam for our files.

YOUR NAME \_\_\_\_\_

<u>PROBLEM</u>	<u>SCORE/POSSIBLE</u>
I	____ / 35
II	____ / 15
III	____ / 20
IV	____ / 20
V	____ / 25
VI	____ / 10
VII	____ / 28
VIII	____ / 24
IX	____ / 27
X	____ / 22
XI	____ / 24
<b>TOTAL</b>	____ / 250
Bonus points	____ / 2

YOUR NAME \_\_\_\_\_

I. (35 pts total; 5 pts each) Fill in the blanks with the appropriate word, phrase, or abbreviation.

A. In the urea cycle, citrulline is formed from ornithine and \_\_\_\_\_.

B. In the urea cycle, arginininosuccinate is split to form arginine and \_\_\_\_\_.

C. "Classic" phenylketonuria is due to the absence or deficiency in the enzyme \_\_\_\_\_.

D. Tetrahydrofolate is regenerated from folate in a two-stage reaction catalyzed by the enzyme \_\_\_\_\_.

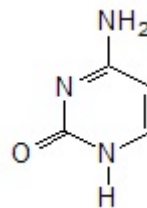
E. In humans the excreted end product of purine catabolism is \_\_\_\_\_.

F. The "committed step" in purine biosynthesis is the conversion of \_\_\_\_\_ into 5-phosphoribosylamine.

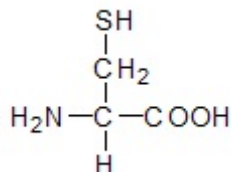
G. The committed step in pyrimidine biosynthesis is the reaction of \_\_\_\_\_ with aspartate.

II. (15 points total; 5 pts each) Name the structures; correct biochemical abbreviations are acceptable.

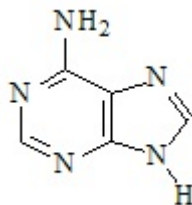
A. \_\_\_\_\_



B. \_\_\_\_\_



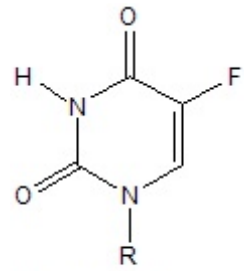
C. \_\_\_\_\_



YOUR NAME \_\_\_\_\_

III. (20 points total) Here is the structure of 5-fluorouridylate.

A. (15 pts) Briefly explain and describe the mechanism of action of this compound in the inhibition of thymidylate synthase.



R = deoxyribose  
monophosphate

B. (5 pts) Explain how this is important in cancer chemotherapy.

YOUR NAME \_\_\_\_\_

IV. (20 points) Explain how, under conditions of fasting or starvation, the production of ATP can continue with a mild ketosis by using glucogenic amino acids. Explain the origin of the ketosis, note which amino acids may be used, and discuss connections to central metabolic pathways.

Name \_\_\_\_\_

**DRUG METABOLISM AND CHEMICAL TOXICOLOGY - Dr. Bolton (160 points total)**

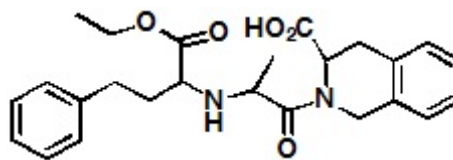
Answer the questions on drug metabolism and chemical toxicology below.

V. There is only ONE answer for multiple choice questions.

A) (5 pts) Which of the following statements is incorrect? Circle your response.

- a. GSH reacts with alcohols and phenols to form GSH conjugates.
- b. GSH reacts with quinones, epoxides, alkyl halides to form GSH conjugates.
- c. GSH conjugation reactions are catalyzed by a transferase.
- d. GSH conjugation is a phase II reaction.
- e. GSH conjugation is a detoxification reaction.

B) (5 pts) Quinapril (antihypertensive) can undergo hydrolysis at two different functional groups. Circle the functional groups that could be hydrolyzed.



Now predict which functional group would be hydrolyzed at the faster rate \_\_\_\_\_

C) (5 pts) Amino acid conjugation occurs with which of the following functional groups?

- a. phenols
- b. amines
- c. carboxylic acids
- d. alkyl halides

D) (5 pts) Aflatoxin is a liver carcinogen which forms an electrophilic epoxide as the ultimate carcinogen. Which of the following would NOT result in reduction in the carcinogenic effects of aflatoxin?

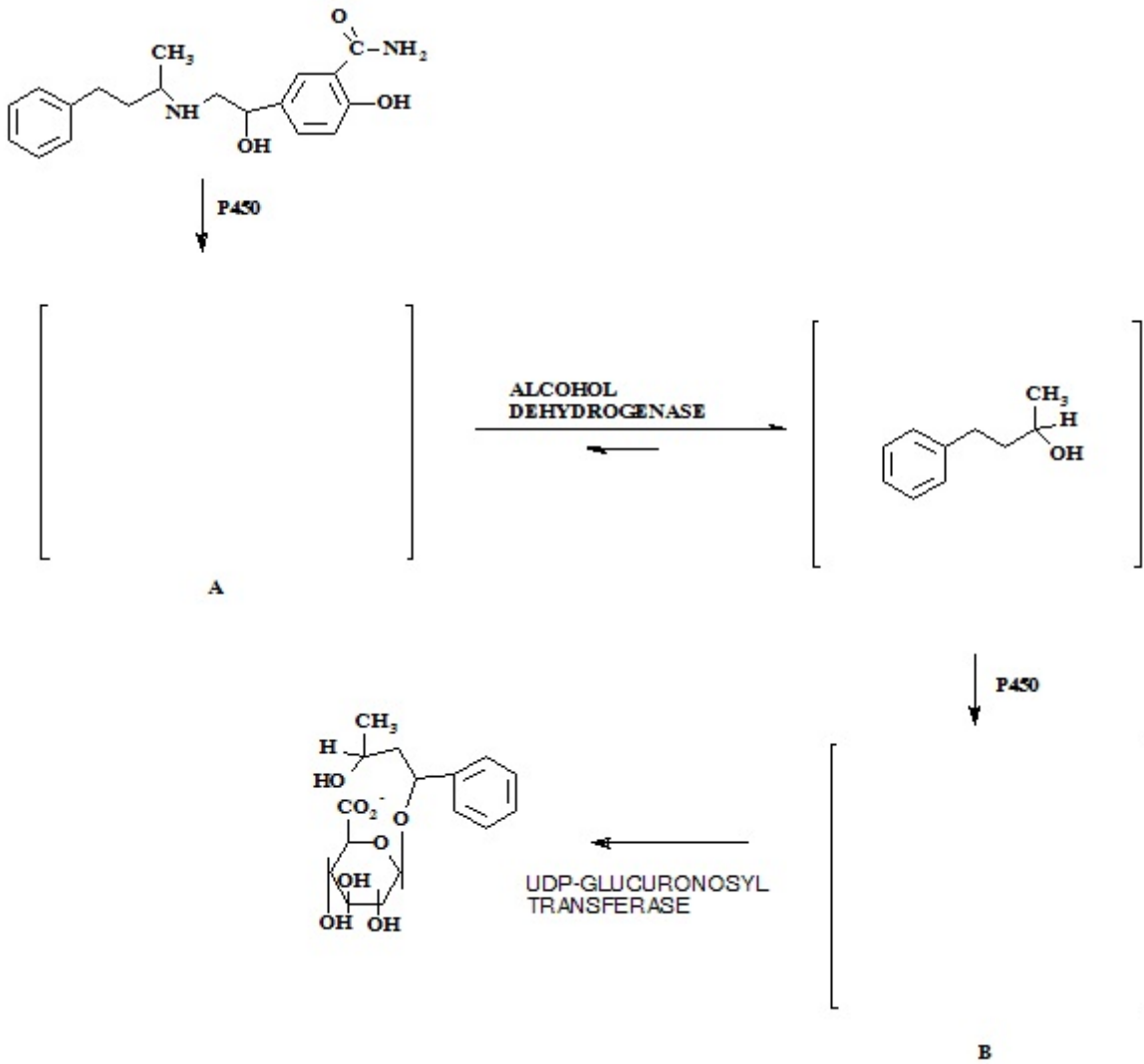
- a. Inhibition of cytochrome P450.
- b. Induction of cytochrome P450.
- c. Induction in glutathione S-transferase.
- d. Education of the population to prevent exposure.

E) (5 pts) The metabolically-based interaction between rifampin and ethinylestradiol could result in pregnancy because:

- a. Rifampin inhibits P4503A4.
- b. Rifampin induces P4503A4.
- c. Ethinylestradiol inhibits P4503A4.
- d. Ethinylestradiol induces P4503A4.

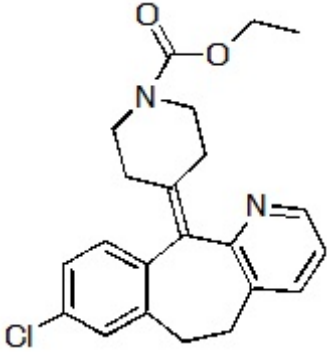
Name \_\_\_\_\_

VI. (10 pts.) Normodyne is a adrenergic receptor blocking agent which could be metabolized as shown below. Give the structures of the intermediate metabolites A and B.



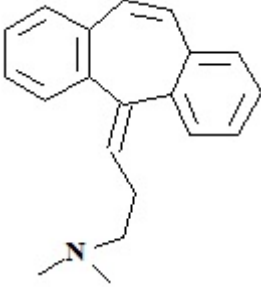
Name \_\_\_\_\_

VII. (28 pts.) The structure of loratadine which is used to treat allergies is shown below. Give three different phase I metabolites of loratadine (Hint: there are at least 8 different phase I metabolites). Name the enzymes catalyzing each reaction. Make sure you do not repeat the same metabolic pathway on a different part of the molecule. Show how one of your metabolites could be metabolized in a phase II reaction and name the enzyme catalyzing the reaction.



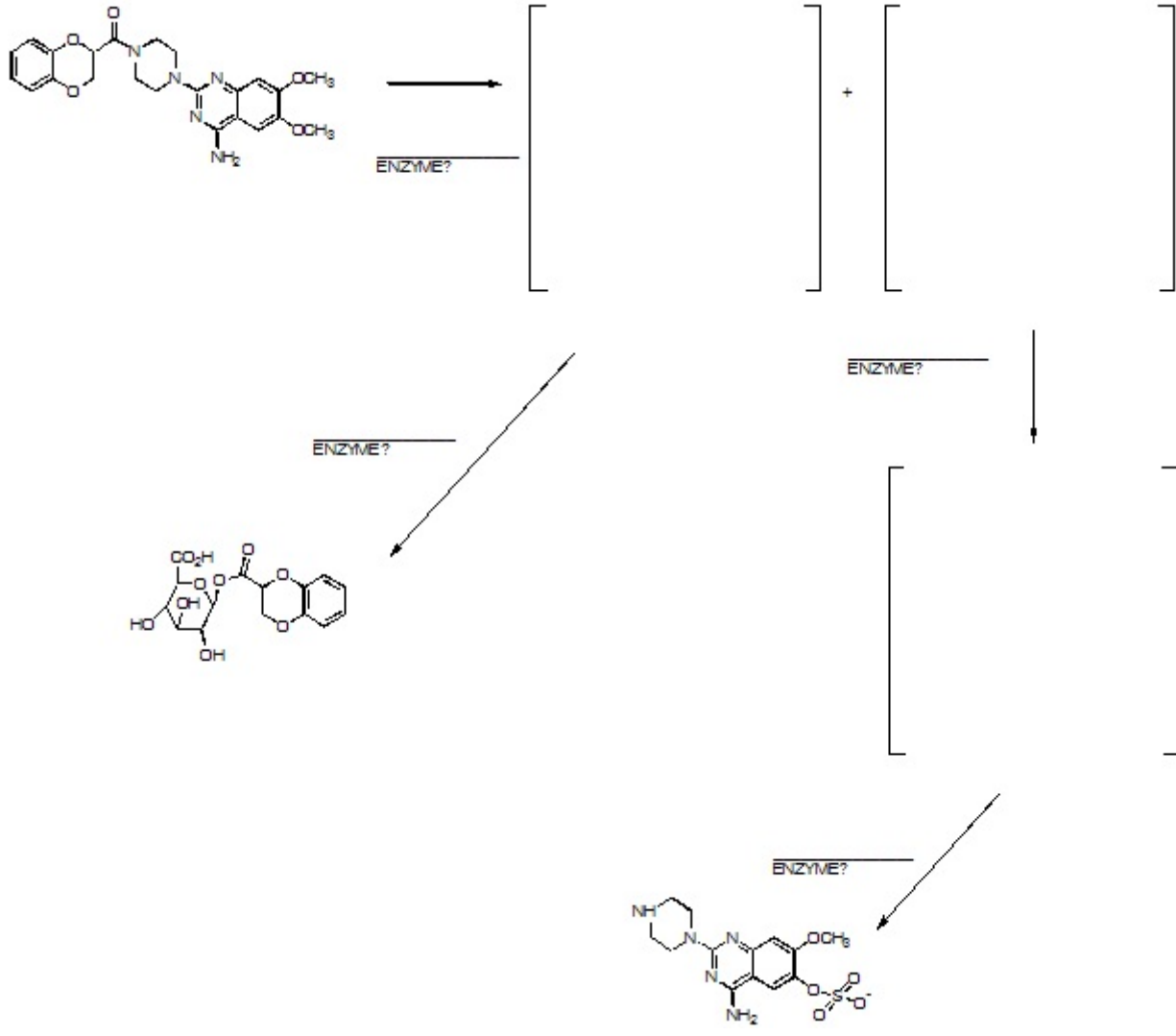
Name \_\_\_\_\_

VIII. (24 pts.) Cyclobenzaprine is used to relieve muscle spasms. Show how cyclobenzaprine could be metabolized by the epoxide/diol pathway (there are two possibilities in the molecule; either one is correct). Name the enzymes catalyzing each reaction and draw the structures of the metabolites. Show the enzyme-catalyzed reaction of one metabolite with glutathione, and name the enzyme.



Name \_\_\_\_\_

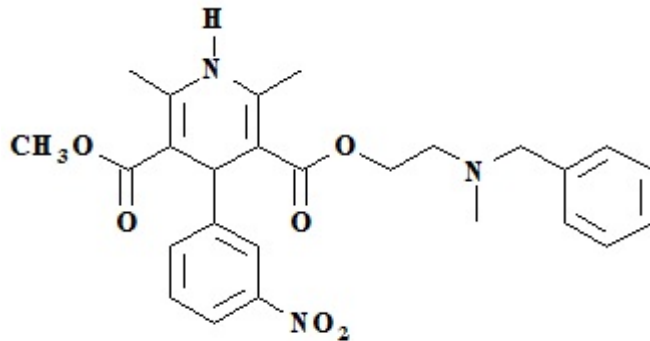
IX. (27 pts) Cardura is an  $\alpha_1$ -blocker used to treat high blood pressure. Carduar could be metabolized by the pathway outlined below. Give the intermediate metabolites and provide names for the enzymes involved in each transformation.



Name \_\_\_\_\_

X. (22 pts) Nicardipine a calcium channel blocker, antihypertensive drug could undergo aromatic hydroxylation at two different sites.

A. Circle which ring will undergo metabolism and briefly explain why.

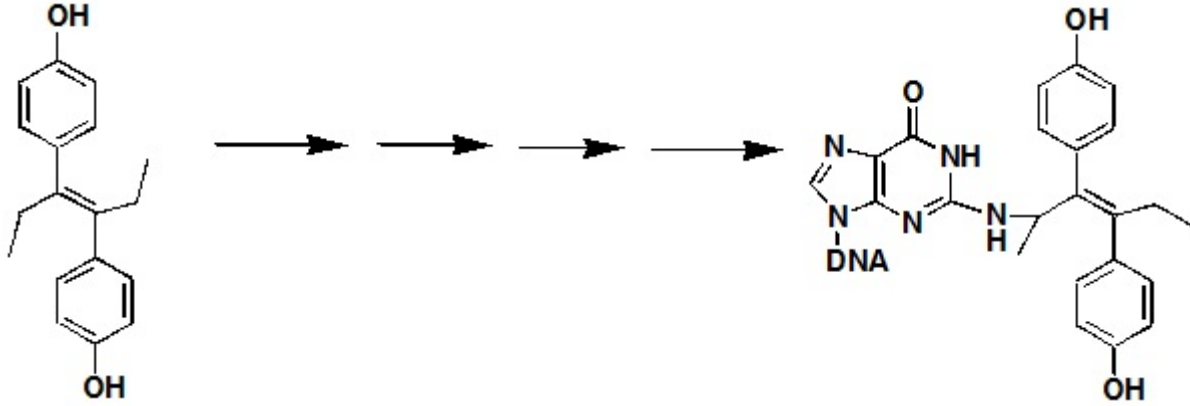


**NICARDIPINE**

B. Nicardipine can be hydrolyzed at two sites. Show the structure of one of the metabolites and name the enzyme catalyzing the reaction. Show the most common phase II metabolic pathway for one of the metabolites of Nicardipine. Name the enzyme catalyzing the reaction.

Name \_\_\_\_\_

XI. (24 pts) Diethylstilbestrol is a potent teratogen. One potential toxic mechanism for diethylstilbestrol is sketched below. Show the intermediate metabolites. Name the enzymes catalyzing each reaction. (Hint: There are three intermediates and only the first two steps are enzyme-catalyzed.) Name the ultimate toxin (i.e. type of reactive intermediate).



YOUR NAME \_\_\_\_\_

Bonus Questions (One point each)

A. Guanine, guanosine, and guanylate are three different compounds. What are the differences?

B. How does allopurinol relieve the condition of gout?