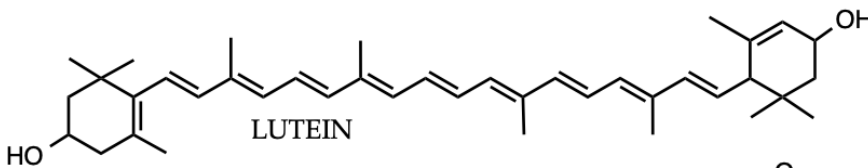
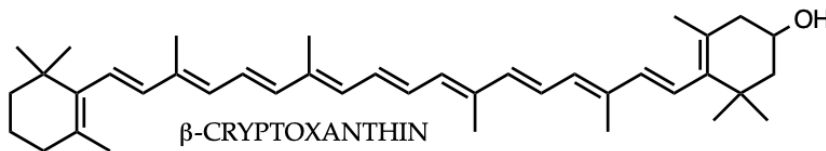
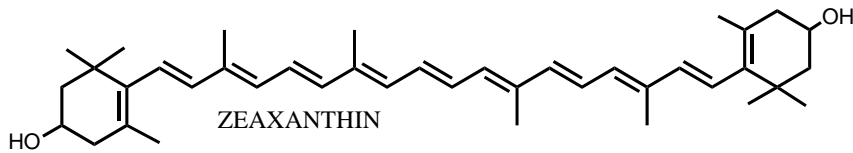


Medicinal Chemistry 562 - Rettie Problem Set 1

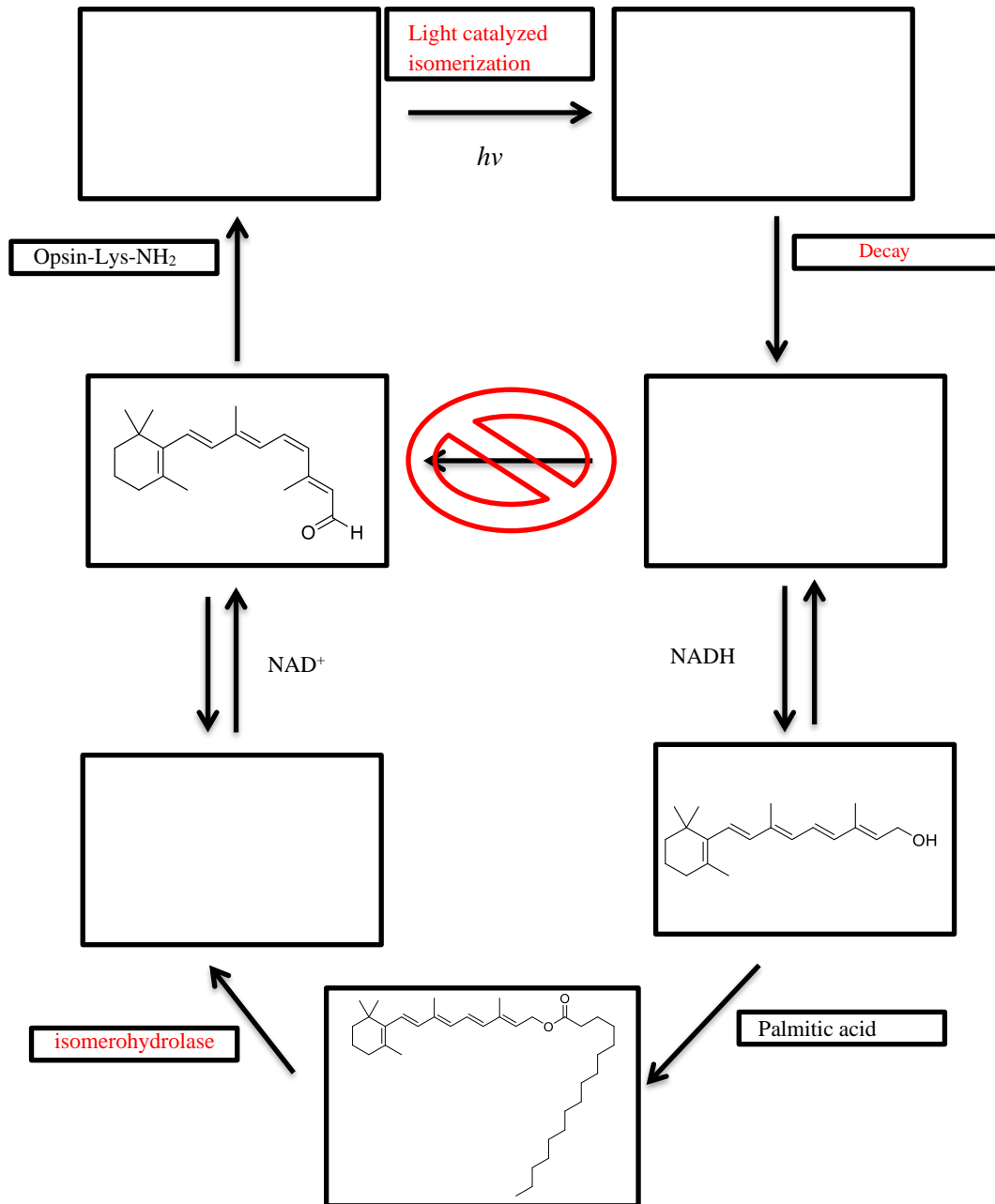
1. List three important differences of physiological consequence between the fat-soluble and water-soluble vitamins.

2. Answer questions a. and b. for each the two carotenoids shown below.



- a. Can these carotenoids yield retinal following BCMO metabolism? If so, how many equivalents of retinal are theoretically possible?
 - b. Lutein and zeaxanthin were constituents of the AREDS2 eye-drop formulation for treating acute acular degeneration. What was the rationale for using them?
3. What 3 basic functions do the active forms of vitamin A support? Briefly discuss the effect of vitamin A deficiency with regard to these basic functions.

4. Fill in the blanks on the rhodopsin cycle.



5. What is a RAMBA? What condition might it be used to treat? Which enzyme does it inhibit?

6. Case study: A 44-year-old man presented with a 3-year history of intermittent night blindness. He suffered from short bowel syndrome due to ileocecal resection in Crohn disease. His serum vitamin A level was measured at 0.11 I g/ml. Oral vitamin A supplementation was ineffective, but subsequent treatment with a liposoluble infusion containing vitamins A, D, E and K once daily for 3 days resolved these visual problems.

Provide a detailed analysis of this case explaining what all the data provided are telling you.

7. Retinoids are administered orally for the treatment of acne and other skin conditions. Are there risks associated with this kind of treatment? If so, discuss briefly.

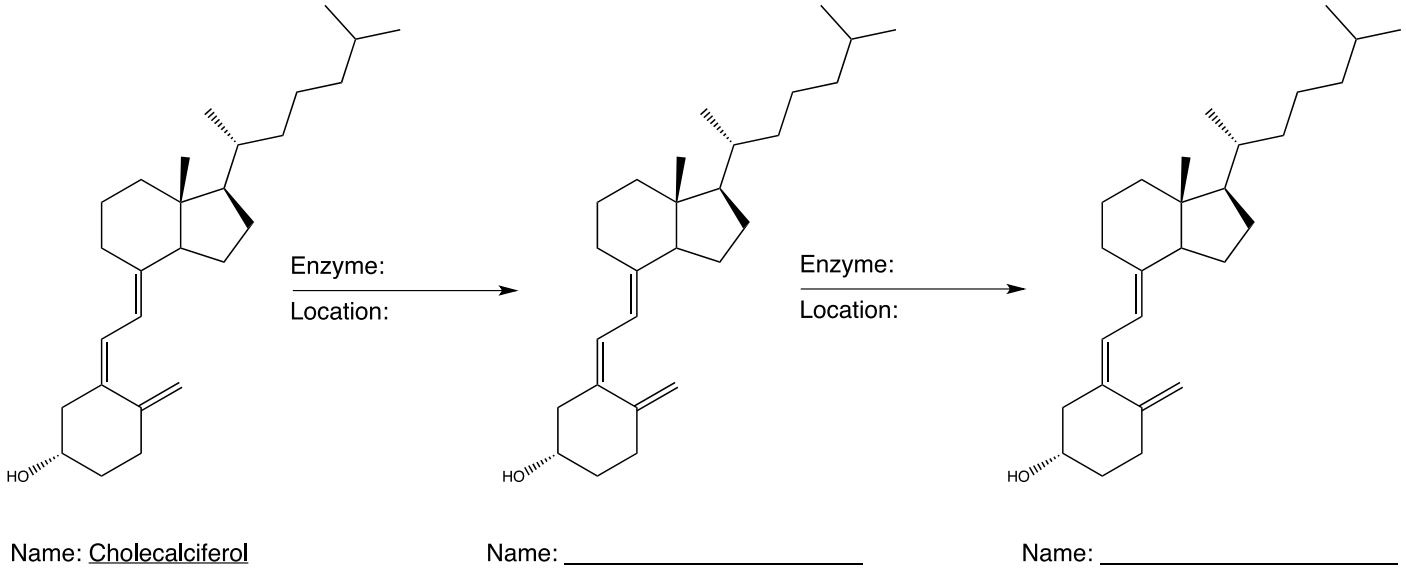
8. Explain fully why the 2nd generation retinoid Etretinate was removed from the market.

9. Identify specific ligands for RXR and RAR.

10. Explain why 1 microgram of all-trans retinol is equivalent to 2 micrograms of all-trans β -carotene in oil.

11. Why should consumers (especially smokers and past smokers) avoid β -carotene as a single dietary supplement?

12. Cholecalciferol is the structure on the far left. Which fat-soluble vitamin is this?



- a. Cholecalciferol is hydroxylated twice by P450s to yield the active form of this vitamin.
 - i. Draw in the hydroxyl groups on the structures provided
 - ii. Indicate which CYP carries out each hydroxylation and the tissue location where it takes place in.
 - iii. Finally, name each molecule (there are multiple names for each!).

13. Vitamin D and parathyroid hormone (PTH) have important roles in metabolic bone disease.

- a. Metabolic bone disease typically happens as a result of failure in which organ?
- b. Metabolic bone disease is associated with deficiency of which mineral?
- c. Describe how PTH interacts with bone, the failed organ in “part a”, and the mineral in “part b”.

14. Complete the table.

Vitamin	Function / Uses	Deficiency States	Toxicities	Daily Value	Upper Limit
A					
D					