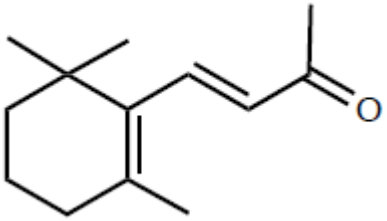
MEDCHEM 562 - 2014
Fat Soluble Vitamins Problem Set

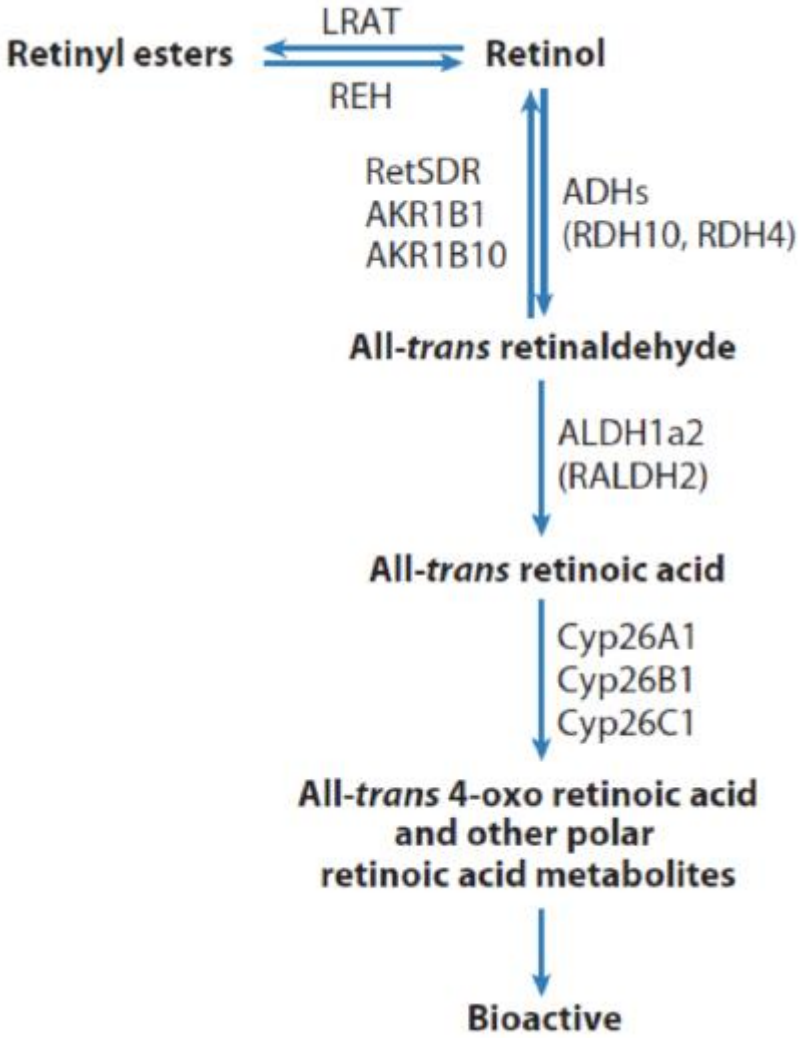
1. Fill out the blanks in the table below.

Vitamin	Physiological Function	Deficiency symptoms	Toxicity
A	-Vision -Cell Differentiation -Inhibition of Cell Proliferation -Antioxidant Activity -Acne Psoriasis	-Night Blindness -Dry skin -Prone to infection -poor tooth development -slower bone growth	-Teratogenic (controversial) -Hypervitaminosis: Vomiting, hypercalcemia, brittle bones, fatigue, etc. -Increased risk of fractures (also a problem with low intake)
D	-Maintaining Calcium Levels -Modulation of cell differentiation and proliferation	- Rickets - Osteomalacia	- Calcification of soft tissues
E	-Antioxidant -Free Radical Scavenging	- Neuromuscular abnormalities - Myopathies - Hemolytic anemia in infants	- Adverse bleeding effect (rare) - Exacerbated bleeding when given with warfarin
K	-Blood Clotting -Inhibiting Artery Calcification -Bone Metabolism -Gla Protein formation -Post translational modification of glutamic acid residues	- Spontaneous hemorrhaging increase	- Allergic reactions

2. What are the key structural requirements for vitamin A activity of the retinol series of compounds?



3. Fill in the boxes for the pathway below:



4. Which sense does this pathway play a part in? Identify two symptoms of vitamin A deficiency.
   Sight.
   When deficient: night blindness & Dry, rough skin

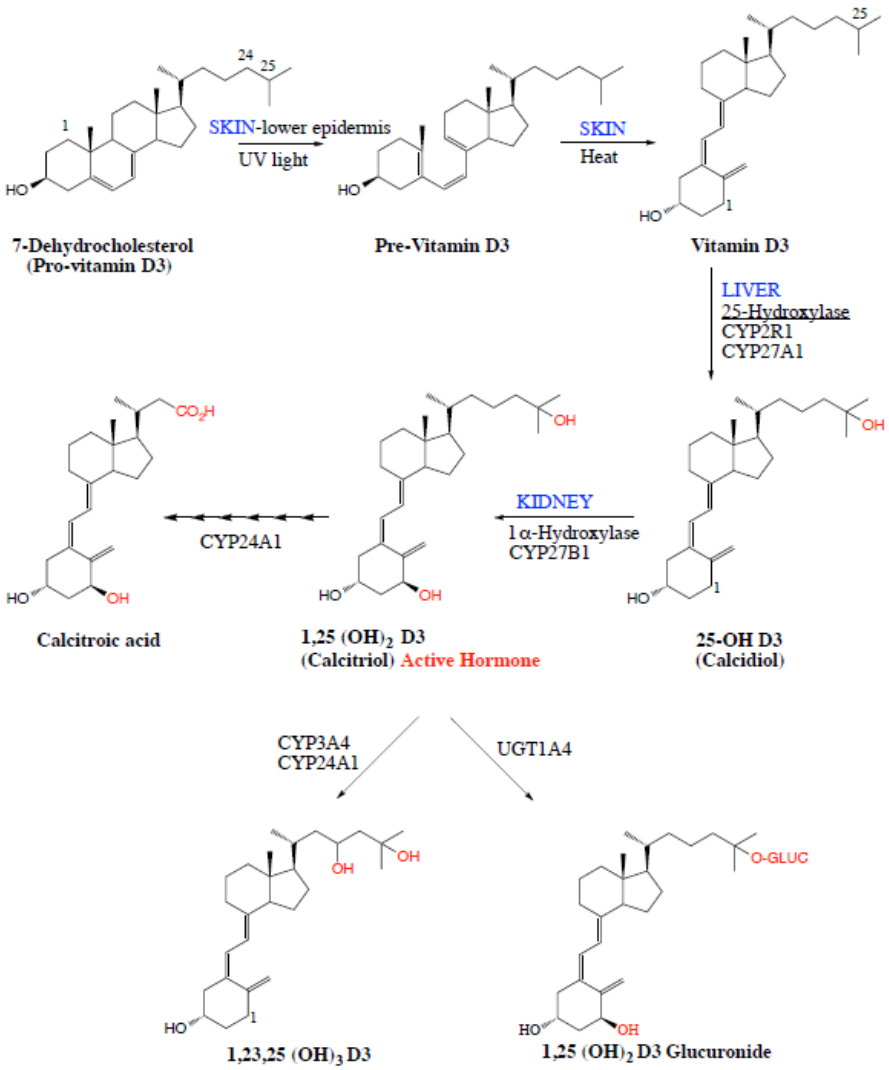
5. Name three good dietary sources of Vitamin A:

   Leafy Greens, Cod liver oil, Animal Livers (Beef, polar bear, etc.)

6. "Vitamin D" is technically not a Vitamin. Explain.

Vitamin D is a prohormone, it's converted to the active hormone form in the body.

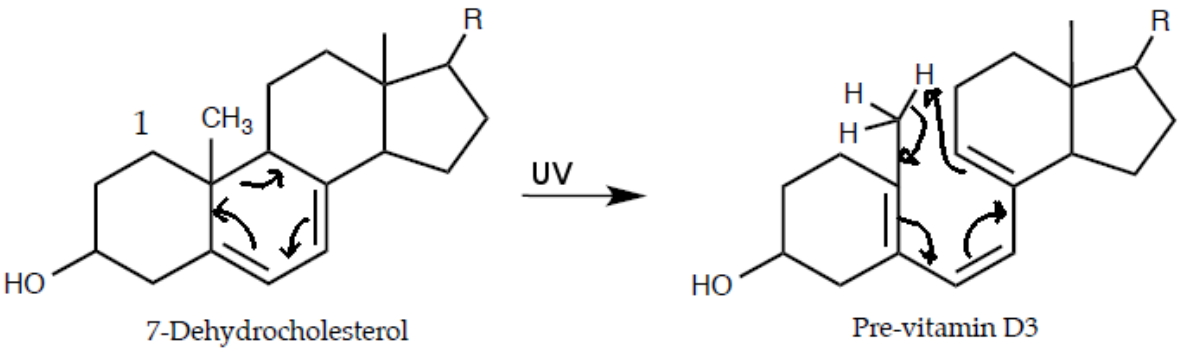
7. Fill in the blanks on this diagram:



8. Where in the body is Vitamin D converted to its active form enzymatically?
   The Kidney

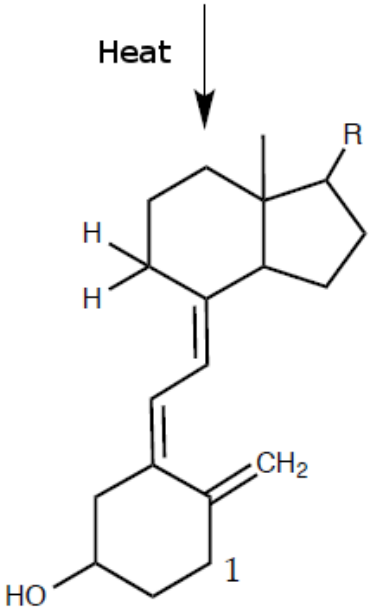
9. How is Pre-Vitamin D3 converted to Vitamin D3? Show this reaction.

   In the skin when exposed to sunlight.



7-Dehydrocholesterol

Pre-vitamin D3

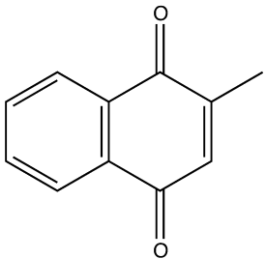


Vitamin D3

10. A patient is worried about hypervitaminosis A because he/she eats a diet high in carrots. Should he/she be concerned by vitamin A produced by the cleavage of β-carotene (found in carrots)? Why or why not?

No, he/she should not because conversion of the carotenoids to form retinals is inefficient as conversion decreases when body stores of vitamin A are high. The patient might experience yellowing of skin, but no negative symptoms associated with high levels of vitamin A. If the patient has high levels of vitamin A, he/she should avoid eating foods with large amounts of cod liver oil, beef liver, or polar bear liver.

11. Menadione is shown below: By what other name is it known?



Vitamin K3

12. Menadione itself has no intrinsic vitamin activity, but can be activated by reaction with what endogenous constituent? What is the product of this reaction?

It is activated with geranylgeranyl phosphate to make MK4, a K2 Vitamin.

13. Why is Vitamin K's cofactor activity so crucial?

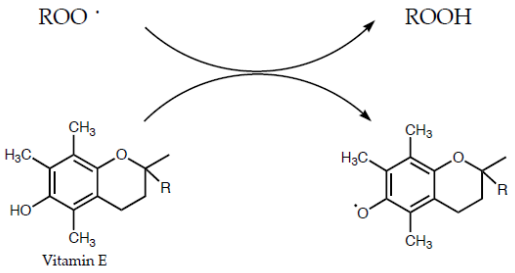
The reaction that Vitamin K assists in creates γ-Carboxyglutamic acid, which then goes to make many clotting factors. Without these clotting factors, people become hemophilic and are prone to bleeding out.

14. How exactly does warfarin exert its anticoagulant effects?

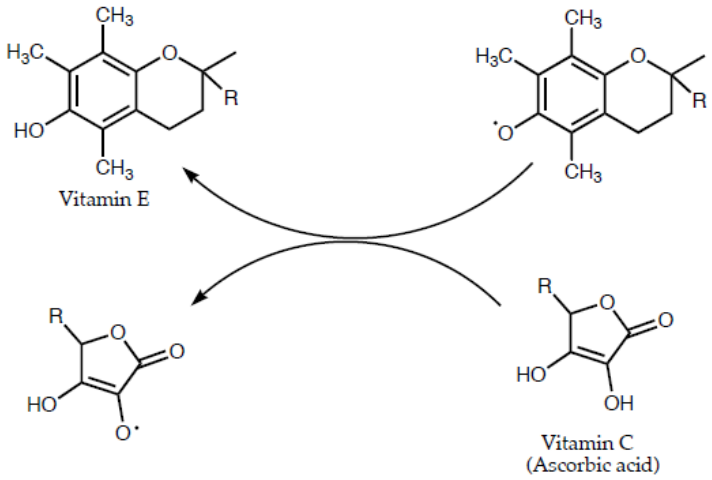
Warfarin inhibits the Vitamin K recycling process, lowering levels of Vitamin K in the body.

15. Explain how vitamin E can function as an antioxidant Vit. E? Show how is it regenerated.

Vitamin E can be used to remove radicals from lipids



It's regenerated with Ascorbic Acid (Vitamin C)



16. Explain why, from a chemical standpoint α-tocopherol is a more potent antioxidant than ɣ-tocopherol.

The methyl groups are electron donating, promoting the non-aromatic form, which helps with resonance

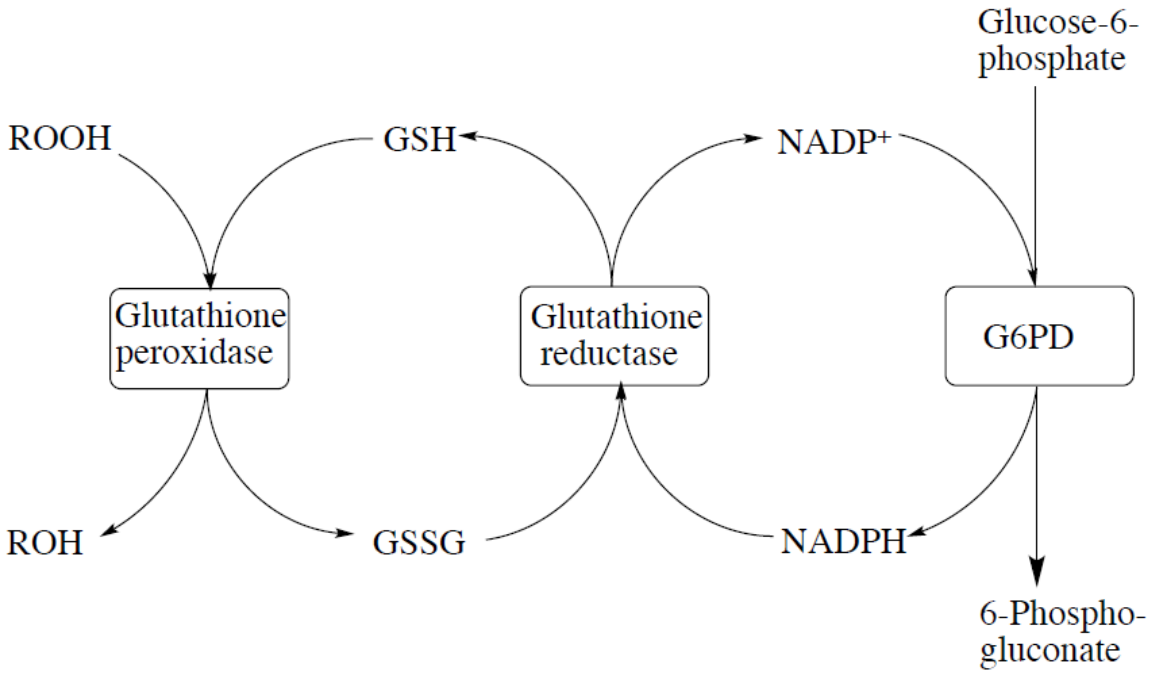
17. Which is the most toxic of the reactive oxygen species? Show how it can be generated from superoxide anion and hydrogen peroxide. What is the name of this reaction?

The most toxic reactive oxygen species is the hydroxyl radical. It is generated in the Harber-Weiss reaction with the aid of iron.

$$Fe^{3+} + O_2^{-\cdot} \text{ -----> } Fe^{2+} + O_2$$

$$Fe^{2+} + H_2O_2 \text{ -----> } Fe^{3+} + OH^- + OH^{\cdot}$$

18. Show how lipid hydroperoxides are detoxified by the glutathione pathway.



19. Which minerals and vitamins are critical to the proper functioning of the glutathione pathway?

Selenium, B2 (riboflavin), and B3 (niacin)