Medicinal Chemistry 562

Final Exam

December 12, 2018

NAME:_____

Q1 – Q35_____(70)
Q36–Q39 _____(28)
Evaluation (2)
Total_____(100)

Q1-Q35 Multiple Choice (70 pts). Choose the single best answer.
USE SCANTRON

1. If the EAR for a vitamin is 3.0 mg/day then the RDA is:
   a. 1.7 mg/day
   b. 2.5 mg/day
   c. 1.2 mg/day
   d. 3.6 mg/day
   e. none of the above

2 – 4. Match each vitamin with the appropriate disease or condition associated with its deficiency

2. _____ Pernicious anemia
   a. Thiamin
   b. Cobalamin
   c. Niacin
   d. riboflavin

3. _____ Neural tube defect
   a. B_{12}
   b. Thiamin
   c. Biotin
   d. Folic acid

4. _____ Beriberi
   a. B_5
   b. Pyridoxal
   c. B_1
   d. Niacin

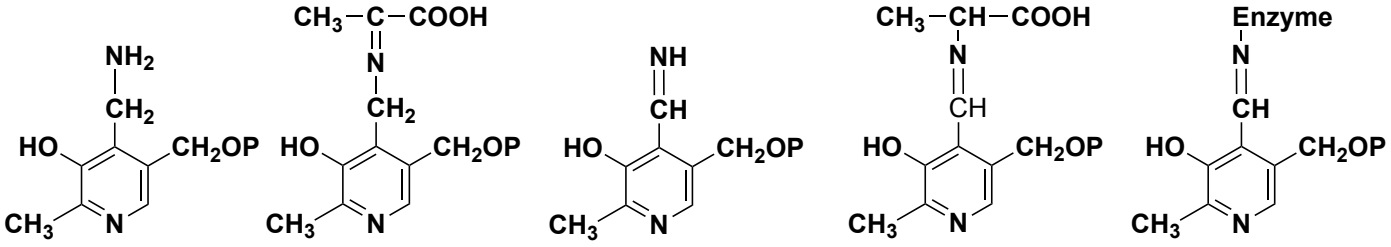
6-8. Match the test for deficiency of a vitamin, with the vitamin:

5. _____ Vitamin B_1
   a. folate level in erythrocytes
   b. urine methylmalonic acid level
   c. transketolase assay in red blood cells
   d. Amino acid decarboxylase

6. _____ Vitamin B_9
   a. Homocysteine levels in red blood cells
   b. erythrocyte glutathione reductase activity
   c. erythrocyte transaminase activity
   d. Folate levels in erythrocytes

7. _____ Riboflavin
   a. transketolase assay in red blood cells
   b. erythrocyte glutathione reductase activity
   c. Homocysteine level in erythrocytes
   d. erythrocyte transaminase activity

8. Which imine form of pyridoxal below yields an amino acid upon hydrolysis [P= HPO_3^-]:



a. b. c. d. e.

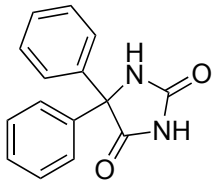
9. Which of the following is FALSE about Leucovorin:
   a. Can allow ordinarily lethal dose of pyrimethamine to be used against malaria
   b. Can allow ordinarily lethal dose of methotrexate to be used against tumor
   c. Is N_5-formyl THFA
   d. Is more effective in killing tumor cells than normal cells

10. Which of the following inborn errors of metabolism is NOT likely responsive to vitamin B_1 treatment?
   a. Transketolase defect
   b. Cystathionurea
   c. Maple syrup urine disease
   d. Pyruvate dehydrogenase defect

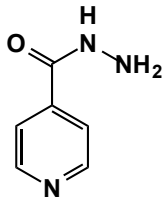
11. What is the reason that vitamin B_{12} deficiency will lead to folic acid deficiency?
   a. Because B_{12} helps enterohepatic circulation of N_5-methyl THFA
   b. Methyl B_{12} can methylate homocysteine
   c. Because B_{12} is needed for N_5-methyl THFA to be converted back to THFA
   d. B_{12} is a required cofactor for DHFA reductase that reduces DHFA to THFA

12. Preparations containing > 0.8 mg of folic acid require prescription because high dose of folate supplements have what risk?
   a. Could reduce the effect of trimethoprim
   b. Could reduce the effect of methotrexate
   c. Could mask the megaloblastic anemia symptoms of B_{12} deficiency and leave the neurological damages unchecked
   d. Could inhibit DNA methylation and lead to megaloblastic anemia

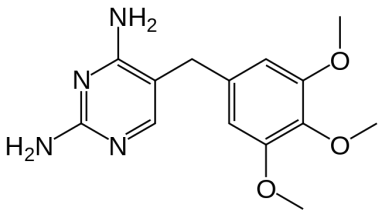
13. In principle, which drugs or vitamins below could possibly result in iatragenic Vitamin B_6 deficiency if used chronically, based on the structures shown:
    a. Phenytoin
    b. Trimethoprim
    c. Isoniazid and Carbidopa
    d. Isoniazid and Trimethoprim
    e. Isoniazid and Pyrimethamine



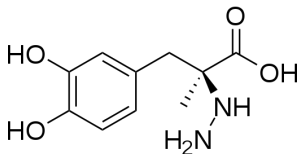
Phenytoin



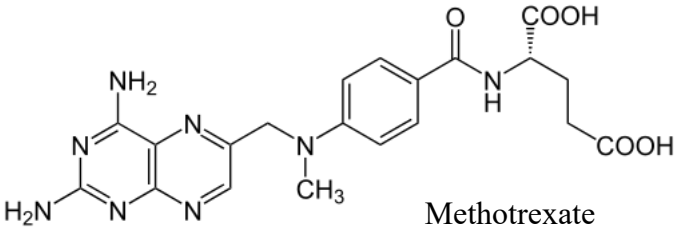
Isoniazid



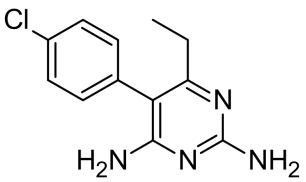
Trimethoprim



Carbidopa

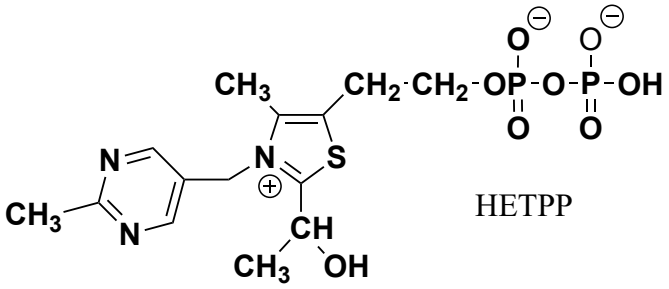


Methotrexate



Pyrimethamine

14. Which of the following is a possible fate for the hydroxyethyl TPP form of thiamine:
    a. Transfer of two carbons to an oxidized lipoic acid
    b. Transformation of carbon-carbon double bonds to carbon-carbon single bonds
    c. Decarboxylation to yield CO_2 and pyruvate
    d. Attack by ethanol to reduce systemic ethanol levels and benefit alcoholics



HETPP

15. Isoniazid can precipitate some symptoms of pellagra because:
    a. Isoniazid binds to vitamin B_3, which leads to B_3 deficiency
    b. Isoniazid binds to vitamin B_1, which leads to B_1 deficiency
    c. Isoniazid binds Zn, which stops the conversion of tryptophan to niacin
    d. Isoniazid binds to pyridoxal phosphate, which stops the conversion of tryptophan to niacin

16. Choose the FALSE statement about vitamin C.
    a. Act as a cofactor for hydroxylation of proline that is important for collagen synthesis
    b. Will make urine test for sugar false positive because vitamin C will oxidize the copper used in the test
    c. Act as a cofactor for the synthesis of norepinephrine
    d. Act as a cofactor for hydroxylation of lysine that is important for collagen synthesis

17. Elevated plasma Homocysteine, associated with decreased conversion to methionine, is correlated with increased risk of cardiovascular disease. Which is the most effective supplementation in lowering the level of homocysteine?
    a. 5-Methyl tetrahydrofolate
    b. Pyridoxal, folic acid, and cobalamin
    c. Methyl cobalamin
    d. Thiamine, folic acid, and cobalamin

18. Vitamin B_6 is contraindicated in levo-DOPA therapy against Parkinson's disease. Which of the following statement on this is TRUE?
    a. Vitamin B_6 enhances decarboxylation of levo-DOPA, which prevents it from crossing blood-brain barrier.
    b. Vitamin B_6 inhibits synthesis of dopamine from levo-DOPA
    c. Levo-DOPA can lead to vitamin B_6 deficiency by reacting with it
    d. Carbidopa can be used as an alternative to levo-DOPA because it can cross blood-brain barrier

19. Choose the TRUE statement about biotin.
    a. Is highly abundant in egg whites, which can cause "egg white injury"
    b. Can be used to lower cholesterol level
    c. Participate as a cofactor for a number of decarboxylation reactions
    d. Can be used to treat an inborn error of metabolism in biotinidase

20. Which one is FALSE for pantothenic acid?
    a. Its coenzyme form participates in pyruvate dehydrogenase
    b. It is part of coenzyme A
    c. Its dimer can be used to lower cholesterol level
    d. It can be used to treat hair loss

21. An patient with pernicious anemia due to intrinsic factor deficiency would most likely benefit from:
    a. Change to a diet that is rich in vitamin B_{12}
    b. IM injection of 100 mg of vitamin B_{12}
    c. IM injection of 100 mg of intrinsic factor
    d. Oral supplementation of long-acting hydroxycobalamin

22. Choose the statement on Niacin that is FALSE.
    a. Is the precursor to the enzyme cofactors $NADP^+/NAD^+$
    b. Its coenzyme form participates in fatty acid β-oxidation
    c. Can be used to lower LDL levels at its daily value
    d. Its coenzyme form participates in P450-catalyzed oxidation

23. Which of the following is <u>True</u> about the fat-soluble vitamins?
    i) mineral oil impairs their absorption
    ii) they are rapidly degraded by heating
    iii) it takes time to bring on a deficiency state
    Answer **A** if (i) and (ii) are true
    Answer **B** if (i) and (iii) are true
    Answer **C** if (ii) and (iii) are true
    Answer **D** if all are false

24. All-*trans* retinoic acid;

i) regulates cell synthesis of macromolecules after binding to the retinoid X receptor
ii) is synthesized from all-*trans* retinaldehyde by CYP26
iii) is highly effective in the treatment of promyelocytic leukemia
Answer **A** if only (i) is correct
Answer **B** if only (ii) is correct
Answer **C** if only (iii) is correct
Answer **D** if all are correct

25. β-Carotene is;

i) the most effective carotenoid source of vitamin A
ii) the safest form of vitamin A for smokers
iii) present at high levels in sweet potato
Answer **A** if (i) and (ii) are correct
Answer **B** if (i) and (iii) are correct
Answer **C** if (ii) and (iii) are correct
Answer **D** if all are correct

26. Which of the following is/are <u>True</u>;

i) no carotenes contain oxygen
ii) all carotenoids are carotenes
iii) all carotenes have vitamin A activity
Answer **A** if only (i) is correct
Answer **B** if only (ii) is correct
Answer **C** if only (iii) is correct
Answer **D** if none are correct

27. When a photon of light hits rhodopsin, the first isomerization step in the visual cycle generates;

i) all-*trans*-retinal
ii) all-*trans*-retinol
iii) 11-*cis*-retinol
Answer **A** if only (i) is correct
Answer **B** if only (ii) is correct
Answer **C** if only (iii) is correct
Answer **D** if none are correct

28. Vitamin D2 is;

i) obtained by UV irradiation of cholecalciferol
ii) has a longer half-life than vitamin D3
iii) present at high levels in cod liver oil
Answer **A** if only (i) is correct
Answer **B** if only (ii) is correct
Answer **C** if only (iii) is correct
Answer **D** if none are correct

29. CYP24A1 is responsible for formation of;

i) calcidiol
ii) calcitriol
iii) calcitroic acid formation
Answer **A** if only (i) is correct
Answer **B** if only (ii) is correct
Answer **C** if only (iii) is correct
Answer **D** if none are correct

30. The vitamin D plasma level;

i) found in healthy adults with good sun exposure is 50-70 ng/ml
ii) needed to prevent rickets is at least 15 ng/ml
iii) cut-off for deficiency is <20 ng/ml
Answer **A** if (i) and (ii) are correct
Answer **B** if (i) and (iii) are correct
Answer **C** if (ii) and (iii) are correct
Answer **D** if all are correct

31. Menadione

i) is found predominantly in hydrogenated vegetable oils
ii) is converted to MK-4 by reaction with geranylgeranylphosphate
iii) is also known as vitamin K3
Answer **A** if (i) and (ii) are correct
Answer **B** if (i) and (iii) are correct
Answer **C** if (ii) and (iii) are correct
Answer **D** if all are correct

32. Vitamin K

i) deficiency is associated with a high PIVKA-II value
ii) is important to bone health because it is required for synthesis of γ-carboxylated osteocalcin
iii) has an Upper Limit of 1000 micrograms/day
Answer **A** if only (i) is correct
Answer **B** if (i) and (ii) are correct
Answer **C** if all are correct
Answer **D** if none are correct

33. Regarding vitamin E,

i) α- β- γ- and δ-tocopherols have antioxidant properties
ii) The naphthoquinone ring is critical for antioxidant activity
iii) Tocopherols each have 8 stereoisomers
Answer **A** if (i) and (ii) are correct
Answer **B** if (i) and (iii) are correct
Answer **C** if (ii) and (iii) are correct
Answer **D** if all are correct

34. For vitamin E,

i) the Daily Value is 30 mg RRR α-tocopherol

ii) deficiency causes neurological problems in humans

iii) αTTP selectively transfers 2(R)-tocopherols into VLDL

Answer **A** if (i) and (ii) are correct

Answer **B** if (i) and (iii) are correct

Answer **C** (ii) and (iii) are correct

Answer **D** if all are correct

35. The Haber-Weiss reaction:

i) consumes superoxide anion and hydrogen peroxide

ii) generates hydroxyl radical

iii) requires Fe for catalysis

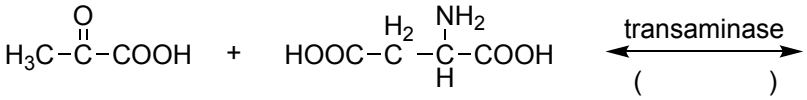
Answer **A** if (i) and (ii) are correct

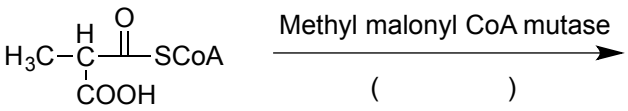
Answer **B** if (i) and (iii) are correct

Answer **C** if (ii) and (iii) are correct

Answer **D** if all are correct

36. Please draw the products for the following transformations (2 pts) and specify which vitamin (1 pt) participated as a cofactor. (total of 6 pts)



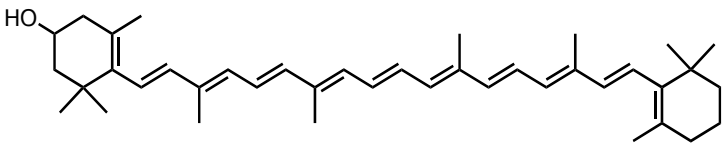


37. (8 pts)
The structures shown below (A and C) are precursors to the active forms of fat-soluble vitamins. Both require an enzymatic transformation to generate the active species.

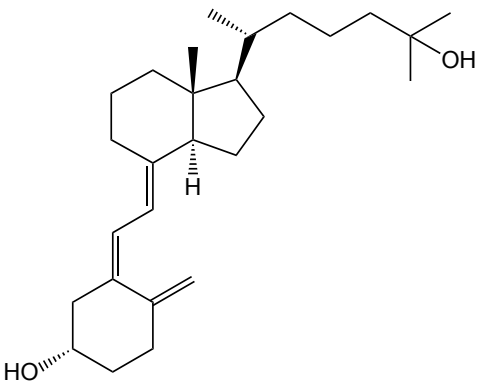
i) Draw the full structures of B and D. (4)

ii) Identify the enzymes responsible for formation of B and D and the major tissues where they catalyze these reactions. (4)

A → **B**

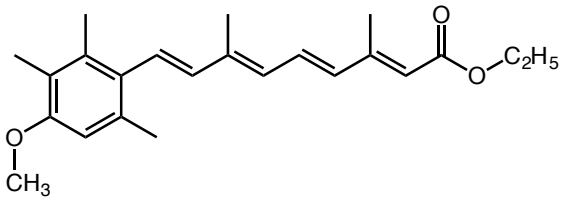


C → **D** (show stereochemistry)



38. (7 pts)

a) Etretinate, shown below, is a _____ generation oral retinoid used to treat psoriasis before it was removed from the market. Fill in the blank. (1)

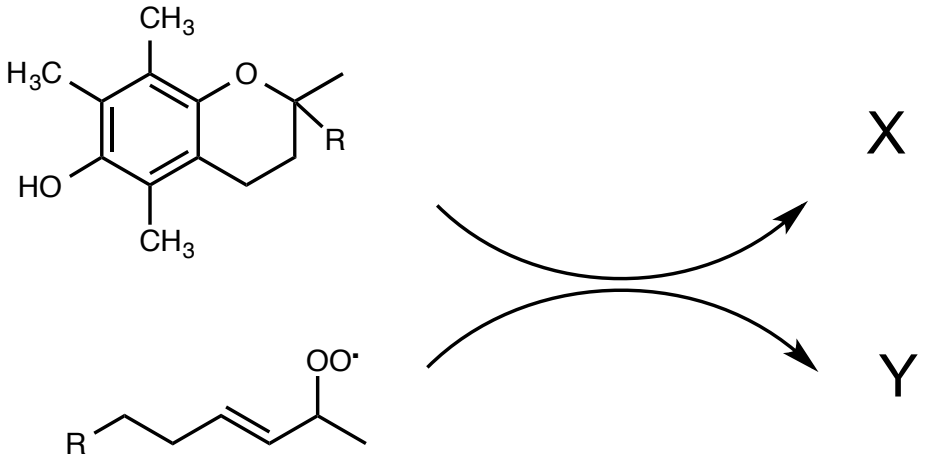


b) Explain fully why etretinate was removed from the market (4)

c) Acitretin is a related compound that remains on the market. What precautions need to be taken with its use to avoid the problems that occurred with etretinate? (2)

39. (7 pts)

a) Vitamin E effectively quenches lipid peroxyl radicals ($ROO^{\cdot}$) according to the scheme below. Draw full structures for X and Y. (2)



b) How can vitamin E be regenerated from X? (1)

c) Y still poses a biological risk because it can alter membrane function. Identify the enzyme that detoxifies Y and the mineral that is critical for its function. (4)