Medicinal Chemistry 562

Final Exam

December 13, 2017

NAME:_____

Medicinal Chemistry 562
December 13, 2017

Q1 – Q37_____(74)
Q38-Q41 _____(24)
Evaluation (2)
Total_____(100)

Q1-Q37 Multiple Choice (74 pts). Choose the single best answer.
USE SCANTRON

1. If the RDA for a vitamin is 2.4 mg/day then the EAR is:
   a. 1.7 mg/day
   b. 2.0 mg/day
   c. 1.2 mg/day
   d. 2.9 mg/day
   e. none of the above

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

2. _____ Scurvy
   a. Biotin
   b. Niacin
   c. Ascorbic acid
   d. Riboflavin

3. _____ Pellagra
   a. Thiamin
   b. Niacin
   c. Ascorbic acid
   d. riboflavin

4. _____ Pernicious anemia
   a. Folic acid
   b. B12
   c. Thiamin
   d. Biotin

5. _____ Wernicke-Korsakoff syndrome
   a. B12
   b. Biotin
   c. Niacin
   d. Thiamin

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

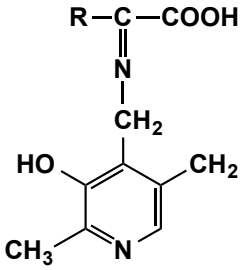
6. _____ Vitamin B_{12}
   a. folate level in erythrocytes
   b. urine methylmalonic acid level
   c. transketolase assay in red blood cells
   d. pyruvate levels in plasma

7. _____ Vitamin B_6
   a. transketolase assay in red blood cells
   b. pyruvate levels in plasma
   c. erythrocyte glutathione reductase activity
   d. erythrocyte transaminase activity

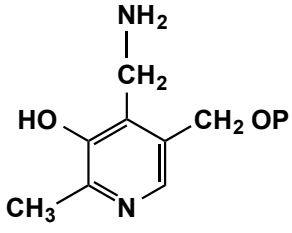
8. _____ Vitamin B_2
   a. transketolase assay in red blood cells
   b. pyruvate levels in plasma
   c. erythrocyte glutathione reductase activity
   d. erythrocyte transaminase activity

9. Which one of the following vitamins or their derivatives DOES NOT participate in reduction-oxidation (redox) reactions as an enzyme cofactor?
   a. Thiamin
   b. Riboflavin
   c. Vitamin B_3
   d. Vitamin C

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



a.



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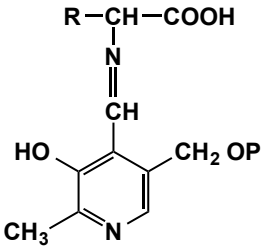

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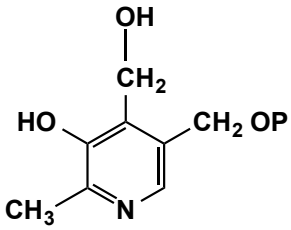

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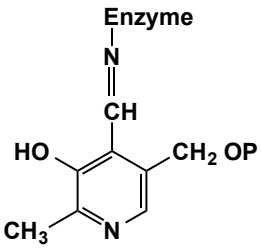


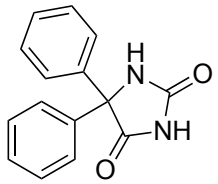
e.

11. Which of the following is FALSE about Leucovorin:
    a. Can lead to folic acid deficiency by inhibiting DHFA reductase
    b. Can allow ordinarily lethal dose of methotrexate to be used against tumor
    c. Is an intermediate of folate cycle
    d. Can allow ordinarily lethal dose of pyrimethamine to be used against malaria

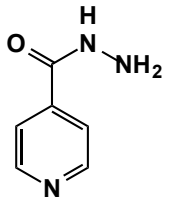
12. Which of the following inborn errors of metabolism is likely responsive to vitamin B_6 treatment?
    a. Transketolase defect
    b. Pyruvate dehydrogenase defect
    c. Maple syrup urine disease
    d. Cystathionurea

13. Preparations containing > 0.8 mg of folic acid require Rx because high dose of folate supplements have what risk?
    a. Could lead to neural tube defect
    b. Could mask the hematological symptoms of B_{12} deficiency and leave the neurological damages unchecked
    c. Could inhibit DNA methylation and lead to megaloblastic anemia
    d. Could counteract the effect of Phenytoin

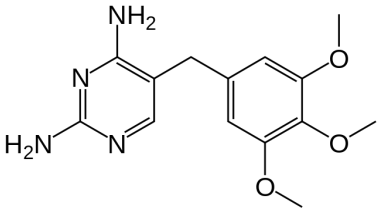
14. In principle, which drugs or vitamins below could possibly result in iatragenic Vitamin B_6 deficiency if used chronically, based on the structures shown:
    a. Phenytoin
    b. Trimethoprim
    c. Only Isoniazid
    d. Isoniazid and Methotrexate
    e. Isoniazid and Hydralazine



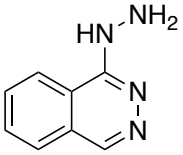
Phenytoin



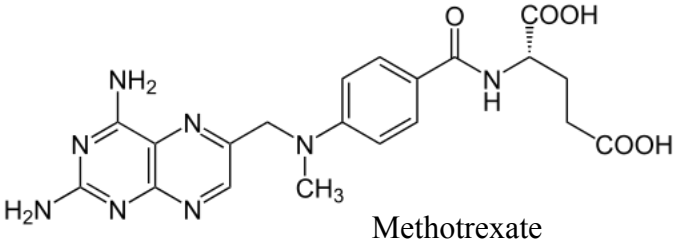
Isoniazid



Trimethoprim

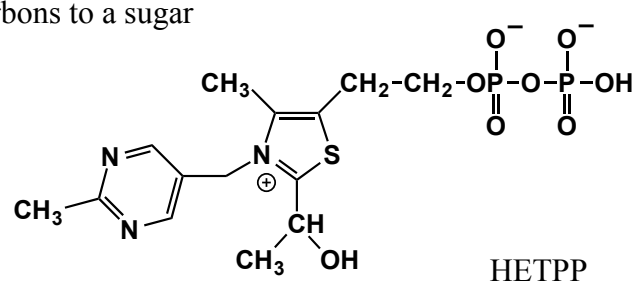


Hydralazine



Methotrexate

15. Which of the following are NOT possible fates for the hydroxyethyl TPP form of thiamine:
    a. Transformation of carbon-carbon double bonds to carbon-carbon single bonds
    b. Transfer of two carbons to an oxidized lipoic acid.
    c. Elimination as acetaldehyde: CH_3-CHO
    d. deprotonation to a carbanion followed by attack at an aldehydic carbon to transfer two carbons to a sugar



HETPP

16. Pellagra was once often seen in "corn belt" in US during early 1900's and possible reason is:
    a. Corn does not contain enough amount of vitamin B_6
    b. Corn lacks the enzyme to convert tryptophan to niacin
    c. Corn contains low levels of niacin and tryptophan
    d. Low levels of Zn consumption through diet

17. Choose the FALSE statement about vitamin C.
    a. Act as a cofactor for hydroxylation of proline that is important for collagen synthesis
    b. Can prevent common cold
    c. Act as a cofactor for the synthesis of norepinephrine
    d. Work as an antioxidant to prevent oxidative damage to DNAs and proteins

18. Choose the FALSE statement about biotin.
    a. Is highly abundant in egg whites, which can cause "egg white injury"
    b. Can be used to strengthen brittle nails, based on available evidence
    c. Participate as a cofactor for a number of carboxylation reactions
    d. Can be used to treat an inborn error of metabolism in biotinidase

19. Elevated plasma Homocysteine, associated with decreased conversion to methionine, is correlated with increased risk of cardiovascular disease. Which vitamin-derived cofactor is directly required for methionine synthase?
    a. 5-Methyl tetrahydrofolate
    b. Methyl cobalamin
    c. Vitamin B_6.
    d. Thiamin pyrophosphate.

20. Vitamin B_6 is contraindicated in levo-DOPA therapy against Parkinson's disease. Which of the following statement on this is FALSE?
    a. Vitamin B_6 enhances decarboxylation of levo-DOPA, which prevents it from crossing blood-brain barrier.
    b. Larobec® (Roche) contains no vitamin B6 and can be used if multivitamin supplementation is desired for patient on levo-DOPA.
    c. Carbidopa is often used in combination with levo-DOPA because it inhibits DOPA decarboxylase.
    d. Vitamin B_6 inhibits synthesis of dopamine from levo-DOPA.

21. Choose the TRUE statement about Dehydroascorbic acid?
    a. It is the reduced form of Vitamin C
    b. It is metabolized to oxalic acid
    c. It is a chemical reductant for ferric iron in the diet to help iron absorption.
    d. It acts as a radical scavenger and antioxidant
    e. all of the above

22. An patient with pernicious anemia due to intrinsic factor deficiency would most likely benefit from:
    a. High oral dose of vitamin B_{12}
    b. Oral supplementation of intrinsic factor
    c. Supplementation of long-acting form of vitamin B_{12}, hydroxycobalamin
    d. IM injection of vitamin B_{12}

23. Choose the statement on Niacin that is FALSE.
    a. Is the precursor to nicotinamide
    b. Is the precursor to the enzyme cofactors $NADP^+/NAD^+$
    c. Can be used to lower LDL levels by just consuming Niacin-containing food
    d. Its coenzyme form participates in fatty acid β-oxidation

24. Which of the following is False about the fat-soluble vitamins?

i) they have clogP values of between 2 and 6

ii) cholestyramine impairs their absorption

iii) they are rapidly degraded by heating

A if (i) and (ii) are false

B if (i) and (iii) are false

C if (ii) and (iii) are false

D if all are false

25. 9-Cis retinoic acid

i) is regulated by the iPLEDGE program

ii) is used to treat chronic eczema

iii) is a ligand for RXR

A if (i) and (ii) are correct

B if (i) and (iii) are correct

C if (ii) and (iii) are correct

D if all are correct

26. The AREDS2 formulation;

i) was designed to improve treatment of xerophthalmia

ii) increased the amount of β-carotene it provided

iii) added lycopene

A if (i) and (ii) are correct

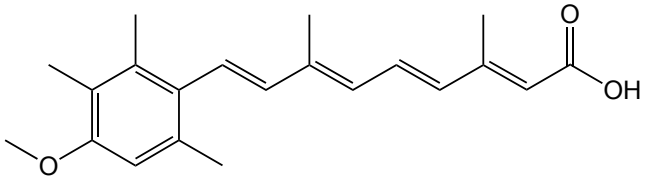
B if (i) and (iii) are correct

C if (ii) and (iii) are correct

D if all are correct

E if none are correct

27. Acitretin (structure below)



i) is a second generation retinoid

ii) is a pro-drug for etretinate

iii) was withdrawn from the market due to a high risk of birth defects

A if (i) is correct

B if (ii) is correct

C if (iii) is correct

D if none are correct

28. CYP24A1 is responsible for formation of;
i) vitamin D3
ii) calcitriol
iii) calcidiol
iv) calcitroic acid

A if (i) is correct
B if (ii) is correct
C if (iii) is correct
D if (iv) is correct
E if none are correct

29. The 25-OH D3 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) that characterize deficiency are <0.7 uM

A if (i) and (ii) are correct
B if (i) and (iii) are correct
C if (ii) and (iii) are correct
D If all are correct

30. The DV and UL for vitamin D3 are:

A 10ug and 20ug, respectively
B 10ug and 100ug, respectively
C 15 ug and 30ug, respectively
D 15ug and 100ug, respectively
E 15ug and 1500 ug, respectively

31. Menadione
i) is also known as vitamin K3
ii) is converted to vitamin K1 by reaction with geranylgeranylphosphate
iii) is found predominantly in hydrogenated vegetable oils

A if only (i) is correct
B if (i) and (ii) are correct
C if (ii) and (iii) are correct
D if all are correct
E if none are correct

32. Vitamin K1 is routinely administered to infants because;
i) breast milk contains only vitamin K2
ii) the gut is sterile at birth
iii) placental transmission of vitamin K is low

A if (i) and (ii) are correct
B if (i) and (iii) are correct
C if (ii) and (iii) are correct
D if all are correct

33. Vitamin K
i) deficiency is associated with a low PIVKA-II value
ii) has a Daily Value of 90 micrograms/day
iii) has an Upper Limit of 1000 micrograms/day

A if only (i) is correct
B if only (ii) is correct
C if only (iii) aiscorrect
D if all are correct
E if none are correct

34. For vitamin E,
i) bleeding can be an adverse effect
ii) deficiency causes neurological problems in humans
iii) aTTP selectively transfers a-tocopherol and a-tocotrienol into lipoproteins

A if (i) is correct
B if (i) and (ii) are correct
C if (i) and (iii) are correct
D if all are correct
E if none are correct

35. Regarding vitamin E
i) α- β- γ- and δ-tocopherols have antioxidant properties
ii) Each tocopherol has 8 stereoisomers
iii) The naphthoquinone ring is critical for antioxidant activity

A if (i) and (ii) are correct
B if (i) and (iii) are correct
C if (ii) and (iii) are correct
D if all are correct

36. The Haber-Weiss reaction;

i) consumes superoxide anion and hydrogen peroxide

ii) generates hydroxyl radical

iii) requires Fe for catalysis

A if (i) and (ii) are correct

B if (i) and (iii) are correct

C if (ii) and (iii) are correct

D if all are correct

37. Riboflavin helps to reduce the damage caused by free radical reactions because;

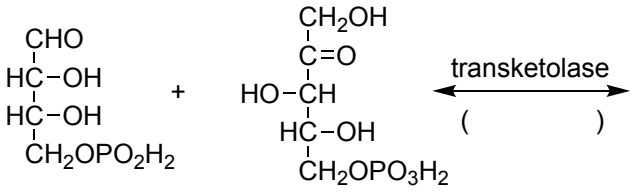
A Glutathione peroxidase requires NADPH

B Glutathione reductase requires NADPH

C Glutathione peroxidase requires FAD

D Glutathione reductase requires FAD

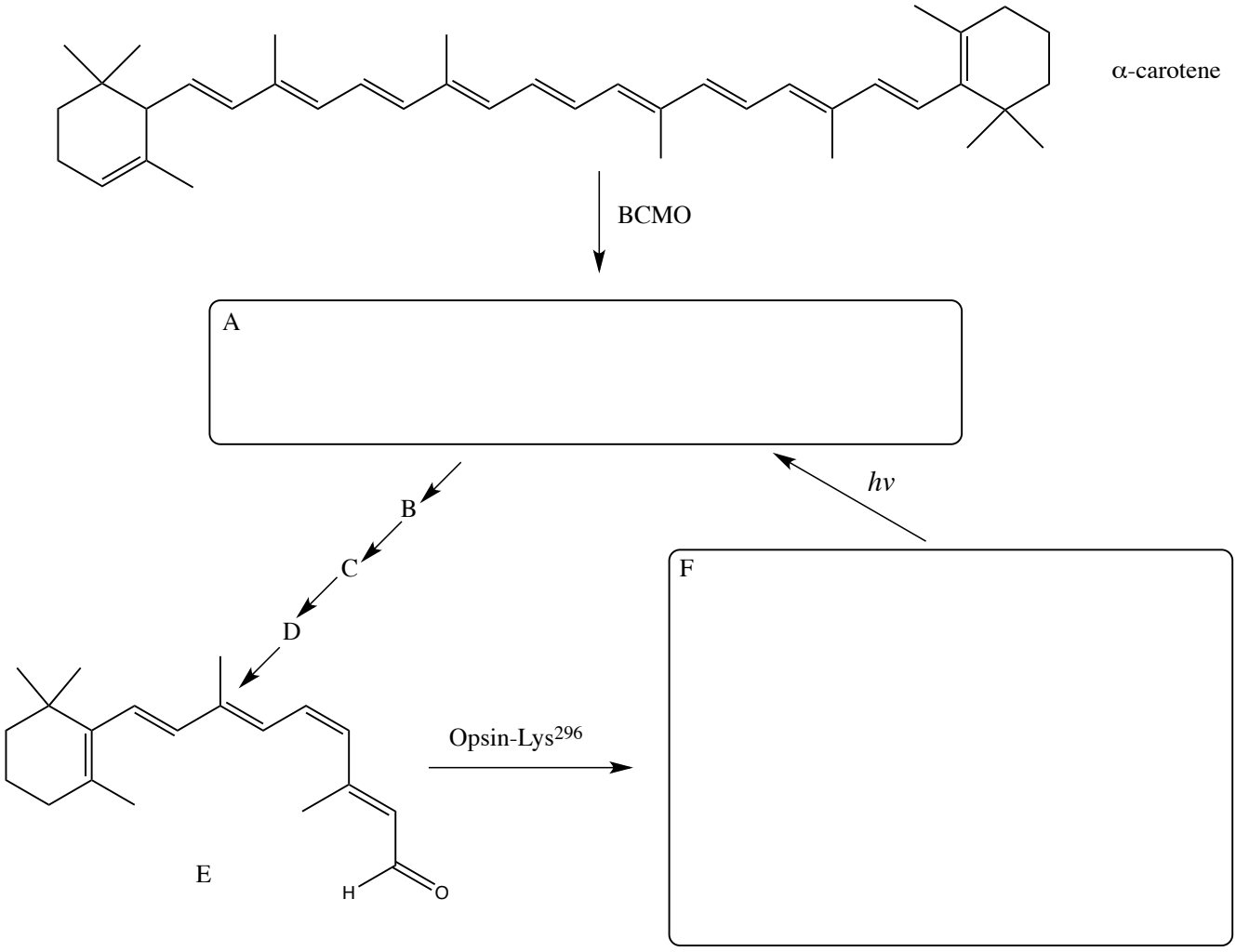
38. Please write the products for the following transformation (3 pts) and specify which vitamin (1 pt) participated as a cofactor. (total of 4 pts)



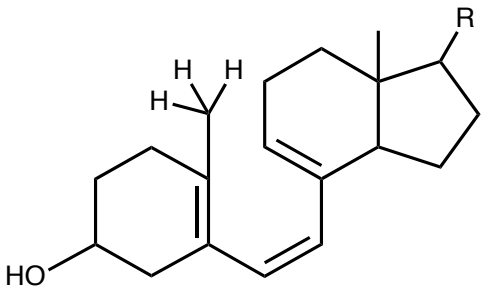
39. Based on your knowledge of the role of vitamin A (and pro-vitamin A) in the visual cycle, **draw structures** in the boxes provided that represent:

a) **A** – the specific vitamin A form generated from α-carotene by the enzyme, BCMO. (3 pts)

b) **F** – the vitamin A linkage to the visual pigment formed by reaction of E with opsin. (3 pts) [Partial structure is OK here]



40. Pre-vitamin D3 (shown below) is the immediate precursor to vitamin D3 formed in the skin from 7-dehydrocholesterol. Draw an arrow-pushing mechanism (and the resulting structure) for the formation of vitamin D3. (6 pts)



Pre-vitamin D3

Vitamin D3

41. The glutathione cycle, shown below, relies on several vitamins and minerals for its primary function of protecting the cell against peroxides, including hydrogen peroxide. Identify W, X, Y and Z in the blanks in the scheme below (8 pts).

W –

X –

Y –

Z –