

Medicinal Chemistry 562

Midterm Examination

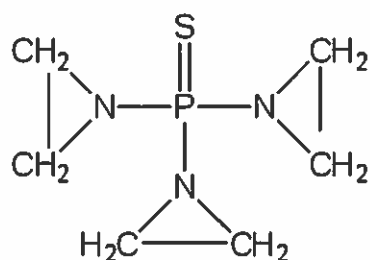
November 21, 2016

NAME: _____

5. Alkylating agents are an older class of anticancer drugs. As discussed in class, which of the following are true about them?

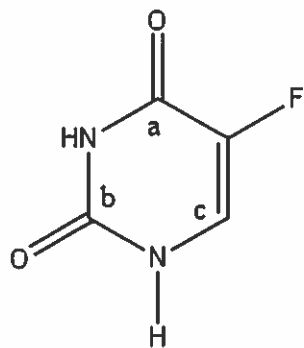
- A. They directly react and bind covalently to DNA.
- B. They can cause new cancers to form years later.
- C. They are not used anymore because better drugs exist.
- D. A and B.
- E. A, B and C.

6. Thiotepa which is shown below, is an older anticancer drug. Which of the following are true about thiotepa?



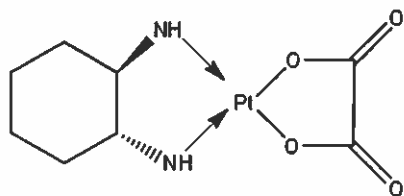
- A. It 's a prodrug.
- B. It's converted to a diazonium ion.
- C. It can be used in bladder cancer by direct instillation into the bladder.
- D. A, B, and C.
- E. B and C.

7. Shown below is the structure of 5-fluorouracil (5-FU). Which of the following are true about 5-FU?



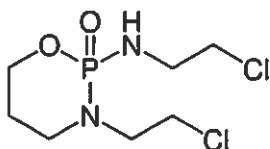
- A. The carbon that becomes attached to the enzyme through a thiol (-SH) is labeled with letter c.
- B. 5-FU inhibits the enzyme dihydrofolate reductase (DHFR).
- C. A prodrug form of 5-FU exists and is called fludarabine.
- D. A, B, and C.
- E. A and C.

10. Oxaliplatin (Eloxatin) is an important anticancer agent. As discussed in class, which of the following are true about this agent?



- A. It is useful in the treatment of colorectal cancer, especially as part of the FOLFOX regimen.
- B. It's main toxicity of concern is peripheral neuropathy.
- C. It can be dissolved in saline or D5W.
- D. A, B, and C.
- E. A and B.

11. Ifosfamide (Ifex), an important anti-cancer drug, is shown below. As discussed in class, what is true about this agent?



- A. It's not a prodrug.
- B. It is a specific enzyme inhibitor.
- C. It can be activated to form an aziridine (aziridinium) ring.
- D. A and B.
- E. A and C.

12. As discussed in class, polymorphic metabolism is associated with which enzyme(s)?

- A. Thymidylate synthetase (TS)
- B. Ribonucleotide reductase (RR)
- C. Dihydropyrimidine dehydrogenase (DPD)
- D. UDP glucuronosyltransferase 1A1 (UGT1A1)
- E. C and D.

13. Topotecan (Hycamtin) is an approved oncology agent. Which are true about this agent?

- A. It inhibits the enzyme topoisomerase 1 (Topo 1).
- B. It's a prodrug.
- C. It is extensively metabolized by UGT1A1.
- D. A and B.
- E. A and C.

19. T cells are an important type of cells among the white blood cell group that are important for immunological control or elimination of cancer cells.

A. True

B. False

20. The use of biomarkers and surrogate markers are not of any use in the development and use of anticancer agents.

A. True

B. False

25. The second 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

26. Vitamin D3 is;

i) derived from ergosterol

ii) has a longer half-life than vitamin D2

iii) circulates in plasma usually at concentrations > 20ng/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

27. CYP27B1 carries out the following reaction on the vitamin D nucleus:

i) 27-hydroxylation

ii) 25-hydroxylation

iii) 24-hydroxylation

iv) 1-hydroxylation

Answer A if only (i) is correct

Answer B if only (ii) is correct

Answer C if only (iii) is correct

Answer D if only (iv) is correct

28. Parathyroid hormone secretion:

i) increases 25-hydroxylation of vitamin D in the kidney

ii) decreases CYP2R1 in the liver

iii) increases calcium reabsorption in the kidney

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

Answer B if only (ii) is correct

Answer C if only (iii) is correct

Answer D if none are correct

33. Oxygen is reduced to water in four one-electron steps that involve formation of several ROS (reactive oxygen species according to the scheme below.



Glutathione peroxidase can scavenge:

- i) X
- ii) Y
- iii) Z

Answer A if (i) is correct

Answer B if (ii) is correct

Answer C if (iii) is correct

Answer D if none are correct

34. Superoxide dismutase contains:

- i) Copper
- ii) Zinc
- iii) Manganese
- (iv) Iron

Answer A if (i) is correct

Answer B if (i) and (ii) are correct

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

Answer D if all are correct

35. Which of the following statements is TRUE about superoxide dismutase?

- i) It is the most efficient enzyme in the body
- ii) It generates ROS
- iii) It is found in mitochondria

Answer A if only (i) is correct

Answer B if only (i) and (ii) are correct

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

Answer D if all are correct

b) Explain why the retinol activity of 1 ug of all-trans retinol = 2ug of trans β -carotene in oil = 12 ug food-based all-trans β -carotene. (4)

c) Identify the enzyme that warfarin inhibits to reduce the formation of clotting factors (1)

d) Circle the important structural elements in warfarin that cause it to be an effective vitamin K antagonist. The structure of warfarin and vitamin K1 are shown below. (2)

