

Key

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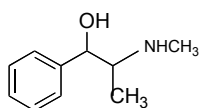
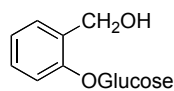
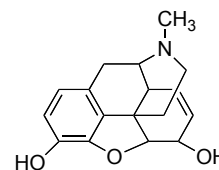
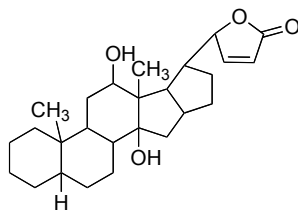
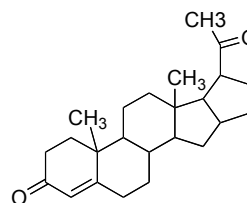
Multiple choice (33 questions, 3 points each, 99 points, 1 point for proper pin #). Supply the best answer for each question.

1) Of the structures below which represents a cardioactive glycoside?

- _____ A.
_____ B.
_____ C.
_____ **D.**
_____ E.

2) Which structure represents an NSAID

- _____ A.
_____ **B.**
_____ C.
_____ D.
_____ E.

**A****B****C****D****E**

3) Many herbal products act as free radical scavengers, anti-oxidants and in many cases they are dark colored compounds known as:

- A) alkaloids
- B) steroids
- C) **proanthocyanidins**
- D) terpenes
- E) none of the above

4) Which of the following is used to relieve symptoms of PMS and painful menstruation?

- A) Chaste berry
- B) Wild Yam
- C) **Black Cohosh**
- D) Ginkgo Ginseng
- E) None of the above

5) A plant purported to be useful in the treatment of colds, flu, and as an immunostimulant.

- A) Feverfew
- B) **Echinacea**
- C) Chaparral
- D) Ephedra
- E) None of the above

6) Which of the following may be of utility for individuals with dementia or Alzheimers disease?

- A) Ginkgo biloba
- B) Wild Yam
- C) Turmeric
- D) Pomegranate
- E) **A and C above**

Following question dropped due to the information not being included in the lecture or the notes.

7) Which of the following is a herbal carminative?

- A) *Serenoa repens*
- B) *Digitalis purpureaa*
- C) *Ephedra sinic*
- D) *Mentha piperita***
- E) *Larrea tridentata*

8) Safety related issues with herbal medicines include

- A) contamination with microorganisms
- B) time release formulations
- C) mislabeling
- D) A and C above**
- E) A, B and C above

9) A patient comes in with a prescription for an antidepressant that is a known MAO inhibitor. Which of the following natural products would you ask the patient if they are taking?

- A) Ginger
- B) St. John's Wort**
- C) Black Cohosh
- D) Turmeric
- E) none of the above

10) An alkaloid that is used as an anti-sialagogue and mydriatic:

- A) Atropine**
- B) Cocaine
- C) Morphine
- D) Ephedrine
- E) all of the above

11) Which of the following can lead to a SNP not being observed at the phenotypic level?

- A) It occurs in a region of the DNA that codes for a protein
- B) It occurs in a region of the DNA that does not code for a protein
- C) It yields a new codon that codes for the same amino acid as the original codon
- D) All of the above

_____ **E) B and C above**

12) A monogenic haplotype

_____ A) is not an allele

_____ **B) is a cluster of SNPs on a single gene that may cause a disease state**

_____ C) is a cluster of SNPs spread across multiple genes that may cause a disease state

_____ D) will always have a high penetrance

_____ E) B and D above

13) Expression profiling includes

_____ **A) variations in mRNA levels as a function of disease state**

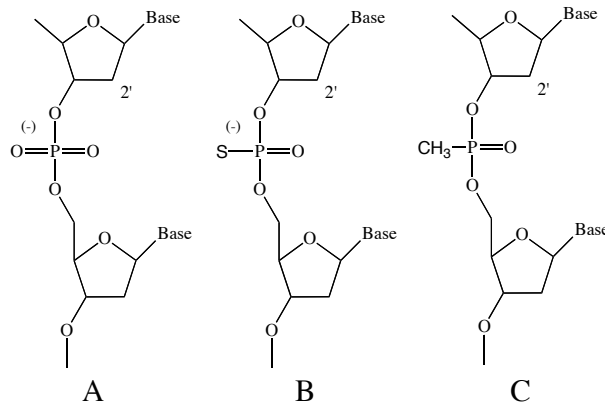
_____ B) prediction of drug outcomes based on family history

_____ C) variation in protein levels as a function of drug therapy

_____ D) measurement of the distribution of SNPs in DNA

_____ E) none of the above

14) Which of the following would be expected to not be susceptible to hydrolysis by proteases?



_____ A) A

_____ B) B

_____ C) C

_____ D) B and C

_____ **E) all of the above**

15) An advantage of a ribozyme-based therapy over an antisense agent that does not work in conjunction with a protein:

- A) readily permeable across cell membranes
- B) the ability to bind to a specific mRNA
- C) avoids non-specific polyanion effects
- D) the ability to cleave multiple target mRNAs**
- E) B and C of the above

16) The disease that many individuals being treated with Factor VIII in the early 1980s were exposed to is

- A) hemophilia
- B) AIDS**
- C) dwarfism
- D) Creutzfeldt-Jakob (Jacob-Kreutzfeld) syndrome
- E) transplant rejection

17) Loss of efficacy of a protein-based drug following administration may be due to

- A) peptide bond hydrolysis
- B) antigenic response
- C) binding to the asialoglycoprotein receptor
- D) all of the above**
- E) A and C above

18) The most reliable method to determine the stability of a protein-based drug during storage is

- A) SDS Page
- B) reversed phase HPLC
- C) potency determination**
- D) bacteriostats
- E) lyophilization

19) If a protein-based drug was shown to be unstable due to deamidation of a side chain, which of the following amino acids would be considered to be the possible cause?

- A) Lysine
- B) Glutamine**
- C) Aspartate

- D) Methionine
- E) B and C above

20) An siRNA-based therapy could

- A) be developed based on data from expression profiling
- B) be delivered via gene therapy
- C) require humanization prior to clinical trials
- D) all of the above
- E) A and B above**

21) A protein-based therapeutic agent that has successfully been delivered via inhalation is

- A) Herceptin
- B) Captopril
- C) Insulin**
- D) Somatostatin
- E) Erythromycin

22) Properties that distinguishes protein-based drugs from low molecular-weight drugs include

- A) they can undergo chemical degradation
- B) their folded, tertiary structure is important for activity**
- C) they can bind to specific proteins
- D) they never have adverse side effects
- E) there are no distinguishing properties

23) Advantages of molecular dynamics simulations over energy minimization include

- A) ability to find the local minimum
- B) ability to find the global minimum
- C) determination of entropy
- D) inclusion of forces
- E) B and C above**

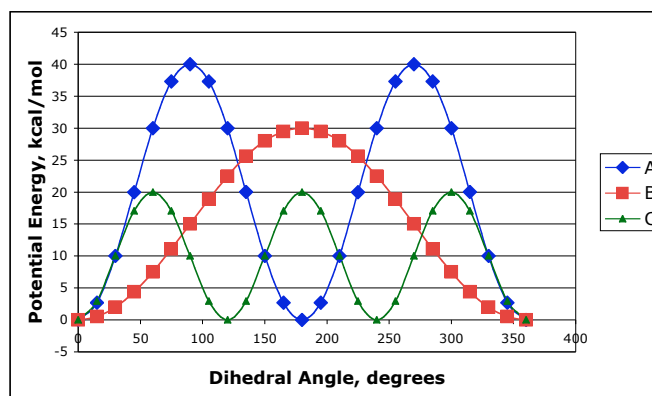
24) Using genomics and proteomics you have discovered a protein that is overexpressed in skin cancer. siRNA targeting the mRNA for this protein leads to apoptosis of the cancer cells. Recently, the 3D structure of the protein was determined. Considering that you do not have access to synthetic

chemistry, which of the following approaches would you apply to initiate a project to discover low-molecular weight inhibitors of the overexpressed protein?

- A) structural genomics
 B) database searching
 C) de novo design
 D) free energy perturbation
 E) none of the above

25) Based on the following graph and equation, what is the force constant of the curve with a multiplicity of 1?

$$V = \sum K[1 + \cos(n\phi - \delta)]$$



- A) 10
 B) 15
 C) 20
 D) 30
 E) 40

26) A free energy perturbation study is performed from drug 1 to drug 2. From the calculations the free energy difference in solution is 4 kcal/mol and the free energy difference for the receptor bound drugs is -4 kcal/mol. Based on that data which of the following are true.

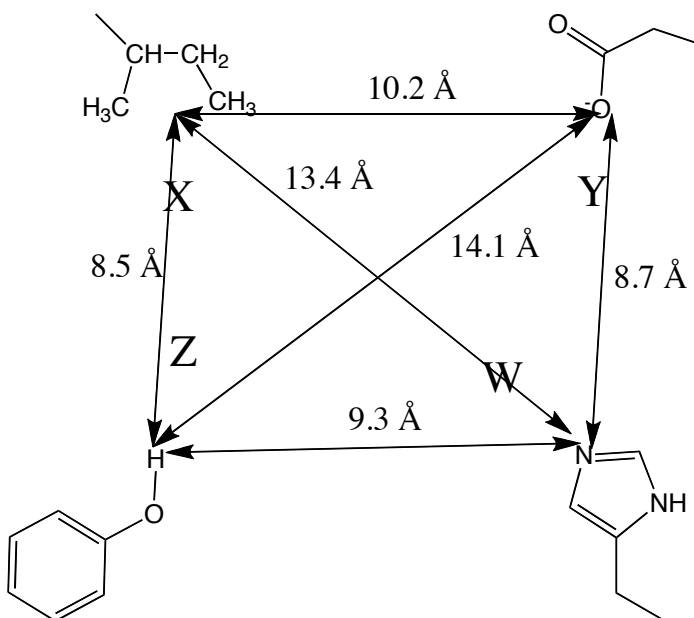
- A) drug 2 is more soluble than drug 1
 B) the overall binding of the two drugs is the same

- C) drug 2 interacts more favorably with the receptor
 D) the drug 1 has significantly better overall binding than drug 2
 E) there is not enough information given to determine changes in overall binding.

27) Parameters that are important for the calculation of external interaction energies include

- A) the equilibrium bond length
 B) the phase
 C) the temperature
 D) the well depth
 E) none of the above

Based on the following model of a receptor answer questions 29 and 30



28) The distance between pharmacophore points X and Y should be

- A) 14.1 Å
 B) 10.2 Å
 C) 8.4 Å
 D) 6.6 Å

_____ E) 13.4 Å

29) Which of the following classes of functional groups would be suitable at position W

- _____ A) hydrogen bond acceptor
 _____ B) hydrogen bond donor
 _____ C) cation
 _____ D) anion
 _____ E) **B and C above**

30) A number of analogs of the following compound were synthesized and QSAR performed from which the equation shown below was determined.

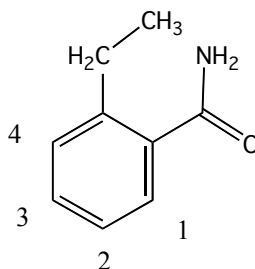
$I_1 = 1$ when position 1 is substituted with a chlorine group; = 0 when position 1 is unsubstituted.

$I_2 = 1$ when position 2 is substituted with an amino group; = 0 when position 2 is unsubstituted

$I_3 = 1$ when position 3 is substituted with a hydroxyl; = 0 when position 3 is unsubstituted

$I_4 = 1$ when position 4 is substituted with a methyl; = 0 when position 4 is unsubstituted

If a position is not listed, assume it is unsubstituted



$$\log \frac{1}{C} = 1.1I_1 - 0.7I_2 + 0.8I_3 - 1.3I_4 + 2.7$$

Based on the above information, which of the following is true?

- _____ A) The fully unsubstituted compounds will have the highest activity
 _____ B) The fully substituted compound will have the highest activity
 _____ C) **A chlorine at position 1 and a hydroxyl at position 3 will have the highest activity**
 _____ D) A chlorine at position 1, an amino at position 2 and a methyl at position 4 will have the highest activity

_____ E) An amino at position 2 and a methyl at position 4 will have the highest activity.

31) For the above ligand bound to its receptor, what type of functional group would be on the receptor directly adjacent to position 2 when the optimal substituent at that position is present?

- _____ **A) hydrophobic**
- _____ B) hydrogen bond donor
- _____ C) hydrogen bond acceptor
- _____ D) cationic
- _____ E) anionic

32) What enzyme(s), besides dihydrofolate reductase (DHFR), could be targeted to design anticancer agents that block the conversion of dUMP to dTMP?

- _____ A) DNA methyltransferase
- _____ B) DNA polymerase
- _____ **C) serine hydroxymethyltransferase**
- _____ D) all of the above
- _____ E) A and C above

33) The nitrogen in the pteridine ring of methotrexate ($pK_a = 4$ in solution) is protonated when bound to DHFR at pH 7 because

- _____ A) it is in a hydrophobic environment
- _____ **B) there is an aspartic acid residue adjacent to it**
- _____ C) there is a lysine residue adjacent to it
- _____ D) there is the NH from a peptide bond adjacent to it
- _____ E) A and B above