PHCO329 left.

Answer Key - Midterm #1

Student Name: _____

Student #: _____

1. What is the definition of "Biopharmaceutics"? **(2 marks)**

(2) study of the properties of therapeutic substances & their dosage/bioactivity relationship

2. Provide a definition of "Pharmaceutical sciences". **(2 marks)**

(2) - a gp of interdisciplinary areas of study involved in the design + synthesis, mode of action, delivery & use of drugs

3. In the early 1900's the average lifespan was approximately 50 years. Now the average lifespan is 80+ years. List 4 reasons (not including better food and water etc.) that have contributed to this. **(4 marks)**

- 1 each

(4)

a) Workplace infrastructure is better
b) Vaccines
c) drugs
d) better diagnostics

4. List two top selling drugs from the past decade and explain what each is used for. **(4 marks)**

any 2

(4)

Lipitor - ↓ cholesterol
Nexium - proton pump inhibitor (stomach acid)
Plavix - blood thinner
Advair - asthma.
Abilify - antipsychotic
Singulair - asthma
Seroquel - antipsychotic
Humira - anti-inflammatory

Hydracodone - pain
Generic Zocor - cholesterol ↓

Student Name: _____

Student #: _____

5. List the <u>two</u> most commonly utilized technologies for detection of a "hit" in a high throughput screen (HTS). **(2 marks)**

(2)
- SPA - Scintillation Proximity Assay
- FLIPR - Fluorescent Imaging Plate Reader

6. What are the <u>four major</u> phases recognized in drug development? Name <u>each</u> of these and give approximate timelines for each. **(8 marks)**

(1) Preclinical R+D ⇒ 3-8 yrs (1)
(2) Clinical Trials ⇒ 4-8 yrs (1)
(3) New Drug Application Review (NDA) ⇒ 1-2 yrs. (1)
(4) Post-market surveillance ⇒ ongoing. (1)

Student Name: _____

Student #: _____

7. Preclinical research and development has six stages. Briefly explain what happens in each of these stages. **(12 marks)**

(2) a) Understand nature of disease.
- explanation.

(2) b) Where to intervene.
- explain.

(2) c) Identify lead structure. - explain.

(2) d) Develop Bioassay - explain.

(2) e) Chemical Synthesis - explain

(2) f) toxicity testing - explain In vitro + in vivo with appropriate models

8. What is the difference between efficacy and efficiency? Use an appropriate example in your answer. **(2 marks)**

(1) efficiency ⇒ maximize an effect

(1) efficacy ⇒ "power" to produce the desired affect (dose).

Student Name: _____

Student #: _____

9. Name the **three** phases of clinical trials. What is the goal or purpose of each phase? How many patients are involved in each phase and what is the timeframe of each phase? **(12 marks)**

a) Phase I - determines "safety" (1)
- 20 healthy volunteers (1)
- 1-2 months (1)

b) Phase II - assess efficacy + efficiency (1)
- (1) < 50 patients w condition
- 3 month → 1 year.

c) Phase III - assess efficacy + safety (1)
- large diverse gp of patients (1)
- 3-8 yrs

10. What are the two main reasons that Pharma will decide to develop a drug for treatment of a disease. **(2 marks)**

(1) (1) Filling a need
(1) (2) Reacting to opportunity (a new one)

11. 80% of drugs on the market today work via one of four biological mechanisms. List these four biological mechansims. **(4 marks)**

(1) (1) Enzyme Inhibitor
(1) (2) Receptor Antagonist
(1) (3) Receptor Agonist
(1) (4) Ion channel modulator

Student Name: _____

Student #: _____

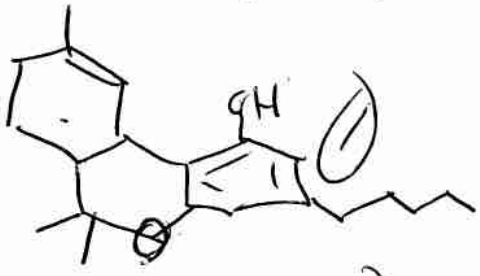
12. List the PROs/CONs of "combinatorial libraries" used in drug development? **(3 marks)**

PRO = ① chemical synthesis/generate ↑ # cmpds

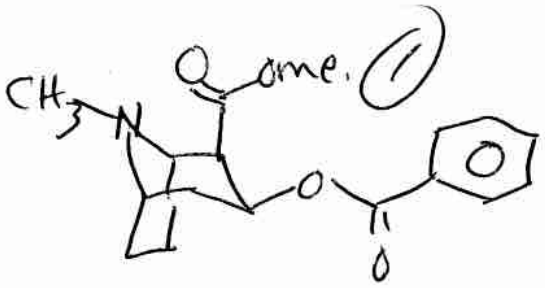
CON = ① structural diversity limited (all same "family")

② can be difficult separations

13. Provide the structures and names of two natural products obtained from plant sources. **(4 marks)**



THC ✓



Cocaine. ✓

Morphine, mescaline, taxol & Quinine also accepted.

14. What is "ethnopharmacology"? **(1 mark)**

- study + use of plant derived materials in traditional societies to maintain + improve health

(1)

Student Name: _____

Student #: _____

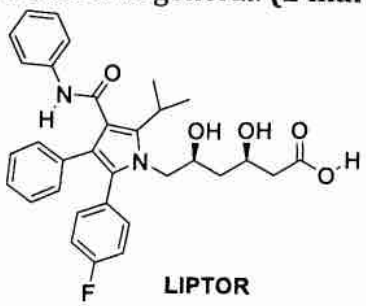
15. The development of the statins as cholesterol lowering drugs required the understanding of cholesterol biosynthesis. Explain with one or two phrases and by drawing the structures and enzyme involved in the key step. **(5 marks)**

5

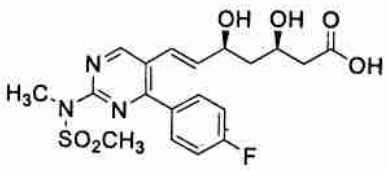
HMG CoA reductase (HMG Reductase) catalyzes formation of mevalonate (), & is RDS. A-molecule with similar structure can-inhibit this enzyme.

+1

16. The structures of the important statins Lipitor and Crestor are shown below. Each has a fluorine substituent on one of its aromatic rings. Give <u>two</u> potentially important functions of a fluorine substituent on an aromatic ring in these molecules and in drug molecules in general. **(2 marks)**



LIPTOR



CRESTOR

(1) (1) Increased lipophilicity

(1) (2) Deactivate aryl ring towards oxidation (metabolism)

Student Name: _____

Student #: _____

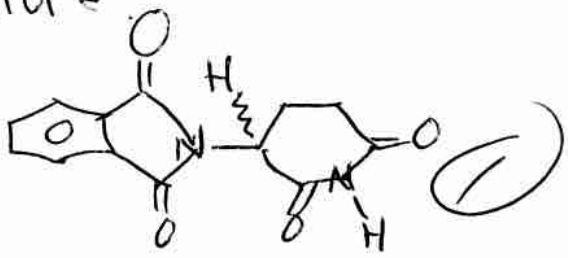
17. Explain briefly why drugs such as ASA, and the various non steroidal anti-inflammatory drugs (NSAIDs) often result in stomach lesions upon prolonged usage. **(2 marks)**

- 2 COX enzymes: both mediate inflammation but inhibiting COX-1 also affects renewal of stomach lining & thus get ulcers.

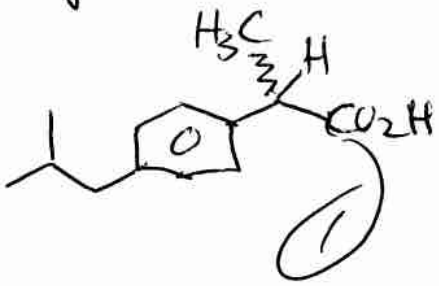
18. Generally, drugs are not marketed as racemates. Why? Provide the names and structures of two drugs that are currently marketed as racemates. **(4 marks)**

b/c the two enantiomers can have different biological activities (or their metabolites)

- thalidomide

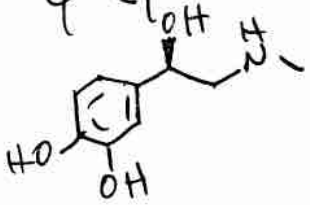


- ibuprofen.



Common mistake: ASA = achiral

Also acceptable: epinephrine



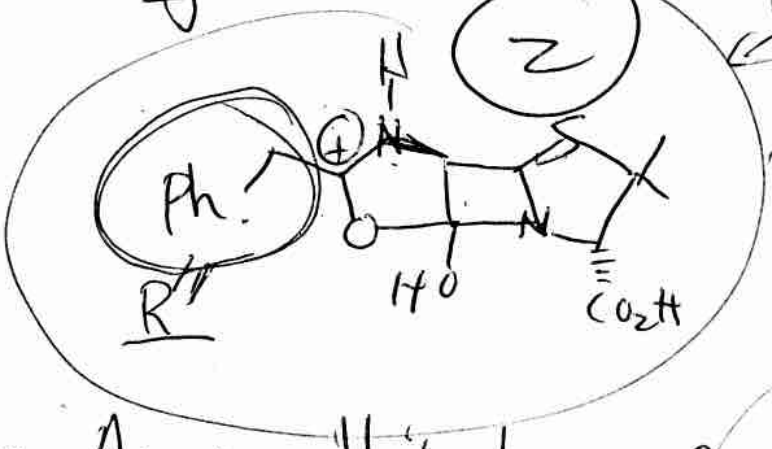
Student Name: _____

Student #: _____

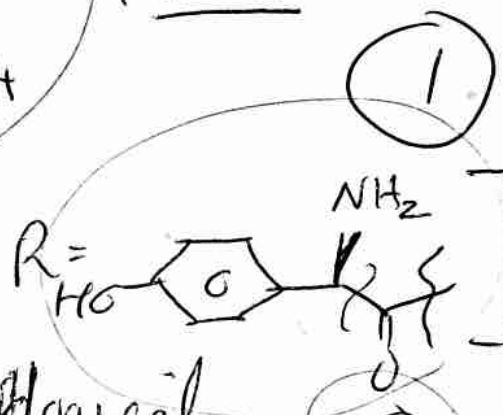
19. Amoxycillin is orally active but Penicillin G is not (generally injected) as it is not stable under acidic conditions. Explain why is amoxicillin is acid stable. As part of your answer you will need to discuss the key intermediate in hydrolysis of a beta lactam. **(5 marks)**

Key intermediate

Resonance structure



Pen G.



Amoxycillin has

& under physiological pH we get $-\overset{+}{N}H_3$

very EWG.

& disfavors formation of Key intermediate.