Medicinal Chemistry 1030042

Midterm Exam

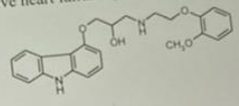
Class:

Name:

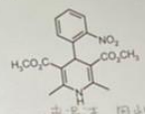
Dr. An-Rong Lee
March 18, 2022

1. For anti-arrhythmic drugs : (a) describe the classification of Class I drugs and give each class an example. (15%)

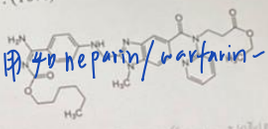
2. Speculate how carvedilol (structure shown below) can be employed as a drug in the treatment of congestive heart failure. (10%)



3. The structure of nifedipine is shown as below. Describe its synthesis, chemical properties and clinical uses (15%)



4. Use dabigatran (structure shown below) as an example to illustrate the "novel oral anticoagulants (NOACs)". (10%)



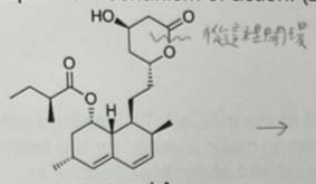
1. Direct 凝血酶抑制劑 (不用如 heparin / warfarin 一樣轉化)
2. 抑凝血酶活性
   → 阻止血液凝集 ⇒ 預防血栓
3. v.s. traditional : available controlled.
   不需經血檢 or diet limit
   ⇒ 方便、有效的治療藥物 for 長期服用 anticoagulants 者.

Medicinal Chemistry Exam

Dr. Hui-Ju Yen
Mar. 18, 2022

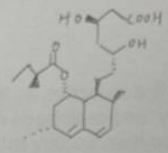
Class：P106
Student number：
Name：

1. The structure of compound A is as shown below.
   (a) Give the name of compound A and draw down its active metabolite. (4%)
   (b) Depict its mechanism of action. (2%)



compound A

Lovastatin



3R,5R-dihydroxy acid

① 抑制HMG-CoA reductase

② 增加LDL receptor的量

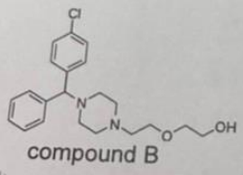
③ 增加HDL的量

→ 降血脂保護作用 { 促進NO釋放 血管內皮釋放 / 穩定 plaque

2. Please complete the pairing of drugs and their heterocyclic ring. (4%)

fluvastatin	pyrimidine
atorvastatin	pyrrole
pitavastatin	indole
rosuvastatin	quinoline

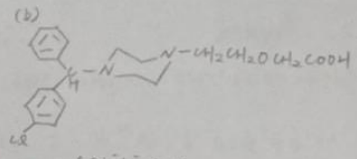
3. *Compound B is a first-generation antihistamine as follows.*
   (a) Give the name of compound B and draw down its active metabolite. (4%)
   (b) Depict its general features in term of the structure and special advantages of clinical application. (4%)
   (c) Comparison of Compound B and its metabolites in clinical use. (2%)



compound B

(a) hydroxyzine

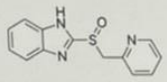
屬於 piperazine 類，第一代抗組胺藥，可止吐、鎮靜



cetirizine

	hydroxyzine	cetirizine
性質		
作用		

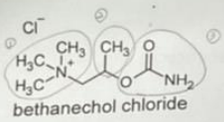
4. Proton pump inhibitors are commonly and more frequently used in the treatment of peptic ulcer. The 2-pyridylmethylsulfinylbenzimidazole motif is conserved in all members of the PPI family. PPIs are prodrugs, and enteric-coated formulations. Please explain the mechanism of action of PPIs, and how it works. (7%)



timoprazole (never marketed)

PPIs類藥物為prodrug，需在酸中催化成 sulfonic acid & sulfonamide，才能與 H^+/K^+ ATPase 的 cysteine 的 thiol group 產生雙硫共價鍵，不可逆地抑制 H^+/K^+ ATPase

5. Bethanechol chloride is a selective agonist at the mAChR. Its localized action, direct action selectivity, and prolonged duration make it useful for the treatment of postsurgical and postpartum urinary retention and abdominal distension. Please explain which structure causes its localized action, direct action selectivity, and the prolonged duration. (8%)



bethanechol chloride

① ammonia head：使其離子化，不易自由，用於局部作用

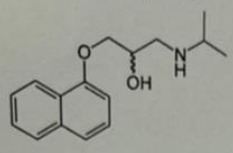
② β-alk：
- M_N 作用大於 M_N
- S form 作用大於 R form
- 形成立體結構，AchE不易水解，延長作用時間

③ carbamate：AchE不易水解，延長作用時間

6. Please try to make a comparison of the thiazide diuretics with loop diuretics, both are sulfonamide derivatives.
It can be compared from the position of action, the intensity of action, the mechanism of action, the concentration of electrolytes in the blood, and the side effects. (10%)

	Loop diuretics	Thiazide
位置	亨利氏環	遠曲小管
作用	抑制 $Na^+/K^+/2Cl^-$ symporter	抑制 Na^+/Cl^- symporter
電解質	$Na^+\downarrow$ $K^+\downarrow$ $Cl^-\downarrow$ $Ca^{2+}\downarrow$	$Na^+\downarrow$ $K^+\downarrow$ $Cl^+\downarrow$ Ca^{2+}
副作用	高尿酸血症 耳毒性	高尿酸血症

7. The β-blockers are of vital importance in clinical pharmacy.
   (a) Describe at least three clinical applications. (3%)
   (b) Describe the significance of β_1/β_2 selectivity in practice and the structure relationship. (2%)



propanolol

(a) 因嗜鉻細胞瘤引起的高血壓、心律不整、心絞痛、心肌梗塞、偏頭痛
青光眼

(b) β-blocker 因子