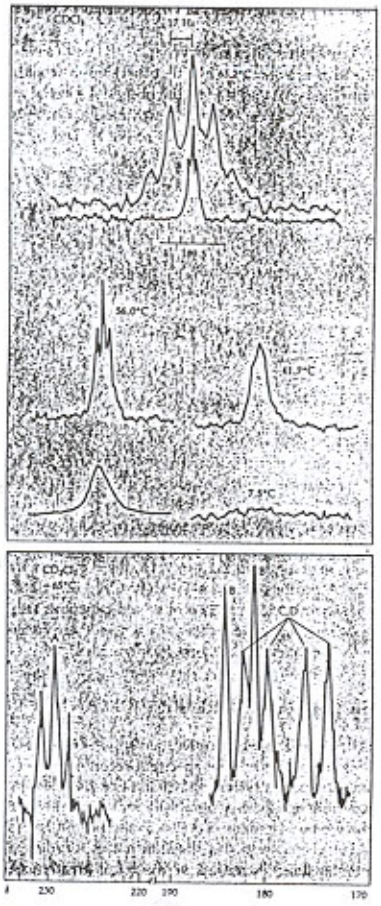
1. Explain the following term: (16%)
   1) Superacid. 2) B-strain, 3) crystal radii, 4) macrocyclic effect
2. Determination the point group of the following compounds: B_2H_6, allene(H_2CCCH_2), and SF_6(6%).
3. To calculate the nuclear charge Zn, 1) for the 4s electron and 2) for 3d electron.(6%)
4. Write a catalytic cycle for olefin hydrogenation using Wilkision's catalyst. (10%)
5. What do the following pairs or groups of structure have in common, and how do they differ in $3.3PT_{1/2}T_{1/2}$ and 3.2 PT.(4%)
6. Predict the structure of the following compounds: TeF_5^-, ClF_3, ClO_2^+.(6%)
7. Give the valence electron count for the following species.(6%)
   a) $(\eta^5\text{-}C_5H_5)(CONHMe)Cr(NO)_2$, b) $CH_3Mn(CO)_5$, c) $(\eta^5\text{-}C_5H_5)_2ZrCl_2$,
8. Compare and explain the order stretching frequency(υ_{CO}) for the following compound: $Fe(CO)_4^{2-}$, $Co(CO)_4^-$ and $Ni(CO)_4$.(6%)
9. Compare and explain the ΔH of adduct formation of the following compounds, NH_3, Me_3N, Me_2NH, $MeNH_2$, reacting with a) BF_3 and b) $B(t\text{-}Bu)_3$. (6%)
10. For complexes of $Pt(NH_3)(SCN)$ and $Pt(PR_3)(SCN)$, would you expect coordination of SCN^- through S or N to Pt cation and Why? (6%)
11. Give the symmetry of IR-active CO normal modes and number stretching frequency(υ_{CO}) expected for the trans form of $M(CO)_4L_2$, and fac $M(CO)_3L_3$. (8%)
12. Predict the structure of following compound from the Walsh diagram.1)BH_2^+, 2) the first excited state of BH_2^+.(4%)
13. Describe the characteristic of borazine.(4%)
14. Give the bond order and the number of unpaired electrons for B_2^+, O_2^-.(4%)
15. Figure shows proton NMR spectra of $Rh_4(CO)_{12}$ in CD_2Cl_2 solution at various temperature and rationalize the spectra changes.(8%)



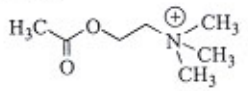
D_{4h}	E	$2C_4$	C_2	$2C_2'$	$2C_2''$	i	$2S_4$	σ_h	$2\sigma_v$	$2\sigma_d$	(x axis coincident with C_2')	
A_{1g}	1	1	1	1	1	1	1	1	1	1		x^2+y^2, z^2
A_{2g}	1	1	1	−1	−1	1	1	1	−1	−1	R_z	
B_{1g}	1	−1	1	1	−1	1	−1	1	1	−1		x^2-y^2
B_{2g}	1	−1	1	−1	1	1	−1	1	−1	1		xy
E_g	2	0	−2	0	0	2	0	−2	0	0	(R_x, R_y)	(xz, yz)
A_{1u}	1	1	1	1	1	−1	−1	−1	−1	−1		
A_{2u}	1	1	1	−1	−1	−1	−1	−1	1	1	z	
B_{1u}	1	−1	1	1	−1	−1	1	−1	−1	1		
B_{2u}	1	−1	1	−1	1	−1	1	−1	1	−1		
E_u	2	0	−2	0	0	−2	0	2	0	0	(x, y)	

C_{3v}	E	$2C_3$	$3\sigma_v$		
A_1	1	1	1	z	x^2+y^2, z^2
A_2	1	1	−1	R_z	
E	2	−1	0	$(x, y), (R_x, R_y)$	$(x^2-y^2, xy), (xz, yz)$

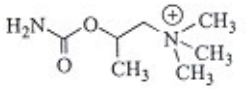
I. Define the following terms: (32%)

1. Hypoxanthine-guanine Phosphoribosyltransferase (HGPRTase)
2. DNA Gyrase
3. Phosphoribosylamine Synthetase
4. HMG-CoA Reductase
5. COX-2
6. Transpeptidase
7. Competitive Reversed Transcriptase Inhibitors (Give an example)
8. Non-competitive Reversed Transcriptase Inhibitors (Give an example)

II. Why is Bethanechol a more potent and more selective cholinergic drug than Acetylcholine ? (6 %)



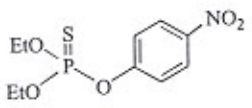
Acetylcholine



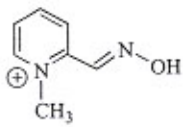
Bethanechol

III. It is known that *l*-epinephrine is a more potent adrenergic agent than its *d*-form isomer, give your explanation. (6 %)

IV. Show schematically how Parathion irreversibly inhibits cholinesterase and how to re-activate enzyme with Pralidoxime (PAM) ? (8 %)

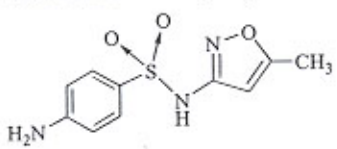


Parathion

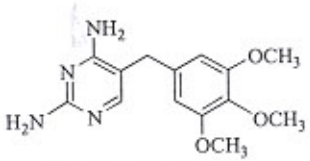


PAM

V. Explain why trimethoprim is usually used in combination with sulfa drugs such as sulfamethoxazole. (8 %)

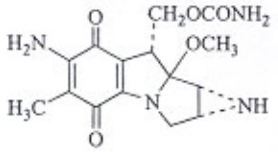


Sulfamethoxazole

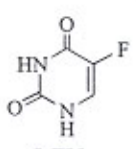


Trimethoprim

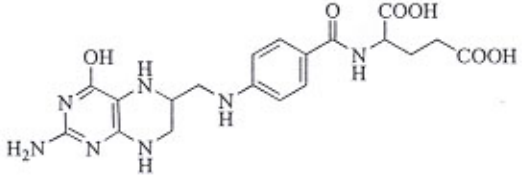
VI. Describe how Mitomycin C alkylates double helical DNA. (8 %)



VII. Describe how 5-Fluorouracil (5-FU) inhibits thymidylate synthetase. (8 %)

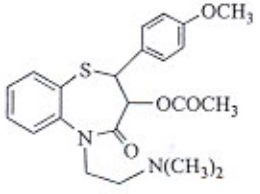


5-FU



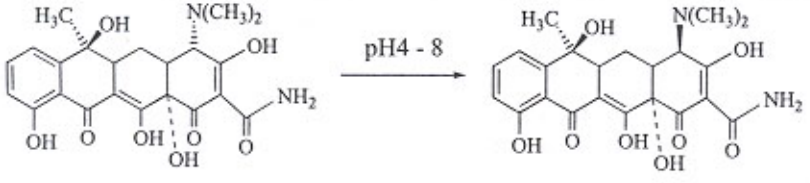
Tetrahydrofolic acid (THF)

VIII. Give four most possible *in vivo* metabolites (phase 1 only) of Diltiazem.(8 %)



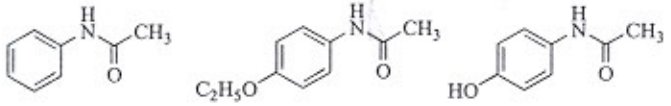
Diltiazem

IX. Explain why tetracycline epimerize to form epitetracycline at pH 4 – 8 ? (8 %)



Tetracycline　　Epitetracycline

X. Explain why acetanilide and phenacetin are hepatotoxic while acetaminophen is less toxic? (8 %)



Acetanilide　　Phenacetin　　Acetaminophen

一. 解釋下列各項(24 分)

1 bathochromic shift
2 Lambert-Beer Law
3 Stoichiometric point
4 Iodometry
5 Specific rotation
6 conjugate acid/conjugate base

二. 配製下列標準溶液時，各選用何種基準標準試藥(primary standard)測定其溶液濃度？(a)硫酸標準溶液 (b)甲醇鈉標準溶液(c)高錳酸鉀標準溶液 (6 分)

三. Sulfamerazine(磺拉嘧胺)(pKa = 5.6)溶於 pH 4.6 緩衝溶液中，則溶液中 Sulfamerazine 之解離度(Percent of ionization)為何？(6 分)

四. 說明藥物適合螢光分析其構造之基本條件。(6 分)

五. 某 Amoborbital 溶液，以紫外光光譜分析後，於 239nm 下測得吸光度為 0.41,另測得 amobarbital 標準液(1.2 mg/ml)之吸光度為 0.45，則該溶液之濃度為何？(6 分)

六. 請說明紫外光分析法與螢光分析法之異同點。(6 分)

七. 說明原子吸光度測定法之原理及適用對象。(6 分)

八. 中華藥典第四版中 methylparaben (HO-⟨⟩-$COOCH_3$ MW: 152.2)之定量方式如下: 取 methylparaben 2.0 g 於 flask 中，加入 1.0 N NaOH 30 ml 後，加熱 1 小時，冷卻後加入 bromothymol blue 為指示劑，再以 1.0 N H_2SO_4 滴定之，並進行空白試驗(blank determination)，其反滴定所耗去 1.0 N H_2SO_4 之體積，檢品試驗及空白試驗分別為 21 ml 及 31ml，請回答下列問題: (1) 以方程式表示滴定過程 (2)其 titer 為何? (3)藥品純度為何? (8 分)

九. 高壓液相層析管進行二種化合物之分離，其滯留時間分別為: V_0: 0.5min; A 化合物, 3.5 min; B 化合物, 4.5 min; 請計算下列各項: (8 分)
(1) 成分 A, B 之 capacity factor (2) 兩者之 selectivity factor

十. 下列氣相層析管在適當層析條件下,何者滯留時間較長，並說明理由。(8 分)
(1) squalane 層析管對 methylbenzene (bp = 110℃) 與 ethyl 2-methylpropanoate (bp = 110℃) 之分離。
(2) PEG 層析管對 butan-1-ol(bp 116℃) 與 4-methylpentan-2-one(bp 117℃) 之分離。

十一. 說明高壓液相層析法中，離子對層析法(ion - pair chromatography)之分離原理及適用對象。(8 分)

十二. Aspirin (acetylsalicylic acid) 之紅外光分析，其圖譜之特徵吸收為何？(8 分)

(一) 敘述透皮藥物輸送系統 (TRANSDERMAL DRUG DELIVERY SYSTEMS),其劑型設計、考慮因素及效應。(20%)

(二) 敘述速效錠 (IMMEDIATE RELEASE TABLET)、腸溶錠 (ENTERIC COATING TABLET),其劑型設計、考慮因素及效應。(20%)

(三) 詮釋藥學倫理 (限 200 字以內)。(13%)

(四) 敘述 ADVERSE DRUG REACTIONS (ADRs) (可包括 causes of, classification of, costs of, description of, home care, in elderly patient, incidence of, prevalence of, information resources regarding and scope of)。(20%)

(五) 說明下列藥品/藥品或藥品/食品合用時可能之交互作用,其機制及適宜之處理方法。(27%)

(1) TERFENADINE-CITROUS FRUIT JUICE

(2) WARFARIN-PHENOBARBITAL

(3) METHOTREXATE-NSAIDs

壹、 問答題:

1. 依「藥事法」之規定，何種藥品須實施「檢驗封緘」制度? 其檢驗封緘之執行機關為何? (12 %)

2. "罰鍰與罰金" 有何不同? 試說明之。(6 %)

3. 針對"診所租用藥事人員執照，另聘用高中畢業的拼號小姐調配處方"一事，試說明其違法(違反何法規?)及應處之情形。(15 %)

4. 臨床藥學服務項目有那些? 試舉出其中那些項目是申請醫學中心應實施的藥事作業項目? (10 %)

5. 何謂"新藥監視期 (PMS)"? (7 %); 何謂藥事? 藥 物?" (6%)

6. 根據藥事法，查獲之偽藥、禁藥、劣藥其處置情形如何"? (8 %)

7. 何謂"妨礙衛生之物品"? (8 %)

8. 何謂"管制藥品[1]"? 分幾級[2]? 如何管理[3]? (12 %)

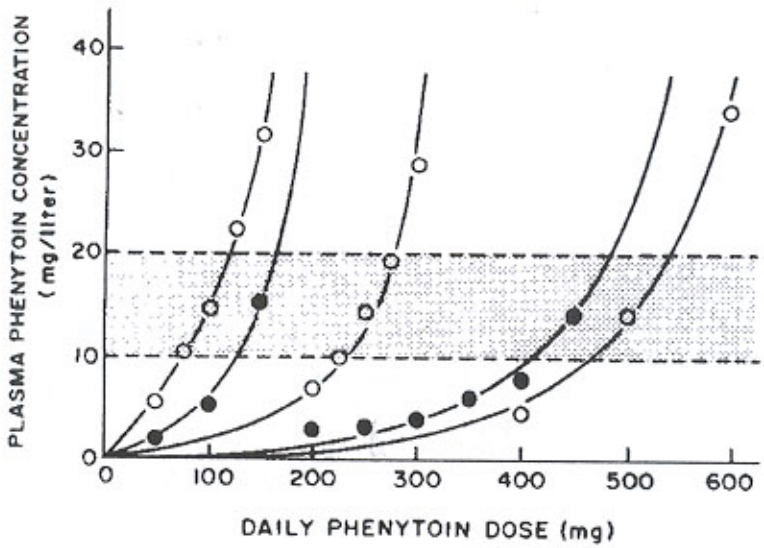
9. 何謂"藥害"? 藥害救濟分幾種? (8%)

10. 試說明現行全民健康保險醫療費用的總額支付制度施行情形? (8%)

1. 請敘述造成痛風的病理生理學並說明藥品治療痛風的方法。(10%)
2. 請比較治療高血壓的鈣離子阻斷劑 (calcium channel blockers, CCB) 與血管加壓素轉換抑制劑 (angiotensin-converting enzyme inhibitors, ACE-I) 的優缺點。(10%)
3. 請解釋下列名詞：Drug Information Services (DIS), Therapeutic Drug Monitoring (TDM) Services 與 Drug Use Evaluation (DUE). (15%)
4. 請將下列英文翻成中文：(10%)

> Omeprazole was 76% bioavailable when a single 40 mg oral dose of omeprazole (at buffered solution) was administered to healthy elderly volunteers, versus 58% in young volunteers given the same dose. Nearly 70% of the dose was recovered in urine as metabolites of omeprazole and no unchanged drug was detected. The plasma clearance of omeprazole was 250 mL/min (about half that of young volunteers) and its plasma half-life averaged one hour, about twice that of young healthy volunteers. In pharmacokinetic studies of single 20 mg omeprazole doses, an increase in AUC of approximately four-fold was noted in Asian subjects compared to Caucasians. Dose adjustment, particularly where maintenance of healing of erosive esophagitis is indicated, for the hepatically impaired and Asian subjects should be considered.

5. 請使用藥品動力學 (pharmacokinetics) 或藥品藥效學 (pharmacodynamics) 的觀念來解釋下面的圖：(15%)



6. 請敘述肺炎感染的病理生理學 (含常見的感染菌種)，並分別列出治療的首選抗菌劑。(15%)
7. 請列出第一代、第二代、第三代與第四代 cephalosporins 抗生素各兩個，並說明 1-4 代 cephalosporins 抗生素的抗菌範圍為何。(20%)
8. 已知一位使用 phenytoin 的病患其 K_m = 12 mg/L，V_{max} = 600 mg/day，如果每天 phenytoin 的劑量為 300 mg，試問該劑量下可達到多少的穩定狀態濃度 (C_{ss}) (mg/L)？(不考慮藥物交互作用或其疾病狀況等因素) (5%)