



Faculty of Health Sciences

School of Pharmacy & Pharmaceutical Sciences

B.Sc. (Pharm.) Degree
Junior Sophister

Semester 2 Exam 2020/21

PHU33111: Malignant Disease, Immune & Ocular Systems and Clinical Therapeutics

Time/Date exam available from	12 noon	Thursday, 13 th May 2021
Submission deadline	3:30 pm	Thursday, 13 th May 2021

Please note that you have received an extra 10 min per hour of the exam for uploading/downloading. **Your paper must be uploaded by 3:30 pm**

Contact details during exam period: pharmacy@tcd.ie
9 am to 5 pm GMT+1 only Telephone: + 353 1 896 2938

Examiners: Assoc. Prof. C. Cadogan, Prof. J. Gilmer, Assoc. Prof. C. Medina, Asst. Prof. N. O'Boyle, Dr. O. Gobbo, Prof. L. O'Driscoll, Assoc. Prof. A. Sasse, Assoc. Prof. J. Walsh

External Examiners: Dr. Sarah Bailey and Prof. Barrie Kellam

Honour Declaration

I understand that by submitting this exam/assignment I agree to the following:

- I am fit to undertake the exam/ assignment
- I acknowledge and accept that this assessment will be reviewed by plagiarism detection (Turnitin) software.

I have read and understand College Regulations *Conduct of examinations and submission of assessed work*: <https://www.tcd.ie/calendar/undergraduate-studies/general-regulations-and-information.pdf>

I have read and understand the Student Code of Conduct (School of Pharmacy and Pharmaceutical Sciences): <https://pharmacy.tcd.ie/assets/pdf/2.16%20Code%20of%20Conduct%20for%20Pharmacy%20Students.pdf>

I declare that all work I submit as part of this exam/assignment is entirely my own work and does not involve plagiarism, collusion, or any other form of cheating.

Student Number: _____ Date: _____

Submissions without this honour declaration confirmed by student number and date will be deemed inadmissible.

Instructions to Candidates:

- Please use this examination paper file for your answers.
 - The maximum word count for each question is given.
 - Please submit your completed examination through Blackboard as a Microsoft Word document (.doc or .docx file).
 - Please use referencing as appropriate, this will not be included in your word count.
 - Do not modify the file name of this exam paper, there is no need to include personal identifiers.
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INSTRUCTIONS FOR THE EXAMINATION

Section A: Five essay questions. All questions must be answered. 70%

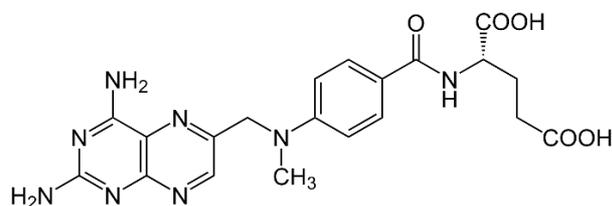
Section B (in Blackboard): 30 by 5-part Multiple Answer Questions (MAQs) 30%
which may have more than one correct answer, marked pro-rata
Negative marking applies: (unanswered = 0; incorrect answer = -0.25).

Overall time available for the exam is 3 hours, plus 30 minutes.

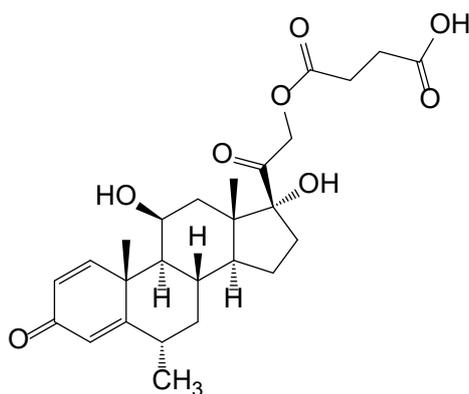
Ensure that you have completed the honour declaration before submission of the **entire** examination paper.

Section A – All 5 questions must be answered [20 marks each].

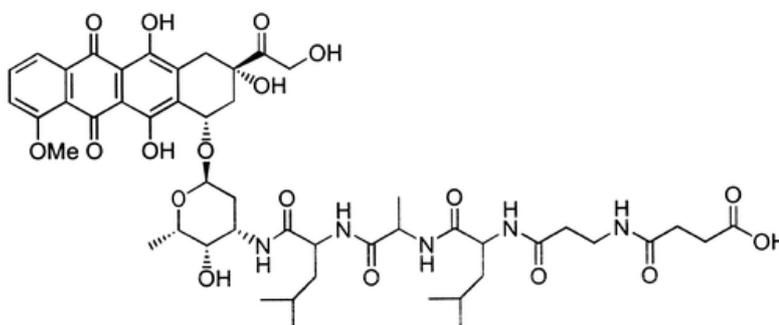
Question 1 (no max. word count)



Compound A



Compound B



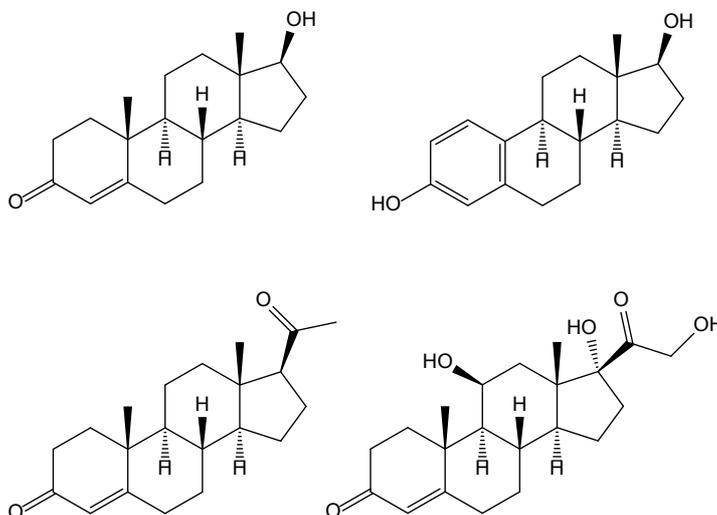
Compound C

- Identify three functional groups in each of the compounds above. (3 marks)
- Are any of the drugs above a prodrug? Briefly explain. (2 marks)
- Given their structures, what is the likely biological target of each of the compounds A, B and C above? What is their molecular mechanism of action? Describe briefly. (4.5 marks)
- Describe why the ionizable groups in compounds A and B above are important with regards to mechanism of action and/or route of administration? (4 marks)
- Discuss the mechanism of action for compound C in detail. (6.5 marks)

Question 2 (no max. word count)**Part A (14 marks)**

Steroidal hormones and their derivatives are used across a number of therapeutic indications.

- a) Match the structure of the physiological hormones shown below to their name (estradiol, progesterone, hydrocortisone, testosterone). (2 marks)
- b) Position 17-alpha is often substituted to achieve better bioavailability and/or pharmacologic activity. Review the effect of substituents on the 17-alpha position in androgens, oestrogens, progestins and corticosteroids. (10 marks)
- c) Derive the IUPAC name for one of such 17-alpha substituted derivatives. (2 marks)



Part B (6 marks)

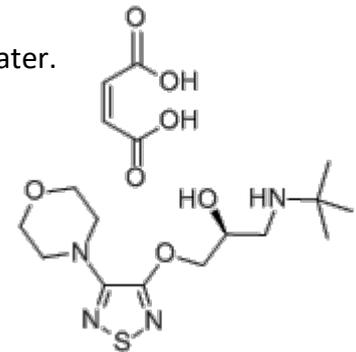
The European Pharmacopoeia states for Timolol Eye Drops:

DEFINITION

Timolol Eye Drops are a sterile solution of Timolol Maleate in Purified Water.

Content of timolol, $C_{13}H_{24}N_4O_3S$

90.0 to 110.0% of the stated amount.

**ASSAY**

Dilute a volume containing the equivalent of 25 mg of timolol to 50 mL with water. To 5 mL add 15 mL of carbonate buffer pH 9.7 and extract with three 20-mL quantities and one 10-mL quantity of toluene. Wash each extract successively with the same 10 mL volume of carbonate buffer pH 9.7, combine the toluene extracts and extract with four 20-mL quantities of 0.05M sulfuric acid.

Combine the extracts, dilute to 100 mL, filter and measure the absorbance at the maximum at 295 nm, Appendix II B, using in the reference cell a solution prepared by treating 5 mL of water in the same manner, beginning at the words 'add 15 mL...'. Calculate the content of $C_{13}H_{24}N_4O_3S$ taking 279 as the value of $A(1\%, 1\text{ cm})$ at the maximum at 295 nm.

You are presented with an eye drop formulation claiming to contain 0.5% timolol and are asked to confirm if the eye drops meet the specifications of the Pharmacopoeia with regards to the assay.

- Describe how you would carry out the experiment, including details on glassware, equipment and instrumentation used. [Note: density of toluene = 867 kg/m^3] (2 marks)
- Explain why the extraction procedure is carried out in this particular sequence. (2 marks)
- In order to predict the expected absorbance reading, calculate the absorbance range that would be obtained if the eye drops meet the specifications of the monograph. (2 marks)

Question 3 (max. 1,200 words)

A 65-year-old male is diagnosed with stage IIIA squamous cell lung carcinoma. This patient has a 40 pack-year history of smoking. Because of his decreased pulmonary function, the patient is deemed to be unsuitable for surgical resection. Instead, his oncologist selects combined modality treatment with radiation therapy and adjuvant chemotherapy. Specifically, treatment includes cisplatin (70 mg/m² on Days 1 and 22) and etoposide (50 mg/m² on Days 1–5 and Days 22–26) plus radiation therapy.

- a) Would prophylactic antiemesis treatment be needed beginning with the first cycle of chemotherapy and continuing through all subsequent cycles of chemotherapy? Why? If prophylactic treatment is needed, which antiemetic drugs would you recommend? (4 marks)
- b) Explain the mechanism of action of the drugs that you have chosen under a) above. (4 marks)
- c) Explain the drugs and their mechanism of action that should be used to treat chemotherapy-induced nausea and vomiting when conventional treatment has failed. (4 marks)
- d) The patient develops chronic diarrhoea. Explain how you would manage this clinical situation (pharmacological and non-pharmacological approaches). (4 marks)
- e) The patient develops oral mucositis. Explain the pathophysiology of this condition and its management (4 marks)

Question 4 (max. 1,200 words)

Alkylating agents are used in chemotherapy.

- a) Drawing also on your knowledge of the chemistry of these drugs, precisely describe their mechanism of action. (6 marks)

- b) Taking cyclophosphamide as example, describe its use in pharmacological treatments, its pharmacokinetics and its side-effects. (14 marks)

Question 5 (max. 1,200 words)

Ms RR is 32 years of age and has been visiting your pharmacy for 2 years. She has a past medical history of psoriasis. She is approximately 150 cm in height and weighs approximately 85 kg. Her fingers appear now swollen at the knuckles and her hands appear slightly deformed. In the time you have known her, she had complained of stiffness in her fingers and wrists, especially in the mornings, and now her mobility appears to have diminished. She has been taking ibuprofen for two years. In the last year, Ms RR had been on methotrexate. Recent laboratory findings indicate an erythrocyte sedimentation rate (ESR) of 85 mm/hour, the presence of normochromic, normocytic anaemia. She is now presenting with a prescription for etanercept. The drug is to be administered as a 25-mg dose by subcutaneous injection, twice weekly.

- a) What is psoriatic arthritis? What are the predisposing factors? (2 marks)
- b) Briefly describe how psoriasis is treated. (4 marks)
- c) What are TNF- α inhibitors? What is etanercept? When would etanercept be prescribed and is it appropriate for Ms RR? (6 marks)
- d) How should the response to etanercept be monitored? (3 marks)
- e) What advice should you give Ms RR? (5 marks)

Section B (in Blackboard)