FOURTH YEAR UNIVERSITY B.Sc. EXAMINATION IN SCIENCE
(INCLUDING DENOMINATED DEGREES)

Biopharmaceutical Chemistry (CH441)

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Time Allowed: Two Hours

Answer three questions from Sections A-C:
One from each Section

Use a separate answer book for each Section.

All questions carry 100 marks distributed as shown.

Leave the first page of the answer book blank and list on it clearly the numbers of the questions attempted.
Section A
(Answer only one question)

1. Answer each of the following:

(i) Give examples of structures of N-glycans & O-glycans and summarise their functions. Why are they important in the biopharmaceutical industry?

[20 marks]

(ii) Show how ‘methylation analysis’ can be carried out to give information on oligosaccharide structure. Illustrate your answer with a description of how ‘methylation analysis’ could be effectively used with the trisaccharide below to gain information on structure.

[40 marks]

(iii) Discuss application of nuclear magnetic resonance (NMR) spectroscopy in the determination of anomeric configuration, carbohydrate conformation & in determination of oligosaccharide sequence. You could illustrate your answer by predicting key features that might appear in NMR spectra of the trisaccharide above.

[40 marks]

2. Answer each of the following:

(i) Based on the binding data presented in Figure 1, compute the dissociation constant (K_D) and the binding free energy (∆G). You can assume room temperature = 300K.

[40 marks]

Figure 1. Binding data for a ligand-protein complex at room temperature. A linear fit to the Scatchard plot results in the equation: y = \(-0.0502x\)
(ii) For the SPR sensorgrams presented in Figure 2, what is the $K_D$ (in $\mu$M) for this interaction? [20 marks]

(iii) Would it be appropriate to have determined the $K_D$ from a steady state (equilibrium) analysis of the sensorgrams in Figure 2? Explain your answer. [40 marks]

![Figure 2. SPR sensorgrams for a ligand binding to a protein.](image)

The kinetic binding rates $k_{on}$ and $k_{off}$ were determined to be $5290 \text{ s}^{-1}\text{M}^{-1}$ and $0.0081 \text{ s}^{-1}$, respectively, by fitting to the sensorgrams.

Section B

(Answer only one question)

3. Answer each of the following:

(i) What is the logP value? Explain its importance and discuss the ideal (and non-ideal) logP values for a molecule in the context of ‘Lipinski’s rule of five’ and drug-likeness. [30 marks]

(ii) Name and briefly explain methods that can be used for the extraction of marine macroalgae (seaweeds) for drug discovery studies. [30 marks]

(iii) Yondelis (also known as ecteinascidin-743, ET-743 or Trabectedin) is the first marine derived compound approved in the European Union as an anticancer drug. Explain its chemical class, source organism (with Latin binominal name), its supply route, and brief mechanism of its anticancer action. [40% of the marks] [40 marks]

4. Answer each of the following:

DNA repair is the primary defence of the cellular genome integrity. Among the available repair pathways, base excision repair (BER) deals with the most common lesions in DNA.

(i) Name one DNA lesion primarily repaired through the BER pathway and what reaction causes that lesion to occur. [35 marks]
(ii) What is the collective name used to define the family of enzymes responsible for removing the damaged bases in the BER pathway? Name one enzyme from this family specialized in the repair of a specific lesion. [35 marks]

(iii) What are the key steps in the BER pathway these enzymes are responsible for? [30 marks]

Section C

(Answer only one question)

5. Answer each of the following:

(i) Using a curly arrow mechanism describe the conversion of ATP and methionine into S-adenosyl methionine (SAM).

\[
\text{methionine} \quad \xrightarrow{\text{SAM}} \quad \text{S-adenosyl methionine (SAM)}
\]

[25 marks]

(ii) Give a curly arrow mechanism for the conversion of theobromine into caffeine using SAM (Scheme 1).

\[
\text{Theobromine} \quad \xrightarrow{\text{SAM}} \quad \text{Caffeine}
\]

Scheme 1

[15 marks]

(iii) Describe the formation of DNA crosslinks from mitomycin C. In your answer briefly account for a bioreductive activation pathway, and use curly arrows to describe the reaction with DNA. Draw an isolated DNA nucleoside dialkylated adduct with accurate stereochemistry. Give a brief reason for the anti-tumour activity.

\[
\text{Mitomycin C}
\]

[60 marks]
6. Answer each of the following:

(i) Describe with the aid of appropriate labelled diagrams how the following single channel detectors operate: PMTs, APDs, and SPADs. Give a concise over-view of the pros and cons of each type of detector for microscopy applications.

(ii) Describe briefly what is multi-photon excitation (MPE) microscopy? What are the primary advantages of MPE microscopy.

[75 marks]

[25 marks]