Autumn Examinations 2013/2014

Exam Code(s)  4BPC
Exam(s)  4th year Biopharmaceutical Chemistry

Module Code(s)  CH441
Module(s)  Biopharmaceutical Chemistry

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Instructions:

Answer all four questions

Use a separate answer book for each question

All questions carry 100 marks distributed as shown.

Leave the first page of the answer book blank and list on it clearly the number of the question attempted.

Duration  2 hours
No. of Pages  3 (incl. this cover page)
School(s)  Chemistry

Requirements:  None

MCQ  
Handout  
Statistical Tables  
Graph Paper  
Log Graph Paper  
Other Material
1. **Answer any two parts of (a) – (c):**

(a)  
(i) Draw pyranose structures for the following saccharides:  
- D-galactose  
- L-fucose  
- D-xylose  
- L-iduronic acid  
- D-glucuronic acid  

(ii) Draw the chemical structure for Gal(β1→4)Glc. Identify the glycosidic linkage and the hemi-acetal. You may assume that Gal and Glc both have D-configurations.

(iii) Show in detail how D-GalNAc would be chemically connected to a protein in an O-glycan. Show the structure of the amino acids of the protein most likely to be involved in the linkage.

(iv) An electrospray ionisation mass spectrum is recorded for Gal(β1→4)Glc. Predict the most likely features of the spectrum including the chemical structure of the ions that would be expected to be observed.

(b)  
(i) Predict the main expected feature of the $^1$H-NMR spectrum of compound A recorded in D$_2$O. Why is the spectrum recorded in D$_2$O? Show how the NMR spectrum could be used to support the stereochemical configuration at the anomeric centre and support the assignment of the $^4$C$_1$ conformation to A.

(ii) Compound A is subjected to methylation with excess (CH$_3$)$_2$SO$_4$. This is followed by acid catalysed hydrolysis, treatment with NaBD$_4$ and subsequent acetylation. Draw the product that would be obtained from this series of reactions and predict the main features of its mass spectrum obtained after GC-MS analysis. In GC-MS you may assume that electron impact mass spectrometry is the technique employed.

(c) Discuss the structure of naturally occurring glycolipids. Give examples of the following, illustrating in detail the structural differences between them:  
- Cerebrosides  
- Sulfatides  
- Neutral glycosphingolipids  
- Gangliosides
2. **Answer any two of the following:**

(i) X-ray crystallography has been instrumental to our understanding of how antibodies bind to antigens. Discuss how crystal structures of the antigen lysozyme bound to a conventional antibody or to the single chain antibody from shark have revealed the unique binding features of the latter.  

[50 marks]

(ii) PEGylation is a common chemical modification of therapeutic proteins. Explain what is meant by PEGylation (include diagrams) and why it has become so important.  

[50 marks]

(iii) What problems are associated with PEGylation of a lysine-rich protein with succinimide-functionalized PEG. Include a structural diagram of the lysine-succinimide linkage.  

[50 marks]

3. **Answer any two of the following:**

(i) Explain which type of marine organisms from which depths and water temperature (climate) have been studied most so far for drug discovery, providing a brief explanation why.  

[50 marks]

(ii) Briefly explain the existing strategies for the collection of marine organisms for marine natural product research.  

[50 marks]

(iii) Briefly discuss the following statement: The specific origin of a natural product isolated from a marine macroorganism often remains unclear.  

[50 marks]

4. **Answer any two of the following:**

(i) List the advantages of implantable drug delivery systems. Define the term bioavailability and describe the differences between (a) relative bioavailability and (b) absolute bioavailability.  

[50 marks]

(ii) Explain the terms: zero-order release.  

[50 marks]

(iii) Describe the advantages and disadvantages of transdermal drug delivery over other routes of drug delivery.  

[50 marks]