Semester II 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
School(s) Chemistry

Requirements: None
MCQ
Handout
Statistical Tables
Graph Paper
Log Graph Paper
Other Material
1. Answer any two parts of (i) – (iii):

(i) Monosaccharides A-E are commonly found in naturally occurring glycoconjugates.

(a) Give names for each of these monosaccharides A-E [15 marks]

(b) Draw the chemical structure for GlcNAc(β1→4)GlcNAc [10 marks]

(c) Show in detail how GlcNAc(β1→4)GlcNAc would most likely be chemically connected to a protein in an N-glycan. [10 marks]

(d) An electrospray ionisation mass spectrum is recorded for a solution of GlcNAc(β1→4)GlcNAc in 0.1% aqueous trifluoroacetic acid. Predict the most likely features of the spectrum including the chemical structure of the ions that might be observed. [15 marks]

(ii) Taking any one of the monosaccharides A-E, briefly predict the main expected features of its 1H-NMR spectrum recorded in D2O. Why would the spectrum be recorded in D2O? How is NMR spectroscopy useful in establishing stereochemistry at the anomeric centre? [25 marks]

(b) Using any disaccharide of your choice, indicate how 2D-HMBC spectroscopy could be used to confirm how two monosaccharides are connected in the disaccharide. How does the information obtained by 2D-HMBC spectroscopy differ from that obtained by 2D-HSQC spectroscopy. [25 marks]

(iii) Show in detail how ‘methylation analysis’ would support the assignment given to the structure below. Give details regarding the various reagents and techniques involved in ‘methylation analysis’ as part of your answer. [50 marks]
2. Answer any two of the following:

(i) With reference to the structure of antibody-antigen complexes, discuss the following statement: The discovery of single chain antibodies was revolutionary for the development of antibody-based therapeutics. [50 marks]

(ii) Outline the issue of circulation half-life for protein therapeutics. Describe three general strategies to extend the half-life. [50 marks]

(iii) Describe the advantages of using Cysteine, compared to Lysine, as a site for the chemical modification of a protein. Draw structural diagrams of both side chains and the products formed by reaction with maleimide- or succinimide-functionalized reactants. [50 marks]

3. Answer any two of the following:

(i) Explain why marine organisms produce natural products (secondary metabolites) and what they are used for. [50 marks]

(ii) Discuss how the supply issue with the anticancer marine metabolite halichondrin B was overcome; from the preclinical trials to the entrance to the market as eribulin mesylate (Halaven™). [50 marks]

(iii) Briefly discuss the major complications in marine natural products chemistry research. [50 marks]

4. Answer any two of the following:

(i) List the advantages of implantable drug delivery systems. [50 marks]

(ii) Which biodegradable copolymer is most extensively used for drug delivery? Provide the chemical structure of the monomers. Describe three major factors that influence degradation behaviour. [50 marks]

(iii) Provide the definition of nanocarriers. Briefly explain the characteristics of liposomes and polyplexes. [50 marks]