

Cork Institute of Technology

Bachelor of Science (Honours) in Applied Biosciences – Award

December 2005

BIOCHEMISTRY

(Time: 3 Hours)

Answer one question from each of Sections A, B, C and D. Each question carries equal marks.

Examiners: Dr. H. Tarrant
Dr. J. O'Mahony
Dr. T. Beresford

Use separate answer books for each section and mark the questions attempted.

Section A

- Q1.** Write an essay on free radical damage and its control. (25 marks)
- Q2.** Describe the molecular mechanisms of drug-receptor interaction, using diagrams and specific examples to illustrate your answer. (25 marks)

Section B

- Q3.** Discuss the three basic pharmacokinetic processes of absorption, distribution and clearance. In your answer, include definitions of the parameters used to quantify these processes and describe the significance of such parameters in the clinical environment. (25 marks)
- Q4.** Write an essay on biotransformation reactions using relevant example(s) to support your discussion. (25 marks)

Section C

- Q5.** Outline the main biochemical processes involved in digesting, absorbing and storing food nutrients. In your answer give examples where applicable of the role hormones play in the processes.
(25 marks)
- Q6.** Describe the important physiological and biochemical relationships that exist between the liver, bile production and the hepatic portal system. Refer in your answer to some of the more common disorders associated with these systems.
(25 marks)

Section D

- Q7.** Discuss some of the main recent developments in the area of clinical diagnostics, particularly with regard to detecting myocardial infarctions.
(25 marks)
- Q8.** Describe using suitable examples, the molecular approaches used to create engineered proteins for subsequent clinical therapeutic applications.
(25 marks)

Model Answers

- Q1.** Define reactive oxygen species (ROS) and oxygen free radicals (OFR) and describe sources of ROS/OFR (metabolic by-product, inflammatory immune response, ischaemia, pollution/ionising radiation, free metal ions-Tenton).
- Mechanisms of toxicity (interactions with proteins, nucleic acids, lipid peroxidation, Fenton reaction) and links with disease (ageing/degenerative diseases, cancers, tissue and enzyme damage, mental illness).
- Describe defence mechanisms under headings of non-enzymic (glutathione, uric acid, vitamins, phenols and polyphenols), enzymic (glutathione-dependent, catalase, superoxide dismutase) and use of compartmentalisation (peroxysomes, lysosomes).
- Q2.** Intracellular receptors: lipid soluble ligands (e.g. NO, steroid hormones, PCBs, dioxins), "gene-active" receptors (e.g. NO, Ah and estrogen receptors), consequences of activation.
- Transmembrane receptors (two sub-groups): ligands (e.g. trophic hormones), receptor domains (extracellular drug binding, transmembrane region, intracellular enzyme activity- serine/tyrosine kinase, guanyl cyclase).
- (a) Receptor tyrosine kinases: insulin, EGF (mechanism, down-stream signalling, down-regulation).
- (b) Cytokine receptors: variant of tyrosine kinase receptor (activity located on JAK protein).
- Ligand-gated channels: increased ion flow upon receptor activation (e.g. acetylcholine, GABA), mechanism of action, rapid response time.
- G-proteins and second messengers: members of serpentine family, mechanism of action (effector proteins, second messengers, cAMP, Ca^{++} , phosphoinositides), advantages/disadvantages (amplification, lag period, persistent effects, variety of signals possible).
- Q3.** Pharmacokinetic processes determine how rapidly, at what concentration and for how long the drug is at the target organ (summary diagram).
- Absorption: define bioavailability, influencing factors (drug, dose route, formulation), first-pass effect).
- Distribution: define volume of distribution, uses and limitations.
- Clearance: define (metabolism and excretion combined), capacity-limited elimination, flow-dependent elimination.
- Half-life: define (combination of V_d and C_L), graphical representation (determination of half-life and K_d in laboratory or clinical environment, applications (drug accumulation, dosing intervals, assessment of potential for toxicity e.g. paracetamol).
- Q4.** Removal of drugs largely by renal excretion: polar/ionised compounds excreted directly, lipophilic molecules undergo Phase I and II reactions (may increase or decrease toxicity) to increase solubility prior to excretion. Sites of biotransformation reactions.
- Phase I: mainly catalysed by mono-oxygenases such as the family of Cyt P450s (heme group, FAD, FMN), mechanism of action for hydroxylation reaction, induction (translational and post-translational levels), inhibition and isoforms of Cyt P450s.
- Phase II: catalysed by transferases, conjugates include glucuronate, sulphate, acetate, glutathione, amino acids. E.g. Glutathione: reservoir of reducing power (functions in cell), substrate for glutathione-S-transferases, conjugate degraded by γ -glutamyl cycle to mercaptic acid, substrates. E.g. Glucuronate: UDP glucuronate is donor, substrates.

Q5. A suitable answer would contain reference to some / all of the following

- a) 4 glycoprotein complexes
- b) Absorption mechanisms for carbohydrates (Na dependent and independent)
- c) 5 GLUT transporters
- d) Carbohydrate mal-absorption
- e) Protein peptidase complexes
- f) Role of bile and lecithin in fat digestion
- g) Role of chylomicrons and cholesterol
- h) Impact of insulin on carbohydrate absorption
- i) Mention of Gastrin, secretin, motilin, Ghrelin
- j) Digestive disorders

Q6. A suitable answer would contain reference to some / all of the following

- a) Structural features of the liver and bile duct
- b) The importance of the portal triad
- c) Components of bile and their role in liver function
- d) Hepatic portal circulation
- e) Role of liver and bile in fat digestion
- f) Parenchymal disease
- g) Hepatitis
- h) Cirrhosis, types and biochemical manifestations
- i) Cholelithiasis – predisposing factors
- j) Hemochromatosis – biochemical consequences

Q7. A suitable answer would contain reference to some / all of the following:

- a) Lactate dehydrogenase (5 isoforms).
- b) Creatine kinase (CK-MB).
- c) Aspartate aminotransferase.
- d) High sensitivity C reactive protein, troponin, myoglobin.
- e) Timing and peaks associated with each marker.
- f) Sequential testing, multi enzyme testing.
- g) Biochemical tests for each marker.
- h) Multiple marker arrays and point of care testing.
- i) Influence of European Society and American College of Cardiology.
- j) Abnormal levels

Q8. A suitable answer would contain reference to some / or all of the following:

- a) Definition of protein engineering.
- b) Reasons for the development of protein engineering.
- c) Methods of protein modification.
- d) Purification and downstream processing
- e) Site directed mutagenesis and screening of clones
- f) Insulin and Growth hormones (creation of).
- g) Abzymes.
- h) Commercial markets for protein engineering.
- i) Regulatory constraints.
- j) Likely future developments.