UNIVERSITY OF TORONTO

FACULTY OF ARTS AND SCIENCE

BIOCHEMISTRY 210H1F

DECEMBER FINAL EXAMINATION 2008

DURATION: 3 hours

EXAMINERS: Dr. R. Andreopoulos and Dr. R.Baker

Candidates may use simple, non-programmable calculators (supplied by candidates).

This examination is worth 45% of the final grade for the course. There are 35 multiple choice questions worth 1 mark each for a total of 35 marks and 5 short answer questions, worth a total of 10 marks.
For the multiple choice questions you are to choose ONE answer for each question and fill in the appropriate circle on the computer card with a soft lead pencil (**not pen!**). Marks are not deducted for wrong choices but no marks are given if more than one circle is filled in per question.

***CAREFULLY fill in the appropriate circles on the computer card for your name and student number WITH PENCIL. Please also print your name and number on the card.

We cannot help you if you make transcriptional errors. It is thus not a good idea to leave entering your answers on the card to the last few minutes of the exam. When not entering answers on your card you should cover the answer card with your question paper.

****Please note that the examiners make every effort to ensure there is only one suitable answer for each multiple choice question. However if you are convinced that a particular question has two answers, you should select the answer that seems MOST appropriate.**

Answer all the multiple choice questions and all the short answer questions.
Place your short answers in the examination booklet provided.

Please print your name and student number on your examination booklet.

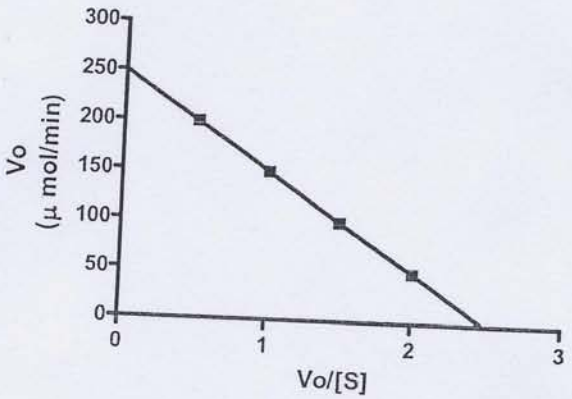
MULTIPLE CHOICE SECTION Answer all questions

Dr. Andreopoulos's Section

1. An alternative plot to the Lineweaver-Burke plot is the Eadie-Hofstee plot which is graphically represented by the following equation:

$$V_o = - K_m (V_o / [S]) + V_{max}$$

Studies of the kinetics of a particular esterase (MW 128 000) generated the Eadie-Hofstee plot seen below:



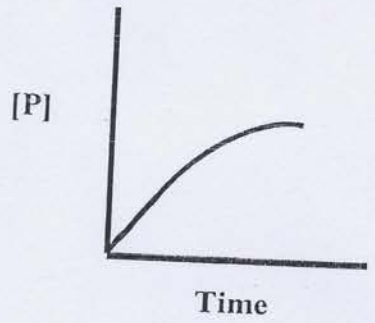
Using the data from the above graph for the Michaelis Menton kinetics of the esterase, calculate the turnover number of the reaction if 0.1 mL of a 0.5 mg/mL enzyme solution was used for the assay.

a) 3.9×10^{-4} min^{-1}
b) 6.4×10^{5} min^{-1}
c) 3.9×10^{-7} min^{-1}
d) 1.5×10^{-6} min^{-1}
e) 6.4×10^{-7} min^{-1}

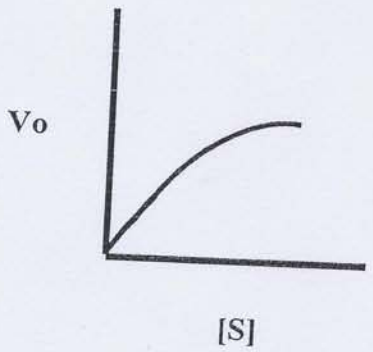
Continued...

2. For the following curves below, choose the graph you would NOT expect to obtain for a simple enzymatic (E + S $\longrightarrow$ P) reaction in the presence of a fixed concentration of a competitive inhibitor.

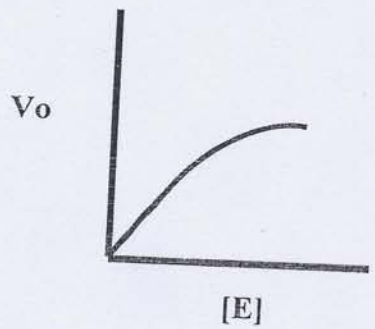
a)



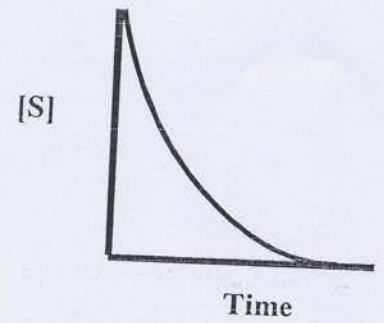
b)



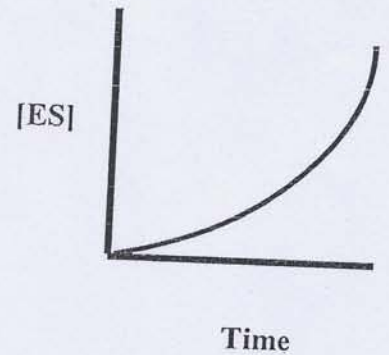
c)



d)



e)



Continued...

3. Which ONE of the following statements concerning ATCase is INCORRECT?

a) The 12 subunit enzyme condenses carbamoyl phosphate and aspartate to form carbamoylaspartate and inorganic phosphate, the first step in the synthesis of pyrimidines.

b) The rate of product formation as a function of substrate concentration for ATCase does not follow Michaelis-Menton kinetics.

c) The larger catalytic subunit alone has catalytic activity, is unresponsive to CTP and displays sigmoidal kinetics.

d) The smaller regulator subunit displays no catalytic activity but can bind CTP and UTP.

e) The binding of CTP to ATCase shifts the equilibrium toward the T-state, thereby increasing the apparent Km for Asp and decreasing net enzyme activity.

4. Which ONE of the following statements concerning RNAse A is INCORRECT?

a) RNase A catalyzes the cleavage of the 3' phophodiester linkages in the following RNA molecule AGUACGUAGUACA yielding 6 fragments.

b) Brief subtilisin cleavage of RNAse A results in the generation of two fragments, the larger of which has 2 important ionic residues (Lys-41 and His-119) that are contained within the active site of RNAse.

c) RNAse A catalyzed hydrolysis produces a leaving group with a 5' hydroxyl group and a nucleoside monophophate product containing a pyrimidine.

d) Chemical modification with iodoacetate of His 119 in RNAse A leads to the formation of carboxymethyl His 119 which would render it incapable of acting as a proton donor to the 5' oxygen atom of the nucleotide leaving group producing an alcohol.

c) The phosphate atom in both transition states in RNase A-catalyzed cleavage is hexacovalent.

Continued...

5. Which ONE of the following statements concerning chymotrypsin is CORRECT?

a) Hydrophilic amino acids line the binding pocket of chymotrypsin and thus aids in the determination of its substrate specificity.

b) Once the acyl-enzyme intermediate is formed, it is stabilized by the oxyanion hole.

c) Exclusion of H_2O from the active site of chymotrypsin would prevent the hydrolysis of the E-TI_2 intermediate.

d)The nucleophilic oxygen of Ser-195 attacks the carbonyl carbon of the peptide bond to form a tetrahedral intermediate E-TI_1.

e) His-57 donates a proton to the hydroxymethyl side chain of Ser-195 thereby making it a powerful nucleophile.

Dr Baker's Section

6. Considering the Case Study Nat, which ONE of the following is INCORRECT?

a) If Nat had a stenosis in his right internal carotid artery, this could have resulted in a loss of feeling in his left arm and hand.

b) Arterial stenosis can be caused by the presence of atherosclerotic plaque in the artery wall.

c) Turbulence in blood flow can result in platelet activation and the production of a thrombus at the surface of an atherosclerotic plaque.

d) Blood within an ischemic brain region that has poor blood flow will likely show depressed NADH levels and decreased pH associated with increased lactate production from glucose.

e) Nat had an elevated LDL cholesterol level, which likely promoted the endocytosis of LDL by scavenger receptors at the liver plasma membrane.

Continued...

7. Which ONE of the following concerning risk assessment for cardiovascular disease is INCORRECT?

a) The higher the risk category, the lower the recommended treatment target for the total cholesterol/HDL ratio.

b) While diet is not a factor used in the calculation of 10-year risk for artery disease (based on the CMAJ assessment sheet noted in class), it is likely that risk can be elevated by consumption of trans or saturated fats.

c) The consumption of soy products, egg plant, almonds and plant sterols and stanols can lower the total cholesterol/HDL ratio.

d) In comparison with VLDL, LDL shows a very highly elevated ratio of cholesterol/esterified cholesterol.

e) Familial hypercholesterolemia is an inherited genetic disease and can be associated with defective LDL receptor and elevated levels of oxidized LDL in the blood.

8. Which ONE of the following concerning blood lipoproteins and arterial atherosclerotic plaque is INCORRECT?

a) If you could elevate levels of lipoprotein lipase in the blood, this should greatly reduce the risk of heart attack and stroke in patients who have FH.

b) Arterial plaque can be associated mainly with the production of VLDL by the liver, rather than the production of chylomicrons by the intestine.

c) Blood cholesterol levels can be influenced by diet, exercise, gender and alcohol consumption.

d) Increased levels of total blood cholesterol above 5 mM can increase the risk for platelet activation and thrombus formation.

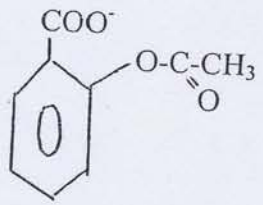
e) Atherosclerotic plaque consists of a lipid pool (rich in cholesterol), a connective tissue cap (produced by proliferating smooth muscle cells) and invading macrophage.

Continued...

9. Which ONE of the following concerning platelet activation is INCORRECT?

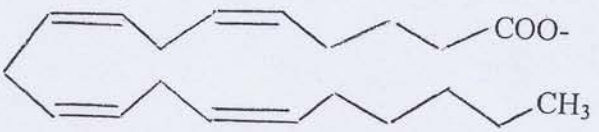
a) Rising calcium ion concentrations in platelets can trigger increased phospholipase A2 (cPLA2) activity in platelets that can selectively release 20:4 from platelet membranes.

b)



The compound above is an NSAID that blocks the formation of TXA_2 in platelets by inhibiting the formation of the eicosanoid PGG_2.

c) The compound below:



can compete with the ω-6 fatty acid arachidonate for the enzyme cyclooxygenase and result in the formation of TXA_3 by this enzyme activity in platelets.

d) ω-3 Fatty acids are found in salmon, anchovy, herring and mackerel and can serve as dietary anti-inflammatories.

e) The 20:4 binding site in COX is accessed by a tunnel defined by α-helices, and blocking or obstructing the tunnel can reduce pain or fever.

10. How many of the following carbohydrates will give a reducing sugar test?

α-D-ribose-1-phosphate, cellobiose, α-D-glucose-6-phosphate,
β anomer of maltose, β-D-fructose-1,6-bisphosphate, β-D-fructose-2,6-bisphosphate,
sucrose

a) 1
b) 2
c) 3
d) 4
e) 5

Continued...

11. Which ONE of the following is INCORRECT?

a) The α anomer of maltose has 10 chiral carbons.

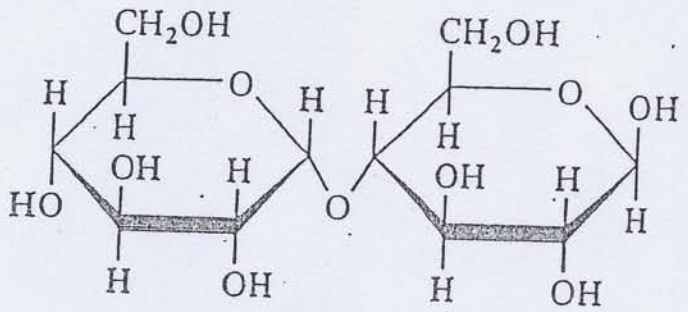
b) α-D-glucosamine cannot be described by the general monosaccharide formula $(CH_2O)n$.

c) There are 8 D and 8 L stereoisomers for straight chain aldohexoses.

d) α-D-Ribose has carbon 1 as its anomeric carbon with the attached –OH group below the plane of the Haworth ring.

e) β-2-Deoxy-D-ribose cannot be converted into a straight chain aldopentose structure.

12. Which ONE of the following concerning the carbohydrate Y shown below is INCORRECT?



a) Y can be formed directly as a product of the attack of α-amylase on amylose.

b) Y is a reducing sugar

c) Y has an α (1→ 4) glycosidic link

d) Likely chemical hydrolysis of the glycosidic bond in Y will directly yield two anomers of D-glucopyranose as products.

e) One of the monosaccharide subunits of Y can open its cyclic structure by loss of the hemiacetal.

Continued...

13. Which ONE of the following concerning carbohydrates is INCORRECT?

a) β-D-glucopyranose is a hemiacetal.

b) β-D-glucuronate production by oral bacteria can be associated with tooth decay.

c) Lactose intolerance is associated with diarrhea and gas production, following ingestion of milk or other dairy products.

d) Chemical hydrolysis of an amylose chain made of 100 α-D-glucose subunits will require 100 molecules of water to release all the monosaccharides from this polysaccharide.

e) It is possible for monosaccharide hemiketals to open up into straight chain ketoses.

14. Which ONE of the following concerning ATP is INCORRECT?

a) ATP is used in phosphorylation reactions catalyzed by hexokinase, PFK-1 and PFK-2.

b) ATP has two high energy anhydride linkages.

c) Catabolic reactions release energy that can support the synthesis of ATP and H_2O from ADP and inorganic phosphate.

d) Catabolic reactions are associated with a positive change in entropy.

e) All reactions that generate ATP have large positive equilibrium constants.

15. If phosphofructokinase (PFK-1) under standard conditions has a $\Delta G^{o'} = -14$ kJ/mole, which value below, under standard conditions, is closest to the equilibrium ratio:

[β-D-fructose-1,6-bisP] [ADP]/[ATP] [β-D-fructose-6-P]

a) 642
b) 446
c) 286
d) 115
e) 67.5

Continued...

16. The $\Delta G^{o'}$ of hydrolysis for β-D-fructose-1,6-bisphosphate is shown below:

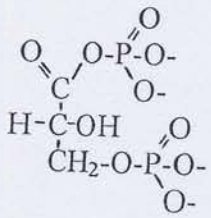
β-D-fructose-1,6-bisphosphate + $2H_2O \rightarrow$ β-D-fructose + 2Pi $\Delta G^{o'} = -29$ kJ/mole

Which value below is closest to the standard free energy change associated with the reaction:

β-D-fructose-6-phosphate + $H_2O \rightarrow$ β-D-fructose + Pi

a) -1 kJ/mole
b) -13 kJ/mole
c) -15 kJ/mole
d) -16 kJ/mole
e) -43 kJ/mole

17. Which ONE of the following concerning the compound Z below, found in Soon-yi's muscles is INCORRECT?



a) If Z were completely hydrolyzed chemically to glycerate, likely the $\Delta G^{o'}$ of this hydrolysis would be greater than -49 kJ/mole.

b) Z is produced by a transferase

c) Z is a substrate for the enzyme phosphoglycerate kinase

d) The enzymatic formation of Z in glycolysis is accompanied by the production of NADH.

e) Z is a substrate for an isomerase that produces a compound important in regulating oxygen binding to hemoglobin.

Continued...

18. Which ONE of the following is INCORRECT?

a) The phosphate group transfer energy associated with the phosphate linkage in phosphocreatine is greater than that associated with the γ-phosphate group of ATP.

b) The 3 isomerase activities of aerobic glycolysis interconvert aldose phosphates and ketose phosphates.

c) Phosphofructokinase-1 is an enzyme in glycolysis that can be allosterically inhibited by ATP and allosterically activated by AMP.

d) The enzyme pyruvate kinase utilizes as substrates ADP and the phosphate ester of a 3 carbon enol.

e) The glycolytic enzyme hexokinase, if supplied with the appropriate substrates, can produce α-D-glucose-6-phosphate, α-D-fructose-6-phosphate, or α-D-mannose-6-phosphate.

19. If Soon-yi develops a muscle cramp in the early part of her exercises and warm-ups, which ONE of the following is INCORRECT?

a) The cramp is an indication of anaerobic glycolysis in muscle.

b) During the cramp there is an accumulation of CH_3-CHOH-COO^-.

c) Pyruvate lost during the muscle cramp is replaced by NADH formed by the enzyme glyceraldehyde-3-phosphate dehydrogenase.

d) Soon-yi can recover from the cramp by converting the accumulating acid into pyruvate by the action of the enzyme lactate dehydrogenase.

e) In anerobic glycolysis there is a net production of 2 molecules of ATP for each molecule of α-D-glucose used as substrate.

Continued...

20. Which ONE of the following concerning glycogen is INCORRECT?

a) Glycogen has α-D-glucose units linked by α (1→4) glycosidic links and certain units also have an α (1→6) glycosidic link that allows chain branching.

b) In Soon-yi's muscle, glycogen can be degraded by the covalently modified and activated glycogen phosphorylase a.

c) Rising adrenaline in Soon-yi's bloodstream is accompanied by an elevation in the levels of cAMP in her muscle cells.

d) In Soon-yi's muscles, rising calcium ion concentrations needed for muscle contraction also promote increased phosphorylase kinase activity.

e) Glycogen synthesis is stimulated by insulin, and in this anabolic path α-D-glucose-1-phosphate is used as substrate by the activated enzyme glycogen synthase that adds the glucose unit to the non-reducing ends of glycogen chains.

21. Which ONE of the following is not a correct match for Soon-yi's tissues, during extended running?

a) Liver, principally influenced by rising glucagon levels in the blood, will use its glycogen to produce α-D-glucose to support blood sugar levels.

b) Brain has no glycogen stores but can rely on its fatty acids to supply ketone bodies for use as fuels during extended running.

c) Muscle, influenced by adrenaline, will show increased adenylate cyclase activities and use its glycogen to supply its own glycolytic needs.

d) Fat may ultimately be mobilized in extended exercise to provide fatty acids as alternate fuels to glucose.

e) Overall Soon-yi, under the influence of rising glucagon and adrenaline and falling insulin, will have a catabolic status centered upon energy production during her extended run.

Continued...

22. Of the following, how many conditions will result in the activation of the pyruvate dehydrogenase complex?

Rising ATP concentrations, falling NADH concentrations, rising acetyl CoA concentrations, rising pyruvate concentrations, rising calcium concentrations, rising NAD^+ concentrations

a) 1 c) 3 e) 5

b) 2 d) 4

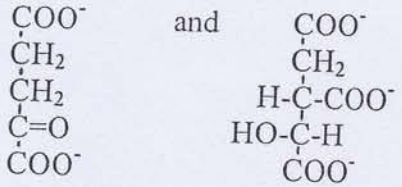
23. Which ONE of the following is INCORRECT?

a) Each turn of the Krebs cycle is associated with GTP production.

b) Carbons entering the Krebs cycle in the form of an acetyl group supplied by acetyl CoA are released as CO_2 during that cycle.

c) Each turn of the Krebs cycle generates 3 NADH and 1 $FADH_2/QH_2$.

d) Each turn of the Krebs cycle involves two oxidative decarboxylations using these two substrates:



e) There is much more ATP generated using reduced coenzyme products of the Krebs cycle via electron transport and oxidative phosphorylation than is made by substrate level phosphorylation within the Krebs cycle.

Continued...

24. Which ONE of the following concerning electron transport is INCORRECT?

a) Mitochondria poisoned with rotenone can transport electrons donated by $CoQH_2$.

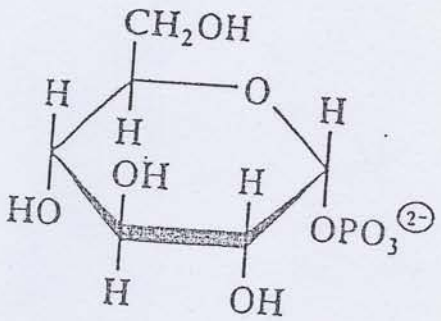
b) The mitochondrial use of $FADH_2$ for ATP production in mitochondria by electron transport and oxidative phosphorylation can be shown by:
$FADH_2 + 1.5ADP + 1.5\ Pi + ½\ O_2 \rightarrow FAD + 1.5\ ATP + 2.5\ H_2O$

c) Complex IV in electron transport is associated with the production of water from oxygen and also with the pumping of $2H^+$ across the inner mitochondrial membrane for each electron pair transported.

d) Cytochromes can serve as electron carriers within the inner mitochondrial membrane, via the reduction and oxidation of iron in component heme groups.

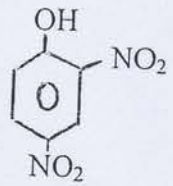
e) As mitochondrial NADH can be used to generate 2.5 ATP in electron transport and oxidative phosphorylation, you would expect the energy of reduction found in this mitochondrial reduced coenzyme (expressed as $\Delta G^{o'}$) to be close to -75 kJ/mol.

25. Which ONE of the following is the best estimate of the net ATP and H_2O production from the compound noted below, released in Soon-yi's muscle cells during prolonged running? Consider glycolysis, PDH complex, Krebs cycle and oxidative phosphorylation.



	ATP	H_2O
a)	31	38
b)	33	41
c)	39	40
d)	42	42
e)	44	40

26. Which of the following concerning the compound below is INCORRECT?



a) It can serve as a weak acid in cells.

b) It is a specific inhibitor of F_0F_1 ATPase in mitochondria, a membrane enzyme found on mitochondrial cristae.

c) It will block mitochondrial ATP synthesis but not electron transport.

d) It can enter the mitochondrial matrix from the cytoplasm.

e) It can reduce the pH of the mitochondrial matrix.

27. Which ONE of the following concerning insulin is INCORRECT?

a) Insulin levels rise in the blood in response to rising blood sugar.

b) In depolarized pancreatic β-cells, rising calcium ion levels in the cytoplasm are associated with insulin release.

c) The binding of insulin to the insulin receptor in the plasma membranes of muscle cells results in increased numbers of GLUT4 at the cell surface.

d) Insulin binding activates protein phosphatase-1 in the cytoplasm of muscle cells.

e) You would expect insulin binding at the insulin receptor to promote dephosphorylation and deactivation of phosphorylase kinase, glycogen phosphorylase, hormone-sensitive lipase, adenylate cyclase and protein kinase A.

Continued...

28. Which ONE of the following is an INCORRECT match, considering Soon-yi's diet after her practice run?

a) Ground flax seed provides lignans and mainly omega 6 fatty acids.

b) Salmon provides EPA, an important anti-inflammatory.

c) Tomatoes are a source of the red coloured antioxidant lycopene.

d) Broccoli and garlic have compounds which are believed to fight cancer.

e) Too much sugar, early in a meal, can raise blood sugar levels and provoke an insulin response that can support inflammation.

29. Which ONE of the following does NOT play a role in promoting the mobilization of fatty acids from triglycerides in Soon-yi's fat tissue?

a) Rising levels of adrenaline in the blood

b) Falling levels of blood glucose

c) Activation of cAMP phosphodiesterase

d) Phosphorylation of hormone sensitive lipase

e) Monoglyceride lipase

30. Which ONE of the following concerning fatty acid β-oxidation in Soon-yi's muscle cells is INCORRECT?

a) A shuttle involving the molecule below is an important regulator of mitochondrial fatty acid β-oxidation: $^{-}OOCCH_2CH_2CH_2N^{+}(CH_3)_3$

b) NADH and $FADH_2/QH_2$ are produced in equimolar quantities in each cycle of fatty acid β-oxidation.

c) There is a hydration step in fatty acid β-oxidation.

d) The last step in fatty acid β-oxidation requires Coenzyme A and produces acetyl CoA.

e) The molecule shown below can decrease rates of mitochondrial fatty acid β-oxidation:

$^{-}OOC\text{-}CH_2\text{-}C(=O)\text{-}S\text{-}CoA$

31. Which ONE of the following is INCORRECT for Soon-yi at the 38 km marker of her marathon in Beijing?

a) Gluconeogenesis in her liver utilizes principally glycerol as a source of C in the synthesis of α-D-glucose, and this pathway depends on the presence of fructose-1,6-bisphosphatase and glucose-6-phosphatase.

b) Falling concentrations of AMP and β-D-fructose-2,6-bisphosphate will stimulate glycolysis and inhibit gluconeogenesis.

c) The complete breakdown of palmitate in mitochondria can give more than 3 times the net amount of ATP produced during the complete breakdown of α-D-glucose as fuel.

d) If Soon-yi ate significant amounts of sugar at the 38 km mark of the marathon she would lose the energy supplied by fatty acid β-oxidation.

e) The complete breakdown of palmitate in mitochondria can give more than 3 times the net amount of water produced during the complete breakdown of α-D-glucose as fuel

32. For Adil, which ONE of the following is NOT associated with his hyperglycemia?

a) Increased loss of potassium from tissues.

b) Increased formation of $CH_3\text{-}\underset{\underset{OH}{|}}{CH}\text{-}CH_2\text{-}COO^-$

c) Elevated production of malonyl CoA from fatty acids

d) Hypotension

e) Elevated levels of $CH_3\text{-}\underset{\underset{O}{||}}{C}\text{-}CH_3$ in expired air from his lungs.

33. Once Adil receives insulin, which ONE of the following does NOT occur?

a) Liver PFK-2 activities decline while fructose-2,6-bisphosphatase activity increases.

b) Free fatty acid levels fall in his blood

c) There is an increase in rates of liver glycolysis.

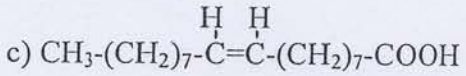
d) His blood sugar values decrease and hopefully stabilize within the normal range.

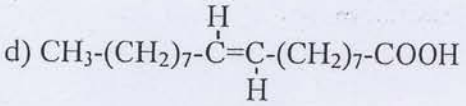
e) Levels of fatty acid synthase increase in liver

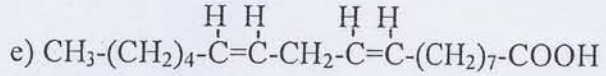
34. Considering possible foods for Julian, the fast food addict, which ONE of the following dietary fatty acids found in ester links in dietary triglycerides would be MOST healthy for him?

a) $CH_3\text{-}(CH_2)_{14}\text{-}COOH$

b) $CH_3\text{-}(CH_2)_{16}\text{-}COOH$

c) 

d) 

e) 

35. Comparing Adil (during his hyperglycemic attack) with Julian, which ONE of the following is INCORRECT?

	Julian	Adil
a) β-hydroxybutyrate levels in blood	Low	High
b) Carnitine acyltransferase Activity	Low	High
c) Rate of blood flow through cerebral circulation	Low	High
d) Activity of glycogen phosphorylase	Low	High
e) Rates of gluconeogenesis	Low	High

Continued...

SHORT ANSWER QUESTIONS: 10 Marks Total Answer all questions

36. Draw the oxidized and reduced forms of the flavin ring in FAD. (2 marks)

37. What two compounds (give names and structures) are the cause of Adil's acidosis, associated with his hyperglycemia? Where are these compounds formed and from what primary substrate? (2 marks)

38. Why is Rosco, the alcoholic patient noted in the Workbook, often hypoglycemic? (2 Marks)

39. Give the substrate level phosphorylation reaction in the Krebs cycle in Soon-yi's mitochondria. Name the enzyme, substrates and products and give the structures of the two Krebs cycle intermediates in this reaction. (2 marks)

40. The pancreatic extract first prepared by Banting and Best was successful in keeping diabetic dogs alive but was much less effective with human diabetics. Give two reasons that might explain this lack of success with diabetic patients. (2 marks)