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Module Code: MANP H4004
CRN:

TECHNOLOGICAL UNIVERSITY DUBLIN
TALLAGHT CAMPUS

TU876

BSc in Pharmaceutical Science

Year 4

SEMESTER 1
EXAMINATIONS 2024/25

Manufacturing Technology and Unit Processes

Internal Examiner:
Dr Adrienne Fleming
Dr Eugene Hickey

External Examiner:
Dr Sandra Lenihan

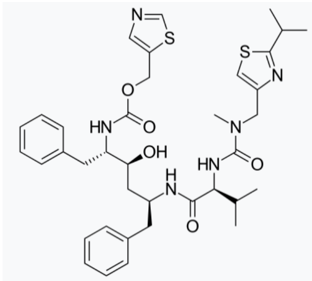
Exam Duration:
Two hours in duration with an additional 15 minutes of reading time in advance
Instructions:
Answer two questions from Section A.
Answer two questions from Section B.
Please use separate answer books for each section.
Formula Sheet at end of exam paper.

SECTION A: You are required to answer TWO complete questions

[Dr. A Fleming]

Question 1 **Answer all parts**

(a) Consider the following drug active compound and identify sites in the structure that could be varied to enhance drug potency and activity in the body. **(20 marks)**



Ritonavir

(b) (i) The Maximum Temperature of a Synthetic Reaction (MTSR) is calculated as the sum of the process temperature and the adiabatic temperature rise. For a large-scale production reaction carried out at 40°C using toluene as the solvent. Determine the MTSR for the reaction. i.e. the temperature above which decomposition can occur (in °C), given that ΔH = -450 kJ mol-1 and the specific heat=1.2 kJ kg $^{-1}$K^{-1} (given that MW = 134 g/mol.). The number of moles is 45 moles and a mass of 450kg.

(ii) The actuator valve controlling the addition of a reagent to the reaction mixture has failed to open during dosing. Based on an initial heat input of 222 W kg^{-1} and an activation energy (E_a) of 1.05 kJ mol^{-1} at 40°C, how many minutes are available to implement emergency measures to prevent a runaway reaction occurring? **(40 marks)**

(c) Assess the following compounds as reagents in a large-scale production from a safety perspective? (i) Acetone (ii) Acetonitrile Explain why, using your knowledge of oxygen balance.

(20 marks)

(d) Determine the batch conversion time for a first order reaction of rate constant k = 0.03 s^{-1}, where the % conversion was 65%. The starting concentration of compound A was 0.600M.

(20 marks)

Question 2 **Answer all parts**

(a) A 25 m^3 reactor is fitted with an agitator of diameter 0.78 m in a vessel of diameter 1.8m. The agitator is used to agitate a reaction mixture of viscosity 1.25 Ns m^{-2} and density 1.3 x 10^3 kg m^{-3}. P_0 has been found to be = 0.88 for the agitator operating at 180 rpm.

(i) Calculate the mixing time (t_{95})

If the limiting reagent is added down the walls of the vessel

(ii) Determine whether product selectivity is determined by micromixing effects or reaction kinetics, using time constant calculations.

The reaction rate is 1.25 x 10^{-3} mol $^{-1}$ s^{-1} and the initial concentration of limiting reagent is to be 145 moles. **(50 marks)**

(b) **Cost Calculations**

(i) Predict the capital cost of implementing an extension to the waste management facility from 10 m^3 to 30 m^3 in size given that the cost of the original installation was set at €35,000.
Use n = 0.6.

(15 marks)

(iii) Given the CEI values below, predict the total cost of a solvent tank of 30 m^3 in size in year B, given that the cost in Year A is €17,356.
CEI Year A = 368 CEI Year B = 453 **(15 marks)**

(c) Describe the steps involved in conducting a Hazard and Operability (HAZOP) study. Use an example to illustrate how the "what if" risk assessment is implemented. **(20 marks)**

Question 3 **Answer all parts**

(a) "*There is an environmental impact of pharmaceutical production, with an emphasis on the waste generated per kilogram of active pharmaceutical ingredient (API)*"
What sustainable strategies can the industry adopt to reduce this waste and promote greener manufacturing practices?

(20 marks)

(b) As a member of a team reviewing the design of a chemical reactor for large-scale pharmaceutical production, you must ensure its efficiency, safety, and compliance with industry standards.

Discuss the critical considerations involved in evaluating the reactor's design. Identify potential obstacles that could arise during full-scale manufacturing and propose practical solutions to mitigate these challenges.

(30 marks)

(c) A six blade agitator of diameter 0.52 m is to be used to stir a reaction mixture of density 1449 kg m^{-3}, and viscosity 0.013 Ns m^{-2} in a 20 m^3 vessel of diameter 1.3 m.
The mixture to be stirred is refluxed in ethanol solvent and agitated at a rate of 150 r.p.m. Given that $P_0 = 0.88$, determine the following:

(i) Power

(ii) Reynolds Number

(iii) Is the fluid flow during the agitation process turbulent or not.

(30 marks)

(d) Compare batch processing and continuous processing in manufacturing, emphasising key differences in production methods and techniques. **(20 marks)**

SECTION B: [Dr. Eugene Hickey]
You are required to answer TWO complete questions

Question 4 (100 marks)

a) Which types of flowsheet (process, block, or P&ID) would:

(i) give a new employee an overview of the plant process?

(ii) trace down a fault in a control loop?

(iii) make a preliminary capital cost estimate to construct a plant?

(iv) indicate whether a controller is to be located in the control room or in the plant?

(v) indicate which pipe lines need insulation?

(vi) represent major pieces of equipment as rectangles rather than icons?

(vii) In what type of flowsheet would one expect to find pipe diameters and materials of construction?

(20 marks)

b) A train of two distillation columns is being used to separate a mixture of hexane, heptane and octane. The feed to the first column contains 40 mole% hexane, 30 mole% heptane and 30 mole% octane and enters at a rate of 2500 kmol/h. In the first column 98% of the octane fed is recovered in the bottom product. Essentially no hexane goes with the bottom product and the mole fraction of octane in the bottom is 99.5%. The overhead product flows to a second column. The overhead product from the second column contains 98 mole% hexane and no octane. In addition, 98% of the hexane fed to this column is recovered in the overhead.

(i) Draw a diagram of the process, labeling all of the streams.

(10 marks)

(ii) Calculate the molar flow rates and mole fractions for each stream in the process. (20 marks)

d) Sodium crystallises in a body-centered cubic form with a lattice parameter of a = 0.4287nm. Use this to calculate the ionic radius of sodium. (20 marks)

e) Explain how stacking of crystal planes in an order ABCABCABC… leads to the formation of the face centred cubic Bravais lattice. (10 marks)

f) Draw rough sketches of cubic unit cells showing the following planes:

(i)	(0 0 1)	(5 marks)
(ii)	(1 0 1)	(5 marks)
(iii)	(0 2 1)	(5 marks)
(iv)	(1 1 1)	(5 marks)

Question 5 **(100 marks)**

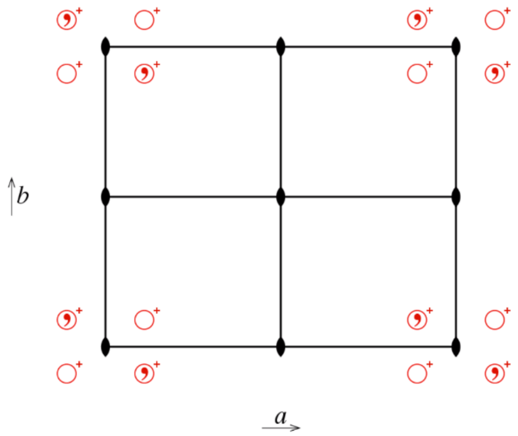
a) An oil stream enters a counter flow heat exchanger at a temperature of 75°C and leaves at 30°C. The cold water stream has an input temperature of 15°C and an output temperature of 50°C. The flow of the hot stream is 2.2kg/s. The heat capacity of the hot stream is 1160J/kg/°C, that of the cold stream is 4190J/kg/°C

(i) Show that the flow rate of the cold stream is 0.783kg/s (15 marks)

(ii) Show that the LMTD for this process is 19.57°C. (10 marks)

(iii) Calculate the UA value of the heat exchanger. (15 marks)

b) The diagram below shows the orthorhombic space group, Pmm2



(i) What does orthorhombic mean in terms of the length of the three sides, a, b, c, and the angles between them, α, ß, and γ? (10 marks)

(ii) Is this space group Primitive, Face Centred, Body Centred, or Base Centred? (5 marks)

(iii) What does m mean in the space group title? (10 marks)

(iv) Is there a centre of symmetry in the cell? Justify your answer. (10 marks)

(v) What is the multiplicity of the general position, (x, y, z), for the space group? (15 marks)

(vi) Locate a special position in the space group and give its multiplicity. (10 marks)

Question 6 **(100 marks)**

a) Draw Explain how a vle diagram can be constructed from a binary phase diagram (10 marks)

b) Use the vle diagram for butane and pentane below to answer the following questions:

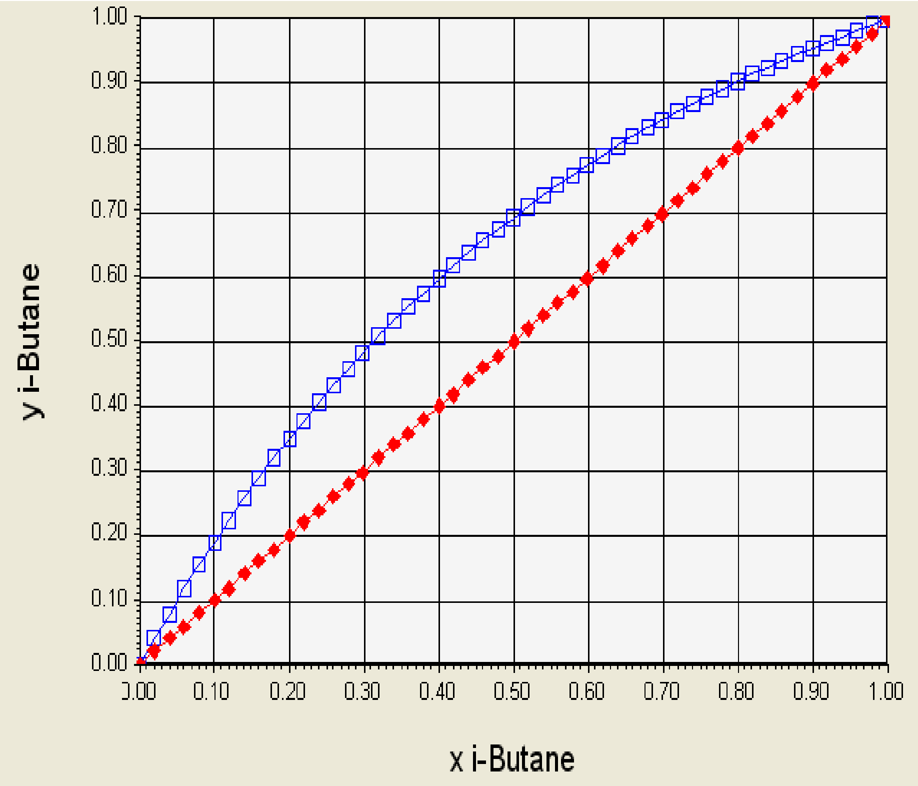
(i) What is the mole fraction in butane of the vapour phase when the mole fraction in butane of the liquid phase is 0.3? (10 marks)

(ii) What is the mole fraction in pentane of the liquid phase when the mole fraction in butane of the vapour phase is 0.75? (10 marks)

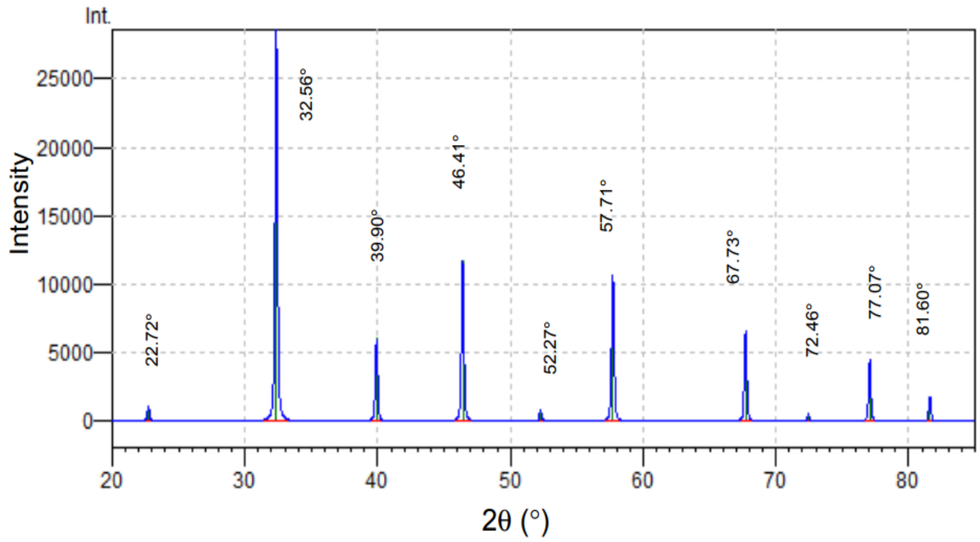
(iii) What is the mole fraction in pentane of the liquid phase when the mole fraction in pentane of the vapour phase is 0.45? (10 marks)

(iv) Calculate the relative volatility of butane in pentane when the liquid mole fraction of butane is 0.35 (10 marks)

(v) What would happen to this vle curve if the pressure was increased? (10 marks)



c) The diagram below shows a powder diffraction pattern using Cu K_{α} radiation from the cubic crystal, $SrTiO_3$. The 2θ position of all the peaks is also given (the first four are: 22.72°, 32.56°, 39.90°, and 46.41°).



(i) Find the inter-planar spacing, d, for the first four peaks (those with 2θ less than 50°) (10 marks)

(ii) Given that the lattice parameter for $SrTiO_3$, a, is 0.3905nm, calculate the value of $h^2 + k^2 + l^2$ for the first four peaks. (10 marks)

(iii) Suggest Miller Indices, (hkl), for the first four peaks. (10 marks)

(iv) Is $SrTiO_3$ primitive, BCC, or FCC? (10 marks)

LIST OF FORMULAE

$$t = \frac{-1}{k \ln(1 - x_A)}$$

$\tau_R = 1/kC_{A0}$

$\tau_R = 1 + a/kC_{A0}$ where $a = V_A / V_B$

$$Re = \frac{\rho v D}{\mu}$$

$$Re = \frac{\rho N D^2}{\mu}$$

$P = P_0 N^3 D_A^5 \rho$

$\varepsilon_{mean} = P / V\rho$

$Re_c = 6370 / P_0^{1/3}$

$P_0^{1/3}$ Re Fo = 5.2

$$Fo = \frac{\mu t_{95}}{\rho T^2}$$

The lifetime of an Eddy is τ_K:

$$\tau_K = 12[\upsilon / \varepsilon]^{1/2}$$

where $\upsilon = \mu / \rho$ (kinematic viscosity)

Engulfment Rate E = $\ln 2 / \tau_K$

$\tau_E = 1/E$

$$C_2 = C_2 \left(\frac{S_2}{S_1}\right)^n$$

C_2 = capital cost of project with capacity S_2
C_1 = capital cost of project with capacity S_1

$$D = \frac{C}{10 \, x \, V}$$

D = depreciation in €/kg
C = capital cost in €
V = production volume in kg/year
10 is the plant life

$Q_r = V(-\Delta H_r)k_0 C_A \exp(-E_A/RT)$

$Q_c = UA(T-T_a)$

$MTSR = T_p + \Delta T_{ad}$

$\Delta T_{ad} = \Delta H.n / m.C_p$

$TMR_{ad} = C_p RT^2 / q_0 E_A$

$$\text{Oxygen balance} = \frac{-[1600(2a + b/2 - c)]}{\text{Mol. Wgt.}}$$

$q = mc\Delta T$

$q = UA \; LMTD$

$$LMTD = \frac{\Delta T_L - \Delta T_R}{\log_e(\Delta T_L / \Delta T_R)}$$

Molar mass CO_2 = 44g/mol

Molar Mass Air = 29g/mol

$n\lambda = 2d \sin\theta$

$$d = \frac{a}{\sqrt{h^2 + k^2 + l^2}}$$

$$\frac{1}{d^2} = \frac{h^2}{a^2} + \frac{k^2}{b^2} + \frac{l^2}{c^2}$$

$\lambda_{Cu\,K_\alpha}$ = 0.154051nm

$$\alpha_{AB} = \frac{y_A / x_A}{y_B / x_B}$$

q = liquid fraction

$$slope = \frac{-q}{1-q}$$

q-line goes between (x_F, y_F) and (0,x_F/(1-q))

rectifying line between (x_D, y_D) and (0,x_D/(R+1))

F = D + B

F x_F = Dx_D + B