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CRN:

TECHNOLOGICAL UNIVERSITY DUBLIN
TALLAGHT CAMPUS

TU876

BSc in Pharmaceutical Science

Year 4

SEMESTER 2
EXAMINATIONS 2023/24

Manufacturing Technology and Unit Processes

Internal Examiner:
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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.

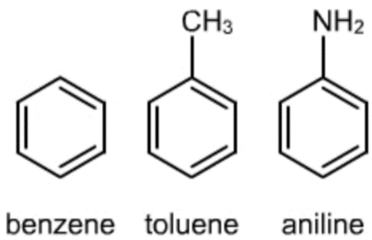
Section A **Answer any two questions**

Question 1 **Answer all parts** **(100 marks)**

(a) A 0.78 m diameter open straight-blade turbine is employed to agitate reaction mixtures within a 20 m^3 batch reactor equipped with baffles. The reactor has a diameter of 1.2 m, and the introduction of one reagent occurs at the outer walls of the vessel, distanced away from the agitator region.
Given that the agitator speed has been fixed at 120 r.p.m. determine the mixing time (t_{95}) in seconds.
$Po = 1.0$; $\rho = 1390\ kg/m^3$; $\mu = 0.012\ Ns/m^2$

(30 marks)

(b) (i) Explain the role of oxygen balance in ensuring safety within the pharmaceutical industry.
(ii) Assess the following compounds as reagents in a large scale production from a safety perspective? Explain why, using your knowledge of oxygen balance.



(30 marks)

(c) Imagine you are part of a team tasked with evaluating the design of a chemical reactor intended for full-scale production within a pharmaceutical manufacturing facility.
Outline the essential factors and procedures your team would employ when assessing the reactor design. Offer concrete instances of possible challenges that could emerge during full-scale production and suggest tactics for managing them.

(40 marks)

Question 2 **Answer all parts** **(100 marks)**

(a) Discuss the environmental implications of production, focusing on the waste generated per kilogram of active pharmaceutical ingredient (API). How can the pharmaceutical industry implement greener practices to mitigate this waste? **(30 marks)**

(b) A 20 m^3 batch reactor is equipped with a curved blade turbine agitator, having a diameter of 1.1 m, operating at 70 revolutions per minute. The reactor is utilised for the reaction of 4.58 moles of reactant A with reactant B at room temperature. The reaction mixture, which is homogeneous, possesses a density of 1856 kg m^{-3} and a viscosity of 1.3 Ns m^{-2}, along with a calculated rate constant of 4.12 s^{-1}. Reactant A is introduced in a controlled manner in the agitator region.

Utilising time constant calculations, determine whether product selectivity is influenced more by micro-mixing or reaction kinetics in this process. The specified value for power number for the turbine agitator (P_0) is 1.1. **(30 marks)**

(c) (i) Compare and contrast batch processing and continuous processing in manufacturing, highlighting significant variances in production techniques and approaches to ensuring product quality control. **(20 marks)**

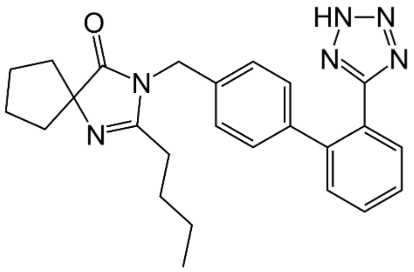
(ii) Explore the distinctions among online, inline, at-line, and offline testing methodologies in the context of quality control and process monitoring within industrial operations. **(20 marks)**

Question 3 **Answer all parts** **(100 marks)**

(a) Discuss the importance and practical applications of polymorphism within the pharmaceutical sector. Offer specific examples and address the manufacturing challenges linked with polymorphism.

(30 marks)

(b) Identify the potential structural modifications to the following structure that could be varied to potentially enhance drug potency and activity in the body.



(20 marks)

(c) A new plant is being designed for the production of the API Ibuprofen.

Given that the installation cost of a $10m^3$ reactor in year A has been calculated to be €150000, predict the cost in year B, given the following CEI cost index data

CEI (A) =463 and CEI (B) = 525 **(20 marks)**

(d) A second order condensation reaction(C_A =56 mol; $k=1.6 \times 10^{-4}\ s^{-1}$) is to be run in a 1500 L vessel of surface area $A=40\ m^2$ with a heat transfer coefficient of $U=3.4 \times 10^{-2}\ W/m^2/K$ at $T=80^0C$.

The following thermodynamic results were obtained from calorimetry experiments:

$\Delta H = -274\ J\ mol^{-1}$; $E_A = 1.54\ J\ mol^{-1}$. $R = 8.314\ J\ K^{-1}\ mol^{-1}$

(i) Determine whether the reaction below becomes self-heating or not when run on a large scale.

(ii) Decide whether steam needs to be continually fed through the jacket of the vessel to maintain reflux throughout the reaction.

(30 marks)

SECTION B: [Dr. Eugene Hickey]

You are required to answer TWO complete questions

Question 4 **(100 marks)**

a) A stream has a composition of 22.0% benzene, 32.9% toluene, 45.1% ethylene, all percentages by mass. The toluene flow rate of the stream is 76.8kg/hr. Calculate the benzene flow rate.

(20 marks)

b) In the chlorination of ethylene to produce DCE, the conversion of ethylene is 83%. If 63mol of DCE is produced from 100mol of ethylene supplied, calculate the selectivity and yield.

(20 marks)

c) CO_2 at a rate of 3.5kg/hr is added to an air stream. After mixing the stream has 0.23% v/v CO_2. Normal air has 0.03% CO2 by mol. Calculate the flow rate of the air stream in kg/hr. Take the average molar mass of air (both before and after mixing) to be 28.9g/mol.

(20 marks)

d) An FCC crystal has a unit cell volume of 11.585nm^3. What is the atomic radius in nm? (15 marks)

e) What is meant by the *Packing Fraction* of crystals? (15 marks)

f) Draw a rough sketch of a cubic unit cell showing the crystal plane given by (hkl) = (210). (10 marks)

Question 5 **(100 marks)**

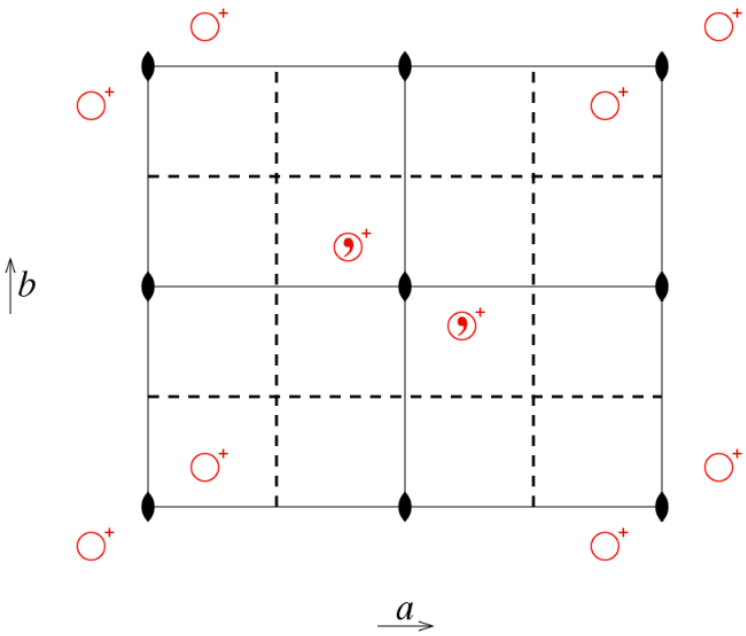
a) An oil stream enters a counter flow heat exchanger at a temperature of 91°C and leaves at 36°C. The cold stream has an input temperature of 21°C and an output temperature of 66°C. The flow of the hot stream is 3.0kg/s. The heat capacity of the hot stream is 1160J/kg/°C, that of the cold stream is 4190J/kg/°C

(i) Show that the flow rate of the cold stream is 1.02kg/s (15 marks)

(ii) Show that the LMTD for this process is 19.6°C. (10 marks)

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

b) The diagram below shows the orthorhombic space group, Pba2



(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 **ba2** mean in the space group title? (10 marks)

(iv) What is meant by the  in the diagram? (10 marks)

(v) What is the multiplicity of the general position, (x, y, z), for the space group? (10 marks)

(vi) What kind of symmetry is denoted by the  symbol in the diagram above? (10 marks)

(vii) What kind of symmetry is denoted by the - - - - symbol in the diagram above? (5 marks)

Question 6 **(100 marks)**

a) Draw a labelled diagram of a distillation column showing the following features:

(i) the location of the feed stream (6 marks)

(ii) the position of the reflux drum (6 marks)

(iii) the location of the reboiler (6 marks)

(iv) the location of the condenser (6 marks)

(v) indicate on the diagram the temperature profile up the column (8 marks)

(vi) indicate on the diagram the pressure profile (8 marks)

b) Three problems that may arise with inappropriately designed distillation columns are:

(i) flooding

(ii) weeping

(iii) entrainment

Explain what is meant by each of these terms and how each effects distillation column performance (20 marks)

c) CuKα radiation (λ = 0.154051nm) is incident on a powder crystal sample. It produces a first order diffraction peak at 2Θ = 40.7°. What is the corresponding interplanar spacing, d?

(15 marks)

d) A tetragonal lattice has lattice parameters of a = b = 2.44nm and c = 1.65nm. What is the interplanar spacing in nm of the (hkl) = (2 1 1) planes? (15 marks)

e) X-ray diffraction on a cubic crystal reveals peaks at (111), (200), (220), and (311). There are no peaks observed at (110) or (210). What type of Bravais lattice is this? (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

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

$Q_c = UA(T-T_a)$

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

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

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

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

$q = mc\Delta T$

$q = UA\ LMTD$

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

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

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

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