UNIVERSITI SAINS MALAYSIA

Second Semester Examination
2011/2012 Academic Session

June 2012

EKC 376 – Downstream Processing of Biochemical and Pharmaceutical Products
[Proses Hiliran untuk Produk Biokimia dan Farmaseutikal]

Duration : 3 hours
[Masa : 3 jam]

Please ensure that this examination paper contains FOUR printed pages and TWO printed pages of Appendix before you begin the examination.

[Sila pastikan bahawa kertas peperiksaan ini mengandungi EMPAT muka surat yang bercetak dan DUA muka surat Lampiran sebelum anda memulakan peperiksaan ini.]

Instructions: Answer **ALL** questions.

*[**Arahan:** Jawab **SEMUA** soalan.]*

In the event of any discrepancies, the English version shall be used.

[Sekiranya terdapat sebarang percanggahan pada soalan peperiksaan, versi Bahasa Inggeris hendaklah digunapakai].

Answer ALL questions.
Jawab SEMUA soalan.

1. [a] What are the fundamental properties of biological material relevant to bioseparation? Give three characteristics and suggest how each can be used to effect separation.

Apakah sifat-sifat asas bahan biologi yang berkaitan dengan bio-pemisahan? Berikan tiga ciri-ciri tersebut dan cadangkan bagaimana ia digunakan dalam mempengaruhi pemisahan.

[9 marks/markah]

[b] Chromatography is similar to adsorption because both involve the interaction between solute and solid matrix. State what is the major different between these two processes? For designing and operating a chromatograph, the yield and purity of the separated products are the two important parameters to be controlled. Explain their differences and express their formulation in integral forms.

Kromatografi serupa dengan penjerapan sebab kedua-duanya melibatkan interaksi antara bahan larut dengan matriks pepejal. Berikan perbezaan utama antara dua proses tersebut. Dalam merekabentuk dan mengendalikan kromatografi, hasil dan ketulenan produk adalah antara dua parameter yang penting yang perlu dikawal. Jelaskan perbezaan antara mereka dan ungkapkan formulasinya dalam bentuk kamiran

[16 marks/markah]

2. [a] With the aid of a diagram, explain the function of a rotary vacuum filter in the downstream processing. Compare the advantages and disadvantages of this filtration system.

Dengan bantuan gambarajah, terangkan fungsi penuras vakum putar dalam proses hiliran. Bandingkan kelebihan dan kelemahan sistem penurasan ini.

[10 marks/markah]

[b] It is desired to achieve complete recovery of bacterial cells from a fermentation broth with a pilot plant scale tubular centrifuge. It has been already determined that the cells are approximately spherical with a radius of 0.5 μm and a density of 1.10 g/cm^3. The speed of the centrifuge is 5000 rpm, the bowl diameter is 10 cm, the bowl length is 100 cm, and the outlet opening of the bowl has a diameter of 4 cm. Estimate the maximum flow rate of the fermentation broth that can be attained. After cell disruption, the cell diameter is reduced by one-third and the viscosity is increased by a factor of 4. Calculate the new feed flow, considering that the centrifuge operates at the same speed and efficiency. Assume that the cell suspension density and viscosity are close to those of water, i.e.: ρ_w = 1.00 g/cm^3, μ = 0.01 g/cm·s

Adalah dikehendaki untuk mencapai pemulihan penuh sel bakteria daripada kaldu penapaian dengan menggunakan pengempar tiub berskala loji pandu. Telah ditentukan bahawa sel adalah hampir sfera dengan jejari ialah 0.5 μm dan ketumpatan ialah 1.10 g/sm^3. Kelajuan pengempar ialah 5000 rpm, diameter mangkuk ialah 10 sm, panjang mangkuk ialah 100 sm, dan bukaan luar mangkuk berdiameter 4 sm. Anggarkan kadar aliran maksimum kaldu penapaian yang boleh dicapai. Selepas pemecahan sel, diameter sel telah berkurang sebanyak satu pertiga dan kelikatan bertambah dengan faktor 4. Kirakan aliran suapan yang baru, dengan mengambil kira bahawa pengempar beroperasi pada kelajuan dan kecekapan yang sama. Andaikan bahawa ketumpatan ampaian sel dan kelikatan adalah hampir dengan air, iaitu ρ_w = 1.00 g/sm^3, μ = 0.01 $g/sm \cdot s$.

[15 marks/markah]

3. [a] Based on the structure of the gram-positive bacteria, suggest three (3) disruption techniques that are suitable to disintegrate the cells. Justify your answer.

Berdasarkan struktur bakteria gram-positif, cadangkan tiga (3) teknik pemecahan yang sesuai untuk memecahkan sel. Wajarkan jawapan anda.

[6 marks/markah]

[b] An adsorption column with a diameter of 2.0 cm and a bed height of 5.8 cm was used to isolate trypsin. The concentration of trypsin in the feed was 0.190 mg/ml. The flow rate of the feed is 0.109 cm^3/s. The external void fraction in the bed was 0.35. The bulk density of the adsorbent (in its hydrated state in the bed) is 1.03 g/cm^3. The volumes at breakthrough and exhaustion point are 150 and 450 cm^3, respectively. Estimate the loading capacity of the adsorbent for trypsin.

Suatu turus penjerapan dengan diameter 2.0 sm dan ketinggian lapisan ialah 5.8 sm telah digunakan untuk memencilkan tripsin. Kepekatan tripsin di dalam suapan ialah 0.190 mg/ml. Kadar aliran suapan ialah 0.109 sm^3/s. Pecahan lompang luar di dalam lapisan ialah 0.35. Ketumpatan pukal penjerap (dalam keadaan terhidrat di dalam lapisan) ialah 1.03 g/sm^3. Isipadu pada titik bubus dan pengakhiran masing-masing ialah 150 dan 450 sm^3. Anggarkan kapasiti beban penjerap untuk tripsin.

[9 marks/markah]

[c] The data in Table Q.3.[c]. has been measured for the growth of crystals for an antibiotic. From this data set, obtain an expression for the relationship between dL/dt and the supersaturation $c - c^*$.

Data di dalam Jadual S.3.[c]. telah diukur untuk pertumbuhan kristal bagi antibiotik. Daripada set data ini, dapatkan ungkapan untuk hubungan antara dL/dt *dan penepuan lampau* c - c*.

Table Q.3.[c].
Jadual S.3.[c].

$c - c^*$ (g/liter)	dL/dt (μm/min)
0.20	0.21
0.35	0.45
0.67	0.90
1.25	1.80
2.05	3.30
2.75	5.00

[10 marks/markah]

4. [a] An antibiotic, cycloheximide, is to be extracted from the clarified fermentation beer by using methylene chloride as solvent. The distribution coefficient, K is 23. The initial concentration of cycloheximide in the feed is 150 mg/L. The solvent containing 5 mg/L of cycloheximide is being used with the flow rate of 1 m^3/h. The required recovery of the antibiotic is 98 percent. With equal solvent flow rate in three (3) stages, how much feed can be processed per hour for counter-current flow.

Suatu antibiotik, sikloheksimida, disari daripada penapaian arak yang dijernihkan dengan menggunakan metilena klorida sebagai pelarut. Pekali agihan, K adalah 23. Kepekatan asal sikloheksimida dalam suapan adalah 150 mg/L. Pelarut yang mengandungi 5 mg/L sikloheksimida dan kadar aliran 1 m^3/jam telah digunakan. Perolehan yang diperlukan adalan 98 peratus. Dengan kadar aliran pelarut yang sama pada ketiga-tiga (3) peringkat, berapakah kuantiti suapan yang boleh diproses per jam untuk aliran arus berlawanan.

[13 marks/markah]

[b] The solubility of a certain protein in water is 250 g/L. When 20 ml of ethanol was added to 100 ml of a 80 mg/ml protein solution in water, 40% of the protein was found to precipitate. If the dielectric constant of pure water and ethanol are 78.3 and 24.3, respectively, calculate the volume of ethanol needed to precipitate 95% of the protein in a 100 mL protein aqueous solution.

Kebolehlarutan suatu protein dalam air adalah 250 g/L. Apabila 20 ml etanol ditambah ke dalam 100 ml larutan protein berkepekatan 80 mg/ml dalam air, 40% daripada protein tersebut akan termendak. Sekiranya pemalar dielektrik air tulen dan etanol adalah 78.3 dan 24.3 masing-masing, kirakan isipadu etanol yang diperlukan untuk memendakkan 95% protein dalam 100 ml larutan akues protein.

[12 marks/markah]

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Appendix

$$\upsilon_g = \frac{\rho_p - \rho_f}{18\mu} D_p{}^2 g \qquad \upsilon_c = \frac{\rho_p - \rho_f}{18\mu} D_p{}^2 \omega^2 r$$

$$Q = \upsilon_g \left[\frac{2\pi l R^2 \omega^2}{g} \right] \qquad Q = \upsilon_g \left[\frac{2\pi n \omega^2}{3g} \left(R_0^3 - R_1^3 \right) \cot\theta \right]$$

$$Q = \upsilon_g \left[\frac{\pi l (R_0^2 - R_1^2)\omega^2}{g \ln(R_0 / R_1)} \right] \qquad g = 980 \text{ cm/s}^2$$

$$t_E = \frac{1}{\upsilon\varepsilon}(K + \varepsilon - K\varepsilon) \qquad \upsilon y_F t^* = L \rho_b q_{sat}$$

$$\theta = 1 - \left(\frac{t_E - t_B}{2t_B} \right) \qquad q = Ky \qquad q = Ky^n \qquad q = \frac{q_0 y}{K + y}$$

$$B = \frac{dN}{dt} = k_n (c - c^*)^n \qquad \frac{dM}{dt} = kA(c - c^*) \qquad G \equiv \frac{dL}{dt} = k_g (c - c^*)^n$$

$$C_{R,n+1} = \left(1 + \lambda + \lambda^2 + .. + \lambda^n\right) C_{R,1} = \left(\frac{\lambda^{n+1} - 1}{\lambda - 1} \right) C_{R,1}$$

$$\ln\left(\frac{S}{S_w} \right) = \frac{A}{RT} \left[\frac{1}{\varepsilon_w} - \frac{1}{\varepsilon} \right]$$

Common Engineering Conversion Factors

Length	Volume
1 ft = 12 in = 0.3048 m, 1 yard = 3 ft 1 mi = 5280 ft = 1609.344 m 1 nautical mile (nmi) = 6076 ft	1 ft^3 = 0.028317 m^3 = 7.481 gal , 1 bbl = 42 U.S. gal 1 U.S. gal = 231 in^3 = 3.7853 L = 4qt = 0.833 lmp.gal. 1 L = 0.001 m^3 = 0.035315 ft^3 = 0.2642 U.S. gal
Mass	**Density**
1 slug = 32.174 lb_m = 14.594 kg 1 lb_m = 0.4536 kg = 7000 grains	1 slug/ft^3 = 515.38 kg/m^3 , 1 g/cm^3 = 1000 kg/m^3 1 lb_m/ft^3 = 16.0185 kg/m^3 , 1 lb_m/in^3 = 27.68 g/cm^3
Acceleration & Area	**Velocity**
1 ft/s^2 = 0.3048 m/s^2 1 ft^2 = 0.092903 m^2	1 ft/s = 0.3048 m/s , 1 knot = 1 min/h = 1.6878 ft/s 1 min/h = 1.4666666 ft/s (fps) = 0.44704 m/s
Mass Flow & Mass Flux	**Volume Flow**
1 slug/s = 14.594 kg/s. 1 lb_m/s = 0.4536 kg/s 1 kg/m^2s = 0.2046 lb_m/ft^2s = 0.00636 slug/ft^2s	1 gal/min = 0.00228 ft^3/s = 0.06309 L/s 1 million gal/day = 1.5472 ft^3/s = 0.04381 m^3/s
Pressure	**Force and Surface Tension**
1 lb_f/ft^3 = 47.88 Pa, 1 torr = 1 mm Hg 1 psi = 144 psf, 1 bar = 10^5 Pa 1 atm = 2116.2 psf = 14696 psi = 101,325 Pa = 29.9 in Hg = 33.9 ft H_2O	1 lb_f = 4.448222 N = 16 oz, 1 dyne = 1 g cm/s^2 = 10^{-5}N 1 kg_f = 2.2046 lb_f = 9.80665 N 1 U.S. (short) ton = 2000 lb_f , 1 N = 0.2248 lb_f 1 N/m = 0.0685 lb_f/ft
Power	**Energy and Specific Energy**
1 hp = 550 (ft.lb_f)/s = 745.7 W 1 (ft.lb_f)/s = 1.3558 W 1 Watt = 3.4123 Btu/h = 0.00134 hp	1 ft lb_f = 1.35582 J, 1 hp·h = 2544.5 Btu 1 Btu = 252 cal = 1055.056 J = 778.17 ft lb_f 1 cal = 4.1855 J, 1 ft.lb_f/lb_m = 2.9890 J/kg
Specific Weight	**Heat Flux**
1 lb_f/ft^3 = 157.09 N/m^3	1 W/m^2 = 0.3171 Btu/(h ft^2)
Viscosity	**Kinematic Viscosity**
1 slug/(ft.s) = 47.88 kg/(m.s) = 478.8 poise (p) 1 p=1 g/(cm.s) 0.1 kg/(m.s) = 0.002088 slug/(ft s)	1 ft^2/h = 2.506 .10^{-5} m^2/s, 1 ft^2/s = 0.092903 m^2/s 1 stoke (st) = 1 cm^2/s = 0.0001 m^2/s = 0.001076 ft^2/s
Temperature Scale Readings	
^oF = (9/5)^oC + 32 ^oC = (5/9) (^oF – 32)	^oR = ^oF + 459.69 ^oK = ^oC + 273.16
Thermal Conductivity*	**Gas Constant***
1 cal/(s.cm.^oC) = 242 Btu/(h.ft.^oR) 1 Btu/(h.ft.^oR) = 1.7307 W/(m.K)	R = 82.057 atm.cm^3/(gmol.K) = 62.361 mm Hg.L/(gmol.K) = 1.134 atm.ft^3/(lbmol.K) = 0.083144 bar.L/(gmol.K) = 10.73 psi. ft^3/(lbmol. ^oR) = 555.0 mm Hg.ft^3/(lbmol. ^oR)

- Note that the intervals in absolute (Kelvin) and ^oC are equal. Also, 1 ^oR = 1 ^oF.

Latent heat: 1 J/kg = 4.2995×10^{-4} Btu/lb_m = 10.76 lb_f.ft/slug = 0.3345 lb_f.ft/lb_m , 1 Btu/lb_m = 2325.9 J/kg

Heat transfer coefficient: 1 Btu/(h.ft^2.^oF) = 5.6782 W/(m^2.^oC).

Heat generation rate: 1 W/m^3 = 0.09665 Btu/(h ft^3)

Heat transfer per unit length: 1 W/m = 1.0403 Btu/(h ft)

Mass transfer coefficient: 1 m/s = 11.811 ft/h, 1 lb_{mol}/(h.ft^2) = 0.013562 kgmol/(s.m^2)