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UNIVERSITI SAINS MALAYSIA

Second Semester Examination  
Academic Session 2008/2009

April/May 2009

**EKC 574 – Downstream Processing of Biochemical and  
Pharmaceutical Products**

Duration : 3 hours

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Please ensure that this examination paper contains THREE printed pages before you begin the examination.

**Instruction:** Answer **FOUR (4)** questions. Answer **ALL** questions.

Answer ALL questions.

1. Outline the integrated bioseparation scheme for streptomycin.

[i] Justify the bioseparation scheme chosen.

[10 marks]

[ii] Draw the flow chart of your bioseparation scheme.

[10 marks]

[iii] Explain the principles, advantages and disadvantages for only two of the unit separations involved in the bioseparation scheme.

[20 marks]

2. [a] How do Good Practices regulations correlate to the life of a drug, starting from basic research through the manufacturing stage? Explain.

[12 marks]

[b] Fumarase is recovered from solution by precipitation at 6°C by the addition of ammonium sulphate.

Preliminary experiments show that at an ionic strength of  $5.5 \text{ mol L}^{-1}$ , we find a soluble enzyme concentration of  $20 \text{ units mL}^{-1}$  and at an ionic strength of  $6.5 \text{ mol L}^{-1}$  a soluble enzyme concentration of  $5 \text{ units mL}^{-1}$ . Estimate the soluble enzyme concentration at an ionic strength of  $7.5 \text{ mol L}^{-1}$ .

[8 marks]

3. [a] Describe what is meant by aqueous two-phase extraction?

[5 marks]

[b] Leucine dehydrogenase is recovered from a homogenate of disrupted *Bacillus cereus* cells using an aqueous two-phase polyethylene glycol-salt system. 150 liters of homogenate initially containing  $3.2 \text{ units enzyme mL}^{-1}$  are processed. A polyethylene glycol-salt mixture is added and two phases form. The enzyme partition coefficient is 3.5.

[i] What volume ratio of upper and lower phases must be chosen to achieve 80% recovery of enzyme in a single extraction step?

[ii] If the volume of the lower phase is 100 L, what is the concentration factor for 80% recovery?

[10 marks]

[c] Explain the differences between crystallization and precipitation.

[5 marks]

...3/-

4. [a] Arrange the following cells in the order of ease at which they can be broken up (most difficult one first) and explain why this is so:

- [i] plant cells
- [ii] bacteria
- [iii] animal cells
- [iv] yeasts
- [v] filamentous moulds

[5 marks]

- [b] Which chromatographic method would you choose to separate:

- [i] a sugar and penicillic acid
- [ii] a large and a small protein
- [iii] two antibodies

[3 marks]

- [c] A 30 ml sample of broth from a penicillin fermentation is filtered in the laboratory on a 3 cm<sup>2</sup> filter at a pressure drop of 5 psi. The filtration time is 4.5 min. Previous studies have shown that filter cake of *Penicillium chrysogenum* is significantly compressible with  $s = 0.5$ . If 500 litres broth from a pilot-scale fermenter must be filtered in 1 hour, what size filter is required if the pressure drop is :

- [i] 10 psi

[6 marks]

- [ii] 5 psi

[6 marks]

Information:

$$\frac{At}{V} = \frac{\mu\alpha\rho_0}{2\Delta P} \left( \frac{V}{A} \right) + \frac{\mu R_M}{\Delta P}$$

$$\frac{At}{V} = K \left( \frac{V}{A} \right) + B$$

$$K = \frac{\mu\alpha\rho_0}{2\Delta P}$$

$$B = \frac{\mu R_M}{\Delta P}$$

$$\alpha = \alpha'(\Delta P)^s$$