CHAPTER 3

STUDIES ON EXTRACTION KINETICS
3.1 Introduction

In order to exploit the principle of reactive-extraction as such, and in liquid membrane in particular, and for simulation and design of extractors for practical applications knowledge on the extraction kinetics is very important. Furthermore, a detail kinetic analysis provides a better insight of the extraction mechanism based on which appropriate mathematical model for the extraction kinetics may be suggested. Results presented in the previous chapter on extraction equilibria using various carrier-solvent systems, it becomes apparent that Aliquat-336-n-butyl acetate is the preferred choice of system in terms of extraction efficiency and re-extraction potential for the beta-lactams under study. Accordingly, this particular carrier-solvent system has been considered for kinetic study further keeping in view that literature report on such a study is very scanty except that for amine extraction of penicillin-G (Reschke and Schugerl, 1984; Lee and Wang, 1995). The results on part or full of the kinetic study presented in this chapter have already resulted in two publications in journals of repute (Bora et al., 1997; Bora et al., 1999).

3.2. Theoretical aspects and kinetic models

3.2.1 Qualitative considerations

The kinetics of solvent extraction of reactive solutes is complex, involving mass transfer with chemical reaction in a heterogeneous system. In case of beta-lactam antibiotics of amphoteric nature, the dissociated anion is amenable for reactive extraction with either amines or Aliquat-336. However, physical extraction may also take place to a considerably lower extent.

Thus, both the rates of mass transfer and chemical reaction or any of them may control the overall extraction rate. The mass transfer involves the transport of solute from the aqueous phase to the organic phase through the aqueous-organic interface. This
comprises transport of solute (i) from the bulk of the aqueous phase to the interface and (ii) from the interface to the bulk of the organic phase. The interface being a three dimensional stationary layer causes an interfacial resistance to the transport of solute from one phase to the other. At the same time, when the solute molecules pass through the interface, a kind of movement called interfacial turbulence, the so-called "Maragoni effect" in practical system occurs and promotes the passage of solute molecules (Lewis and Pratt, 1953). The diffusion through the interface is affected by such factors as the viscosity, diffusion coefficient, concentration, surface tension and is especially affected by the differences in certain properties of the two phases, such the size of the solute and solvent molecules, the area of the interface and the adsorption of surfactants. (Sferling and Scriven, 1959). Thus the interfacial resistance which may be quantitatively described by the well-known theory of mass transfer fully documented in literature (Danckwert, 1970). Such description relies on hydrodynamic effect such as the intensity of the two phase agitation.

The reactive extraction of dissociated beta-lactam anions may be mechanistically represented as shown in Figure 3.1, which is indicative of a reaction-diffusion (and mass transfer) phenomenon. Accordingly, the theory of interphase mass transfer as well as of chemical reaction should be considered to provide an appropriate mathematical model for the extraction rate based on whether mass transfer or chemical reaction controls the overall rate. If the extraction rate is diffusion controlled, it will depend on the interfacial contact area of the two phases and the concentration of the slow diffusing species. When the extraction rate is chemically controlled, it is important to ascertain the location of the rate controlling chemical reaction or reactions, that is, within the bulk phase or at the interface or in a thin zone adjacent to the interface. For a bulk phase rate controlling chemical reaction, the important parameters will be solubility of reactants, their distribution coefficients (which will vary with choice of the diluent and ionic strength of the aqueous phase), ionisation constants if appropriate, and phase volume. For an interfacial chemical reaction under diffusion controlled kinetics, the composition of the interface will correspond to the concentration of species as given by the equilibrium expression for the interfacial reaction. When the interfacial chemical reaction is rate controlling, the important parameters are interfacial area, interfacial activity of reacting
Figure 3.1: Extraction mechanism of beta-lactams with (a) Amines and (b) Aliquat-336.
species, and molecular geometry with respect to preferential molecular orientation at the interface. Under such rate controlling conditions the composition of the interface will be that of reactants only and interfacial physical chemical measurements would assist data interpretation. For instance, interfacial tension measurement may provide useful but not sufficient information for elucidation of the rate controlling step in a given system. Accordingly, fundamental kinetic studies are necessary using three common methods which will be discussed in the experimental section (section 3.3) to follow.

The extraction rates with reaction may be controlled by the kinetics or by diffusion, in five possible regions as shown in Figure 3.2. The two bulk phases can be regarded as well-mixed, so diffusion is unimportant. However, if a very slow chemical reaction occurs in either of bulk phases, it can control the overall extraction rate. On each side of the interface there is a mass transfer boundary layer which may be typically 10 to 100 \( \mu \text{m} \) in thickness. These boundary layers provide the diffusional resistances as expressed by the mass transfer coefficients. However, if a chemical reaction in either phase is fast enough it can occur within the boundary layer in combination with diffusion, resulting in an "enhanced" mass transfer (Danckwert, 1970).

In case of reactive-extraction, species are offered adsorbed at the interface and the kinetics are affected. Thus, the interface should be treated as a zone with a small but finite thickness generally less than 0.01 \( \mu \text{m} \) corresponding to several molecular diameters. Phenomena at the interface can affect not only reaction kinetics and hydrodynamics, but even the measured equilibrium distribution of surface extractant. Thus, the reactive extraction kinetic is generally complex and the kinetic model should incorporate all these factors and must be verified from experimental data, which actually provide a basis for selection or formulation of the kinetic model. However, two common kinetic models i.e. simple mass transfer model and models with interfacial adsorption are reported to have been used for analysing the reactive extraction kinetics of penicillin and other biomolecules (Reschke and Schugerl, 1984 ; Lee and Wang, 1995 ; Matsumoto et al., 1996 ; Juang and Huang, 1995 ; Chan and Wang, 1993 ; Schlichting et al., 1987). A general description of these models is given in the next two section.
BULK ORGANIC PHASE  

↑  

ORGANIC PHASE BOUNDARY  
LAYER  
10 to  
100 µm  
↓  

INTERFACE  
< 0.01 µm  
↓  

AQUEOUS PHASE BOUNDARY  
LAYER  
10 to  
100 µM  
↓  

BULK AQUEOUS PHASE  

(Slow reaction)  

(Diffusion, fast reaction)  

(Interfacial reaction)  

(Diffusion, fast reaction)  

(Slow reaction)  

Figure 3.2: Extraction with chemical reaction: rate controlling zones.
3.2.2 Two-film mass transfer model

The major reaction process concerned with extraction of anionic form of the beta-lactam by amines and Aliquat-336 of high molecular weight may be considered to be interfacial in nature, because the amines have very low solubility in the aqueous phase. The reactive with Aliquat-336 being an ion-exchange type may also be assumed to be very rapid and the rate of extraction is likely to be controlled by diffusion of the reactant.

The two-film model of interphase mass transfer (Danckwert, 1970) is used to describe the mass transfer across the liquid interface as shown in Figure 3.3. The assumption made are (1) the reaction plane is located at the interface, (2) the complex formation is an instantaneous reaction and (3) no chloride gradient exists in the aqueous phase.

The concentration of each species near the interface is obtained in its vicinity such that the interfacial reaction rate is equal to the mass transfer rate. It is apparent that the species H\(^{+}\), HP, P\(^{-}\) and Cl\(^{-}\) reside exclusively in the bulk aqueous phase while QCl and QP reside in the organic phase. Therefore, no subscript has been used (except when noted) for the phases on any of these terms as such as well as on concentration and mass transfer parameters involved in the kinetic and related equation of this chapter. Furthermore, charges of the ions will be omitted from the terms for the sake of simplicity. For the mass flux (mol/cm\(^2\) sec) in the aqueous phase at the interface, the following balance of the beta-lactam holds true

\[
J_P = k_P (C_P - C_{P,ln}) \quad (3.1)
\]

In the organic phase at the interface, the balance for the carrier (Aliquat-336, termed as QCl) is

\[
J_{QCl} = k_{QCl} (C_{QCl} - C_{QCl,ln}) \quad (3.2)
\]

and for the solute carrier-complex

\[
J_{QP} = k_{QP} (C_{QP} - C_{QP,ln}) \quad (3.3)
\]

The flux equation can be coupled by the mass action equilibrium constant given by
Figure 3.3: Concentration profile at the interface of aqueous organic phase for the extraction of beta-lactam antibiotics by Aliquat-336.
\[ K_P = \frac{C_{QP_{2, in}}}{C_{QCl, in} C_{P_{, in}}} \] (3.4)

Under steady-state conditions
\[ J_P = J_{QCl} = J_{QP} \] (3.5)

Elimination of the interfacial concentration yield the following equation for the aqueous phase
\[ -J_P = \frac{V_s dC_P}{S \, dt} = K_P (C_P + 0.5 B \pm \sqrt{0.25B^2 - R}) \] (3.6)

where,
\[ B = \frac{k_{QCl} k_{QP}^2 K_P C_{QCl} + 2 k_P^2 k_{QCl} C_P}{k_P k_{QP}^2 K_P - k_P^2 k_{QCl}} + \frac{2 k_P k_{QCl} k_{QP} C_{QP} - k_P k_{QP}^2 K_P C_P}{k_P k_{QP}^2 K_P - K_P^2 K_{QCl}} \]

and
\[ R = \frac{-k_{QCl} (k_{QP} C_{QP} + k_P C_P)^2}{k_P k_{QP}^2 K_P - k_P^2 k_{QCl}} \]

Numerical integration of equation can be performed to obtain concentration versus time profiles for comparison of experimental and theoretical data at various solutes and carrier concentration. The mass transfer coefficients, particularly \( k_P \) and \( k_{QCl} \) can be identified by fitting the calculated concentration versus time profile to the measures ones. The value of \( k_{QP} \) can be estimated from
\[ k_{QP} = k_{QCl} \frac{D_{QP}}{D_{QCl}} \] (3.7)

Where, \( D_{QCl} \) and \( D_{QP} \) are the diffusivities of the carrier and solute-carrier complexes, respectively. Their values can be estimated from the well-known Wilke-Chang (1955) correlation given by
\[ D = 7.4 \times 10^{-8} \left[ (\phi M_2)^{1/2} T / \mu_2 V_1^{0.6} \right] \] (3.8)

where, \( M_2, T, V_1, \phi \) and \( \mu_2 \) are the molecular weight of solvent, temperature in °K, molar volume of solute (\( \text{cm}^3/\text{g. mole} \)) at its normal boiling point, “association” parameter of the solvent and viscosity of solvent or solution (centipose), respectively.
Apriori estimation $k_P$ and $k_{QC1}$ are possible from the experimentally determined plots of initial extraction and concentrations of carrier and the solute under properly selected condition in a stirred transfer cell of constant interfacial area. In general, linearly of the aforesaid plot under certain concentration ranges is indicative of the mass transfer control process and the value of $k_P$ and $k_{QC1}$ may be approximated from the following correlation

$$J_P = k_P C_P$$

(3.9)

and

$$J_P = k_{QC1} C_{QC1}$$

(3.10)

The values of $k_P$ and $k_{QC1}$ are apparently dependent on the system properties which determine the hydrodynamic conditions too.

### 3.2.3 Model with diffusion and interfacial reaction

Under certain experimental conditions, the extraction rate depends on the concentration of the solute in the aqueous phase which directly reacts with the carrier. This concentration is strongly affected by the concentration of other ionic species and the interfacial reaction process can be elucidated if the reaction condition is properly selected so that the reaction rate process plays a significant role in the overall extraction rate. In this case, the use of a stirred transfer cell with a constant interfacial area provides information on a release slow reaction process, because the effect of hydrodynamics is well understood.

### Model derivation

It is necessary to consider the following dissociation equilibrium of the zwitterionic beta-lactams which can exist in three forms of different charges ($P^+$, $P^-$, $P^0$) depending on the pH of the medium.

$$
P^+ \rightleftharpoons K_{dl} P + H^+ \quad \text{with} \quad K_{dl} = \frac{C_P}{C_P^0} \cdot \frac{C_{H^+}}{C_{P^+}}$$

(3.11)
At 25°C, $K_{d1} = 9.5 \times 10^{-3}$ and $K_{d2} = 3.8 \times 10^{-2}$. Total concentration of the beta-lactam in the aqueous solution can be represented as

$$C_{HP} = C_P^+ + C_P^- + C_{P^2}^- \quad (3.13)$$

$$= C_{P^-} \left( \frac{C_H^{+2}}{K_{d1}} + \frac{C_H^+}{K_{d2}} + 1 \right)$$

$$= \gamma_{-1} C_P^- \quad (3.14)$$

where,

$$\gamma_{-1} = \frac{C_H^{+2}}{K_{d1}} + \frac{C_H^+}{K_{d2}} + 1 \quad (3.15)$$

By using equation (3.13), the concentration of anionic form i.e. $C_P^-$ can be estimated from the values of $C_{HP}$ and pH.

Assuming that the interfacial chemical reaction controls the extraction rate, the following steps may be considered for the extraction process as a whole.

1. Reactants, $P^-$ and $QC1$ diffuse from the bulk aqueous and organic phases, respectively to the interface.
2. $QC1$ adsorbs at the interface according to Langmuir model.
3. $QC1$ reacts with $P^-$ at the interface to form $QP$ and $CI^-.$
4. $QP$ desorbs from the interface.
5. Products $CI^-$ and $QP$ diffuse back to the bulk phases.

Steps 1 and 5 are diffusion processes and steps 2 and 4 are interfacial reaction processes. To establish the model, the following interfacial reaction mechanisms are proposed.

Adsorption of $QC1$

$$QC1 \quad + \quad \overset{k_1}{\rightleftharpoons} \quad QC1^- \quad (3.16)$$

$$\gamma_1 = \frac{k_1}{k_{-1}} C_{QC1in} - k_{-1} \theta_{QC1} \quad (3.17)$$

$$K_1 = \frac{k_1}{k_{-1}}$$
Interfacial reaction between P^- and QC1^\ominus

\[ P^- + QC1^\ominus \xrightleftharpoons[k_2]{k_{-2}} QP^\oplus + Cl^- \] (3.20)

\[ r_2 = k_2 C_{P \text{ in}} \theta_{QC1} - k_{-2} C_{Cl \text{ in}} \theta_{QP} \] (3.19)

\[ K_2 = k_2 / k_{-2} \]

Desorption of QP^\oplus

\[ QP^\oplus \xrightleftharpoons[k_{-3}]{k_3} QP + \oplus \] (3.20)

\[ r_3 = k_{-3} \theta_{QP} - k_3 \theta_0 C_{QP \text{ in}} \] (3.21)

\[ K_3 = k_3 / k_{-3} \] (3.22)

The reaction of equation (3.19) is the rate determining step. Assuming a Langmuir type adsorption isotherm to express the adsorption and desorption steps, the interfacial reaction rate, \( r \) of P^- can be expressed as

\[ r = \frac{k_2 K_1}{K_P} X \frac{(K_P C_{P \text{ in}} C_{QC1 \text{ in}} - C_{Cl \text{ in}} C_{QP \text{ in}})}{(1 + K_1 C_{QC1 \text{ in}} + K_3 C_{QP \text{ in}})} \] (3.23)

where,

\[ K_P = \frac{K_1 K_2}{K_3} = \text{equilibrium constant of the extractive reaction} \]

\[ \theta_0 + \theta_{QC1} + \theta_{QP} = 1 \] (3.25)

The extraction process considers both diffusion and interfacial reaction steps. Assuming pseudo-steady state, the flux of extraction may be determined by

\[ J = -\frac{V_{aq}}{S} \frac{dC_{HP}}{dt} \] (3.25)

\[ = J_{aq} = r = J_{org} = \frac{V_{org}}{S} \frac{dC_{QP}}{dt} \] (3.26)

where,

\[ J_{aq} = k_l (C_{P^-} - C_{P^- \text{ in}}) \]
\[ k_{L} = \frac{(C_{HP} - C_{HP_{in}})}{\gamma - 1} \] (3.27)

\[ J_{org} = k_{org} (C_{QP_{in}} - C_{QP}) \]
\[ = k_{org} (C_{QCl} - C_{QCl_{in}}) \]
\[ = k_{Cl} (C_{Cl_{in}} - C_{Cl}) \] (3.28)

The following mass balance holds

\[ V_{aq} (C_{HP_{i}} - C_{HP}) = V_{aq} (C_{QP_{org}} - C_{QP_{i}}) \] (3.29)
\[ C_{QCl_{i}} + C_{QP_{i}} = C_{QCl} + C_{QP} \] (3.30)
\[ V_{aq} (C_{Cl} - C_{Cl_{i}}) = V_{org} (C_{QCl_{i}} - C_{QCl}) \] (3.31)

Combining equation 3.23 to 3.28 and eliminating the concentration of species at the interface with the help of the above mass balance equations, the overall flux, \( J \) is obtained as follows

\[ J = \frac{-b + \sqrt{b^2 - 4ac}}{2a} \] (3.32)

Where,

\[ a = \frac{K_3 - K_1}{k_{org}} + \frac{k_2 K_1}{k_{org} k_{Cl} K_{P}} - \frac{k_2 K_1}{k_{org} k_{L}} \] (3.33)

\[ b = 1 + \frac{k_2 K_1}{\gamma - 1 k_{org}} C_{HP} + \frac{k_2 K_1}{k_{org} K_{P}} C_{Cl} + K_1 (1 + \frac{k_2}{k_1}) C_{QCl} + (K_3 + \frac{k_2 K_1}{k_{Cl} K_{P}}) C_{QP} \] (3.34)

\[ c = \frac{k_2 K_1}{K_{P}} \left( C_{Cl} - C_{QP} - \frac{k_2 K_1}{\gamma - 1} C_{HP} C_{QCl} \right) \] (3.35)

\[ C_{Cl} = C_{Cl_{i}} + C_{HP_{i}} - C_{HP} \] (3.36)

\[ C_{QCl} = C_{QCl_{i}} + \frac{V_{aq}}{V_{org}} (C_{HP_{i}} - C_{HP}) \] (3.37)
Substituting equation 3.32 into equation 3.26 and integrating numerically, the relation between the total concentration of beta-lactam, $C_{HP}$, and time is then obtained. The initial extraction flux, $J_i$, can also be determined from equation 3.32 as follows

$$J_i = \frac{-b_i + \sqrt{b_i^2 - 4a_i c_i}}{2a_i} \quad (3.39)$$

Where,

$$a_i = \frac{K_3 - K_1}{K_{org}} + \frac{k_2 K_1}{K_{org} K_{Cl} K_L} - \frac{k_2 K_1}{K_{org} K_L} \quad (3.40)$$

$$b_i = 1 + \frac{k_2 K_1}{K_{org}} C_{HP,i} + \frac{k_2 K_1}{K_{org} K_p} C_{Cl}^{-i} + K_1 (1 + \frac{k_2}{k_1}) C_{QCl,i} + (K_3 + \frac{k_2 K_1}{K_{Cl} K_p}) C_{QP,i} \quad (3.41)$$

$$c_i = \frac{k_2 K_1}{K_p} (C_{Cl}^{-i} C_{QP,i} - C_{HP,i} C_{QCl,i}) \quad (3.42)$$

For $C_{QP,i} = C_{Cl,i} = 0$, $J_i$ may be expressed as

$$J_i = \left[\frac{1}{K_3 - K_1 + \frac{k_2 K_1}{k_2 K_1 - \frac{k_2 K_1}{K_{org} K_p K_L}}}ight] \times \left[\frac{k_2 K_1}{\gamma - 1 K_{org}} \left\{1 + \frac{C_{HP,i}}{C_{Cl,i}}\right\} + \left[\frac{K_1 \left(1 + \frac{k_2}{k_1}\right) C_{QCl,i}}{K_3 - K_1 + \frac{k_2 K_1}{k_2 K_1} - \frac{k_2 K_1}{K_{org} K_p K_L}}\right] ^2 + \frac{k_2 K_1}{k_2 K_1} \left[\frac{K_1 \left(1 + \frac{k_2}{k_1}\right) C_{QCl,i}}{K_3 - K_1 + \frac{k_2 K_1}{k_2 K_1} - \frac{k_2 K_1}{K_{org} K_p K_L}}\right] ^2 + \frac{k_2}{k_2 K_1} \left[\frac{K_1 \left(1 + \frac{k_2}{k_1}\right) C_{QCl,i}}{K_3 - K_1 + \frac{k_2 K_1}{k_2 K_1} - \frac{k_2 K_1}{K_{org} K_p K_L}}\right] ^2 + \frac{k_2}{k_2 K_1} \left[\frac{K_1 \left(1 + \frac{k_2}{k_1}\right) C_{QCl,i}}{K_3 - K_1 + \frac{k_2 K_1}{k_2 K_1} - \frac{k_2 K_1}{K_{org} K_p K_L}}\right] ^2\right] (3.43)$$
Equation 3.43 represents the initial extraction flux which incorporates the mass transfer in both aqueous and organic phase and the interfacial reaction. In practical situation, any of these three mechanisms would actually be the controlling mechanism and equation for \( J_0 \) can be simplified for the three limiting cases as follows.

**Aqueous phase film diffusion controlled**: In this case, the organic phase mass transfer constant \( (k_{\text{org}}) \) and interfacial reaction rate constants \( (k_2) \) are very large. Therefore, equation 3.32 can be simplified for extraction flux under this condition

\[
J = \frac{K_P}{k_L} \left( \frac{C_{QP} - K_P C_{QCI}}{k_{CI}} \right) \quad \text{(3.44)}
\]

The initial flux is accordingly given by

\[
J_i = \frac{K_P}{k_L} \left( \frac{C_{HP,i} C_{QCI,i} - C_{QP,i} C_{Cl,i}}{\gamma - 1} \right) \quad \text{(3.45)}
\]

For \( C_{QP,i} = C_{Cl,i} \), \( i = 0 \)

\[
J_i = \frac{k_L}{\gamma - 1} C_{HP,i} \quad \text{(3.45)}
\]

**Organic phase film diffusion controlled**: In this case \( k_L, k_{CI} \) and \( k_2 \) are very large and equation 2.32 simplified to the following form

\[
J = k_{\text{org}} \left[ C_{QCl} - \frac{K_P}{C_{CI} + \frac{C_{HP}}{\gamma - 1}} \right] \quad \text{(3.46)}
\]
The initial flux is

\[ J_i = k_{org} \left[ C_{QCl,i} - \frac{C_{Cl,i} (C_{QCl,i} + C_{QP,i})}{K_p C_{Cl,i} + \frac{K_p}{\gamma-1} C_{HP,i}} \right] \]

For \( C_{QP,i} = C_{Cl,i} = 0 \)

\[ J_i = k_{org} C_{QCl,i} \] \hspace{1cm} (3.47)

**Interfacial reaction controlled**: In this case \( k_L, k_{Cl} \) and \( k_{org} \) are very large and equation 3.32 can be simplified to

\[ J = \frac{K_p}{K_p} \left( \frac{K_p}{1 + K_1 C_{QCl,i} + K_3 C_{QP,i}} \right) \]

The initial flux becomes

\[ J_i = \frac{k_2 K_1}{K_p} \left( \frac{C_{HP,i} C_{QCl,i} - C_{Cl,i} C_{QP,i}}{\gamma-1} \right) \]

For \( C_{QP,i} = C_{Cl,i} = 0 \)

\[ J_i = \frac{k_2 K_1}{K_p} \left( \frac{C_{HP,i} C_{QCl,i}}{1 + K_1 C_{QCl,i}} \right) \] \hspace{1cm} (3.49)

Equation 3.49 is of the Langmuir isotherm form and non-linear in nature and from the plots of experimental data on \( J_i \) versus \( C_{QCl,i} \) and \( C_{HP,i} \), the applicability of the model can be assessed. Equation 3.49 can be rearranged to the following linear form.

\[ \frac{1}{J_i} = \left( \frac{\gamma-1}{K_1 k_2} \right) \frac{1}{C_{HP,i} C_{QCl,i}} + \frac{\gamma-1}{k_2 C_{HP,i}} \] \hspace{1cm} (3.50)
and plotting $1/J_i$ vs $1/ C_{QCl,i}$, the constants $K_1$ and $k_2$ can be obtained from the slope and intercept. $K_3$ can be obtained by curve fitting equation 3.48 with known $K_p$ value and $K_2$ can be consequently calculated from $K_p = K_1 K_2 / K_3$.

3.3 Experimental study

3.3.1 Chemical / reagents and analytical procedure

The chemicals and reagents as well as the analytical procedure used are the same as described in sections 2.3.1 to 2.3.4 (43 to 46)

3.3.2 Kinetic experiments and data reduction

3.3.2.1 Methods available for kinetic experiments

Generally three methods are available for study of fundamental kinetics i.e. (1) single drop technique, (2) stirred contactors and (3) Lewis type stirred cell.

In the single drop technique, drops of known size and hence interfacial area pass through the continuous phase in a vertical column length. Figure 3.4 shown the schematic of a typical droplet contactor. Mass transfer and diffusion are strongly enhanced when there is internal circulation within the drop: however, this is unlikely to be present in several extraction systems of commercial interest. Mass transfer takes place between droplet “swarm” and the surrounding continuous phase, with droplet coalescence and breakdown taking place. There are three different stages during which mass transfer takes place (1) during formation at a nozzle, (2) during free rise or fall and (3) during coalescence at the interface. Methods have been devised to determine the relative magnitude of the three stages. This technique permits enhancement of the diffusional rates of the reactants so that the reaction process play a significant role in the overall extraction rate. This technique however, has significant difficulties arising from the complicated hydrodynamics of drop motion. The kinetic data may involve
Figure 3.4: “Single-file” droplet contactor.

A = mariotte constant head device; B = burette; 
C = capillary tip; D = teflon needle valve; 
E = 5-7 cm diameter glass column; F = interface; 
T = teflon needle valve.
some uncertainties because of the difficulty of separating the effect of hydrodynamics (Inoue et al., 1979).

In stirred contactors, complete dispersion of phases is generally achieved. Actually a variety of model contactors can be used to study the extraction kinetics and the controlling mechanism. A typical stirred contactor is shown in Figure 3.5 and it represents a standard, fully baffled, mechanically agitated contactor provided with a four or six-bladed turbine impeller. This is most suited to determine whether diffusional factors are important in the extraction kinetics. However, this technique suffers from the drawback that the interfacial area cannot be measured. This is disadvantageous when interfacial rate-controlling processes are studied, particularly since the interfacial area is likely to vary with the level of extraction due to interfacial property changes during a kinetic experiment. It is apparent now that the application of the experimental system relies on the basic kinetic model an excellent review on which is available in literature (Danesi and Chiarizia, 1980).

The Lewis type of cell (Bulicka and Prochazka, 1976) is basically a model contactor with known interfacial area and it avoids the problem of boundary layer renewal encountered in the single-drop system. The interfacial area is controlled by the vessel geometry and the rate of interfacial mass transfer per unit interfacial area can thus be measured accurately. A contactor of this type has been used in the present study with the procedure described below. An easy to operate device is stirred membrane-based cell which has been extensively used for metal extraction kinetic and carboxlic acid (Juang and Lo, 1985; Juang and Huang, 1995).

3.3.2.2 Procedure of kinetic experiment

The stirred cell used for the current kinetic experimentals is of standard design schematic diagram of which is shown in Figure 3.6. The cell was a jacketed glass cylinder with inside diameter of 5 cm and a height of 10 cm which was divided into two halves by an acrylic disc placed right at the interface in order to reduce the disturbance at the interface. The interfacial area of the annular gape was varied by changing the size of the disc. The temperature was maintained constant at 25 ± 0.5°C by passing constant
Figure 3.5: A standard stirred contactor with a jacket and internal coil.
A = seating arrangement; B = thermometer pocket; C = liquid inlet/outlet; D = cooling/heating coil.
Figure 3.6: Schematic diagram of all glass stirred cell.
1, glass cell; 2, water jacket; 3, water outlet; 4, water inlet; 5, sample collector; 6, rubber septum for sample collector; 7, magnetic stirrer; 8, teflon stirrer; 9, glass rod; 10, motor with speed regulator; 11, circular disc; 12, aqueous phase; 13, organic phase; 14, interface of two liquid; 15, stainless steel rod; 16, glass lid; 17, O' ring baffle.
temperature water through the jacket from a Julabo thermostated bath. The solute (beta-lactam) was transferred between the aqueous and organic phases of Aliquat-336 solution which has been equilibrated with the buffer used. Both the liquid phases were independently stirred up to 150 rpm however, without causing phase dispersion such that the geometric area of the interface can be considered as the interfacial contact area. A magnetic capsule of 1.5 cm length was used to stir the aqueous phase in the cell for which the cell was kept above a magnetic plate (not shown in the figure) having a speed controlling device. The organic phase was stirred with a teflon made stirrer fitted to a motor with speed regulator. The stirring speed was measured with a non-contact type digital tachometer. The volumes of the upper organic phase as well as the lower aqueous phase were 75 ml each.

The aqueous phase was first introduced into the cell and then the organic solution was poured slowly and carefully without disturbing the interface and the stirrers were started simultaneously. Samples of aqueous phase were drawn with a glass syringe at regular interval of 5 minutes and subjected to analysis in order to obtain solute concentration versus time profiles under various experimental conditions.

### 3.3.3 Determination of interfacial tension

Though the data on interfacial tension are not sufficient to signify the interfacial chemical reaction as the rate controlling step in the extraction process, it is thought desirable to provide such data for the system at least for a qualitative assessment keeping further in view, that Aliquat-336 has surfactant properties (Dutta and Patil, 1993; Deblay et al., 1991). For the measurement, a simple yet reliable method based on drop weight principle was adopted. The schematic diagram of the apparatus is shown in Figure 3.7 design of which was adopted from literature (Weatherley and Wilkinson, 1988). It was also earlier used for measurement of interfacial tension of identical system (Dutta and Patil, 1993; Deblay et al., 1991). The apparatus comprises of a precision bore capillary tube attached to a stopcock (ST) and reservoir (R) at the left end termination in a precision ground glass nozzle (N) at the right end. The procedure for determining interfacial tension involves initially charging the capillary tube and
Figure 3.7: Schematic of the interfacial Tension Apparatus used for this study.
B = Sample bottle; N = Nozzle; R = Reservoir; ST = Stopcock.
reservoir with the required organic phase. This is done by attaching the open nozzle to an external reservoir solvent and allows it flow in by gravity. The stopcock at the left hand end of the apparatus was opened and then closed. A small sample bottle (B) is placed over the precision nozzle and sealed in the position. Solvent (organic phase) is released into the sample bottle through the aqueous phase until solvent/air interface appears in the horizontal calibrated section of the capillary tube. At this point, a series of single droplets was released from the nozzle, the volume of each being directly calculated from the degree of movement of the air/solvent interface in the horizontal section. The interfacial tension of the system was calculated using the original force balance procedure of Harkins and Brown (1919) and later on modified by Mori (1990). A balance of interfacial tension and buoyancy forces yields.

\[ V_f \Delta \rho \ g = 2 \Pi r \sigma \]  

where, \( V_f \), \( \Delta \rho \), \( g \), \( r \) and \( \sigma \) are the experimental drop volume (cm\(^3\)), density difference between two phases (gm/cm\(^3\)), gravitational constant (cm/s\(^2\)), radius of nozzle (cm) and interfacial tension (dynes/cm), respectively. The unit of \( \sigma \) presented here is mN/m as converted from dyne/cm. The effective droplet volume was calculated from the actual droplet volume by allowing non-ideal breakaway at the nozzle using Harkins and Brown correction factor. (Mori, 1990). Before measurement of the interfacial tension between the two phases, the organic phase containing Aliquat-336 was saturated with aqueous buffered beta-lactam solution of appropriate pH. The apparatus was standardized at 30°C for toluene / water hexane / water and n-pentanol / water systems, whose interfacial tension values were 36.15, 50.0 and 2.0 mN/m, respectively.

3.4 Results and discussion

Under various experimental conditions, the initial extraction rate, \( J_i \) (mol/cm\(^2\)sec) was obtained from the concentration change of beta-lactam in the aqueous solution with time. That is the initial rate of extraction across the interface (expressed as flux) was obtained from the following relation
\[
J_i = -\frac{V_s}{S} \left( \frac{dC_p^-}{dt} \right)_{t=0} \text{ mol/cm}^2\text{sec} \quad (3.52)
\]

where, \( (dC_p^-/dt)_{t=0} \) is the initial slope of the curve of \( C_p^- \) vs t. Figures 3.8 to 3.10 shows typical \( C_p^- \) versus t profiles for various beta-lactams studied under specified conditions. All the profiles are generated at stirring speed of 120 rpm for the reasons explained in the following section.

### 3.4.1 Effect of stirring speed and interfacial area

The effect of stirring speed on the initial extraction flux can provide some evidence information on the regime of the transport process i.e. whether the rate is controlled by film diffusion or kinetics of the chemical reaction. This effect was studied at constant interfacial area of 12.5 cm\(^2\) for the 7-ACA molecule only. It is expected that the effects exhibited by the other molecules will be atleast qualitatively identical in as much as the physical properties of the systems may be considered to be identical and do not alter the hydrodynamic conditions of the stirred cell under the operation conditions.

When the mass transfer rate is independent of the stirring speed of the two phases, a kinetic regime can be assumed, i.e. only chemical reaction is controlling the extraction ratio. Figure 3.11 shows the effect of stirring speed on the initial extraction flux. It is apparent that the extraction kinetics is controlled by film diffusion below a stirring speed of 110 rpm and in the range of 100-150 rpm, the rate is independent of the stirring speed implying that the extraction occurs in the kinetic regime. Above a rpm of 150, the flux increases again with increase of speed but the interface becomes unstable above this speed. In view of this, further study on extraction kinetics were performed at 120 rpm i.e. under the kinetics regime.

Studied under the kinetic regime, the extraction rate may be controlled either by the homogeneous phase chemical reaction or by the interfacial chemical reaction. A study on the effect of interfacial area (S) on the specific initial extraction rate (\( J_{s,i} \)) can also provide the inference on the rate controlling reaction. Figure 3.12 shows the relation of \( J_{s,i} \) with (S) for 7-ACA which apparently exhibits a linear dependence. This observation
Figure 3.8: Change of (a) 6-APA and (b) 7-ACA concentration in aqueous phase with time, $C_{pi} = 1$ mM; $pH = 8.0$. 

Symbol $C_{QCl}$ (mM):
- $\bigcirc$: 1
- $\triangle$: 2
- $\square$: 5
- $\bullet$: 10
Figure 3.9: Change of (a) T-ADCA and (b) cephalexin concentration in aqueous phase with time, $C_{p_i} = 1$ mM; pH = 8.0.
Figure 3.10: Change of cephalosporin-c concentration in aqueous phase with time, $C_{Pi} = 1$ mM; pH = 9.5.
Figure 3.11: Effect of stirring speed on the initial extraction flux of 7-ACA. $S = 12.5 \text{ cm}^2$; $C_{\text{Pi}} = 1.5 \text{ mM}$; $C_{\text{QCl}} = 2 \text{ mM}$; pH = 8.
Figure 3.12: Effect of interfacial area on the specific initial extraction rate of 7-ACA. N = 120 rpm, $C_{\text{H}} = 1.5$ mM; $C_{Q_{\text{Cii}}} = 2$ mM; pH = 8.
along with the results of Figure 3.11 imply that the interfacial chemical reaction rather than homogeneous phase chemical reaction may control the overall extraction rate under the conditions studied.

3.4.2 Effect of pH and beta-lactam concentration

The effect of pH of the aqueous phase containing the beta-lactam on the initial extraction flux \( J_i \) was examined for 6-APA and 7-ACA only at various combinations of solute-carrier concentrations. The relationships of \( J_i \) and pH for 6-APA and 7-ACA are shown in Figures 3.13 and 3.14 respectively from which it is apparent that \( J_i \) increases with pH in both the cases. The beta-lactams are zwitterions and their zwitterionic nature imparts unique acid/base characteristics. Increase of pH particularly above the pK\(_{a2}\) value renders prevalence of anionic form amenable for the anion-exchange extraction with Aliquat-336. Thus, these observed results are consistent with the zwitterionic character of the beta-lactams. Similar pH effect may be expected for the other beta-lactams too considered in this investigation. When considered independently, the slopes of the lines in Figures 3.13 and 3.14 for are nearly identical. This implies that under the experimental conditions used, a common extraction mechanism holds good for the extraction. However, this inference should be substantiated from the results on the effects of solute and carrier concentration on \( J_i \).

The effects of initial beta-lactam concentration on \( J_i \) examined at a fixed initial concentration of carrier and different pH of the aqueous phase values are shown in Figures 3.15 and 3.16 (log-log plots) for 6-APA and 7-ACA, respectively while the comparative effects for comparison for various beta-lactams at constant pH is shown in Figure 3.17. It follows from these figures that \( J_i \) increases with initial solute concentration up to around 1.5-2.0 mM beyond which \( J_i \) tend to remain essentially constant. It is also found that \( J_i \) is linearly proportional to solute concentration for all the beta-lactams as is evident from Figure 3.18 which is a plot in cartesian co-ordinate. This observation on solute concentration effect is akin to those reported for extraction of citric acid with tri-n-octylamine (Juang and Huang, 1995), phenylalanine with Aliquat-336 (Chan and Wang, 1993), various organic acids with Tri-n-octylphosphine oxide.
Figure 3.13: Effect of pH on initial extraction flux of 6-APA at various combination of solute-carrier concentrations.
Figure 3.14: Effect of pH on initial extraction flux of 7-ACA at various combination of solute-carrier concentrations.
Figure 3.15: Effect of initial 6-APA concentration on initial extraction flux at various pH. $C_{QCI} = 400$ mM.
Figure 3.16: Effect of initial 7-ACA concentration on initial extraction flux at various pH. $C_{Q_{CH}} = 2$ mM.
Figure 3.17: Effect of initial concentration of various beta-lactams on initial extraction flux at pH = 8; pH = 9.8 for CPC; $C_{QCH} = 2$ mM.
Figure 3.18: Effect of initial concentration of various beta-lactams on initial extraction flux at pH = 8; pH = 9.8 for CPC; $C_{QCl}$ = 1 mM.
(Matsumoto et al., 1996) etc. Since the slopes of the lines of the log-log plot of $J_i$ versus solute concentration below 1.5-2 mM for all beta-lactams are nearly one i.e. 0.99, 1.0, 0.97, 1.0, 0.99, for 6-APA, 7-ACA, 7-ADCA, cephalexin and cephalosporin-c respectively, the extraction rate is first order with respect to solute concentration and a common extraction extraction mechanism seem to hold good for all the beta-lactam. Beyond this solute concentration slope of the lines are much less than unity which imply that a different but common mechanism controls the extraction rate for the beta-lactams studied in this work. It follows from Figures 3.17 and 3.18 that under otherwise identical conditions the values of $J_i$ for different beta-lactams are different and accordingly a relationship of $J_i$ with solute chemical nature may be expected analogous to that deduced for extraction equilibrium constant (section 2.4.5) and reported in our recent publications (Bora et al., 1999 ; Sahoo et al., 1999). However, the present data appear to be insufficient to deduce such a relationship for $J_i$.

3.4.3 Effect of carrier concentration

The effect of carrier concentration ($C_{QCl}$) on initial extraction flux ($J_i$) at constant solute concentration and different pH values of the aqueous phase was examined for 7-ACA only and is shown in Figure 3.19, while the effect at constant pH was examined for various beta-lactams for which the results are shown in Figure 3.20. As discussed in the pervious section, the increase of $J_i$ with pH is consistent with the zwitterionic nature of 7-ACA and this observation may be expected for the other beta-lactams too. Over the range of $C_{QCl}$ studied, $J_i$ increases with $C_{QCl}$ in an exponential way as is evident from Figures 3.19 and 3.20. This increase of $J_i$ with $C_{QCl}$ in an exponential way may be represented by equation (3.49) which is typical of a Langmuir type relationship and is applicable to all the beta-lactams studied under other wise identical experimental conditions. These striking results suggest an interfacial adsorption mechanism and imply the hypothesis of an interfacial reaction control mechanism for extraction of the beta-lactams with Aliquat-336 which has good surfactant properties. Indeed significant lowering of interfacial tension between an aqueous cephalosporin solution and butylacetate solution of Aliquat-336 could be demonstrated as an important factor for
Figure 3.19: Effect of carrier concentration on initial extraction flux of 7-ACA at different pH value of the aqueous phase. $C_{PI} = 1$ mM.
Figure 3.20: Effect of carrier concentration on initial extraction flux of various beta-lactam. $C_{pi} = 1$ mM; pH = 8; pH = 9.8 for cephalosporin-c.
stability and permeability of an immobilized liquid membrane system (Ghosh et al., 1995) wherein the principle of the same reactive extraction was exploited. However, in the low range of \( C_{QCl} \), the role of interfacial adsorption may be less important as will be discussed below.

In order to provide further interpretation on the effect of carrier concentration, the data presented in Figures 1.19 and 3.20 have been reproduced in log-log plots as shown in Figures 3.21 and 3.22. The slopes of the lines in these Figures are nearly one implying that the extraction rates of 7-ACA at various pHs are first order with respect to carrier concentration up to a value of 5 mM and this inference holds good for the other beta-lactams too at least at pH values above the \( pK_a \)s. Beyond the above \( C_{QCl} \) value, the slopes of the lines are much less than unity which implies that a different extraction mechanism holds at higher \( C_{QCl} \).

### 3.4.4 Role of interfacial tension on extraction kinetics

Aliquat-336, known also as a phase transfer catalyst has appreciable surfactant properties which have been shown to enhance reaction rate in certain specific phase transfer reactions through an increase of the \( \sigma \) \( / \Omega \) interfacial area (Dutta and Patil, 1993; Patil and Dutta, 1996). In the present reactive extraction systems, the beta-lactam anion-Aliquat-336 complex can be expected to be more surface active in nature. Accordingly, the change in interfacial tension of the two-phase system due to change in experimental conditions such as concentrations and pH etc. may provide important but not sufficient information about the role of the interfacial process on the extraction kinetics. The interfacial tension data will be interpreted to draw on inference of interfacial chemical reaction as the rate controlling step.

The most important data presented here pertain to the effect of carrier concentration on interfacial tension of the system and are shown in Figures 3.23 and 3.24. As expected, the interfacial tension (\( \sigma \)) decreases with an increase of Aliquat-336 concentration (\( C_{QCl} \)). The other important observation is that the organic phase containing QC1 saturated with the beta-lactam solution exhibits lower interfacial tension than that of the unsaturated solution. The above general observation holds good for all the beta-lactams
Figure 3.21: log-log plot for effect of carrier concentration on initial extractions flux of 7-ACA at different pH values of the aqueous phase. $C_{pi} = 1$ mM.
Figure 3.22: Log-log plot for effect of carrier concentration on initial extractions flux of various beta-lactams. $C_{Pi} = 1$ mM, $pH = 8$; $pH = 9.8$ for cephalosporin-c.
Figure 3.23: Effect of Aliquat-336 concentration on interfacial tension. \( C_{Pi} = 1 \text{ mM}; \) \( \text{pH} = 8. \)
Open symbol: organic phase saturated with beta-lactam solution;
Closed symbol: organic phase not saturated with beta-lactam solution.
Figure 3.24: Effect of Aliquat-336 concentration on interfacial tension. $C_{pi} = 1$ mM; pH = 8; pH = 9.8 for cephalosporin-c.
Open symbol: organic phase saturated with beta-lactam solution;
Closed symbol: organic phase not saturated with beta-lactam solution.
studied in this work. However, the extent of interfacial tension lowering is different for different beta-lactams. From the data, it follows that beta-lactams exhibiting increased interfacial tension lowering may be grouped in the order CPC > 7-ACA > 6-APA > 7-ADCA > cephalexin which is the same in term of the hydrophobicity of the molecules. Thus, it may be inferred that beta-lactam of higher hydrophobic nature exhibits increased lowering of interfacial tension. This may be considered reasonable as more hydrophobic nature would tend to adsorb more at the interface.

Figure 3.25 shows effect of beta-lactam loading ratio \( C_{QP}/C_{QCl} \) on difference in interfacial tension, \( \Delta \sigma \) defined as \( \Delta \sigma = \sigma_n - \sigma \) where, \( \sigma_n \) corresponds to the value of \( \sigma \) for fresh unsaturated solution. The solute concentration in the organic phase was changed by adding solute saturated carrier solution into fresh unsaturated carrier solution. The value of \( \Delta \sigma \) increases with loading ratio of the beta-lactams, the extent of increase being different for different beta-lactams. The data of Figure 3.25 pertain to various initial concentration of carrier and it is apparent that there was almost the same change of interfacial tension for different carrier concentrations. The change in \( \Delta \sigma \) may be attributed to the change in interfacial concentration of the solute–carrier complex by the reaction and adsorption at the interface.

Under the assumption that interfacial chemical reaction is the rate controlling step, the mass transfer resistances of aqueous and organic phases can be neglected, so that the bulk concentrations of the solute–carrier complex \( (C_{QP}) \) and the carrier \( (C_{QCl}) \) are equal to the interfacial concentrations i.e. \( C_{OP} = C_{QPIn} \) and \( C_{Cl} = C_{QClIn} \). Therefore the concentrations of QCl and QP at the interface may be obtained. The concentration of QP at the interface cannot be determined directly, so \( \Delta \sigma \) was used to represent \( C_{QP} \) at the interface indirectly with the help of Figure 3.25. At a known \( C_{QCl} \), \( C_{QP} \) can be translated from the interfacial tension measurements and Figure 3.25. For example, \( C_{QP} / C_{QCl} \) can be obtained as 0.225 at \( \Delta \sigma \) of 1.0. Thus if \( C_{QCl} = 2 \) mM and \( C_{QP} / 2 = 0.225 \); \( C_{QP} \) can be calculated as 0.45mM. The other concentrations can be calculated by the same method providing the effect of \( C_{QCl} \) on \( C_{QP} \) at the interface and the results are represented in Figure 3.26 which is essentially a plot of \( C_{QClIn} \) versus \( C_{QPIn} \) with slope of 1.0 i.e.
Figure 3.25: Effect of beta-lactam loading ratio on $\Delta \sigma$.

$C_{QCH} = 0, 1 \text{ mM; } \triangle, 2 \text{ mM; } \square, 5 \text{ mM; } \bullet, 10 \text{ mM.}$
Figure 3.26: Effect of carrier concentration on $C_{QP, in}$ complex. $C_{Pi} = 1$ mM; $pH = 8$; $pH = 9.8$ for cephalosporin-c.
This finding seems to hold for all the beta-lactams studied in this work and it is in partial conformity with the relationship for chemical equilibrium. It thus provides partial evidence that interfacial chemical reaction controls the extraction rate. Similar approach was applied to study of the interfacial reaction kinetics of Penicillin-G extraction with Amberlite LA-2 (Lee and Wang, 1995).

The relationship of interfacial tension with \( C_{QCl} \): According to the theory of adsorption at liquid-liquid interface (Gibbs, 1928), the following equation holds

\[
-d\sigma = \int RT \, d\ln C_{QCl} \tag{3.54}
\]

With the assumptions of constant adsorption site on an interface, one site adsorbing one molecule and no interactions among adsorbed molecules. The Langmuir adsorption isotherm (1917) for mono-layer adsorption is given by

\[
\Gamma = \frac{\Gamma^* \, k_{QCl}}{1 + k \, C_{QCl}} \tag{3.55}
\]

A relationship between interface excess concentration and bulk concentration can be obtained from equations 3.54 and 3.55. Introducing the later equation in the former and integrating

\[
\sigma_0 - \sigma = \int \frac{\Gamma^* \, k_{QCl}}{1 + k \, C_{QCl}} \, R \, T \, \ln (1 + k \, C_{QCl}) \tag{3.56}
\]

where, \( \sigma_0 \) (25.4 mN/m) is the value for the interface between butylacetate and water. This is the so-called Szyskowski equation (1908). A least square analysis was made to fit the relationship of \( \sigma \) with \( C_{QCl} \) by equation 3.57. The estimated values of the parameters i.e. \( \Gamma^* \) and \( k \) are shown in Table 3.1 and the relationship is shown in Figure 3.27. Thus, the interfacial tension was correlated for the effect of \( C_{QCl} \) in the form of equation 3.56. The observed relationship is consistent with that reported for Penicillin-G-Amberlite LA-2 system (Lee and Wang, 1995).
Table 3.1 Estimated parameters of equation 3.56 for various beta-lactams

<table>
<thead>
<tr>
<th>Beta-lactam</th>
<th>Parameter</th>
<th>Regression coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$k$, cm$^3$/mol</td>
<td>$I^0$ mol/cm$^2$</td>
</tr>
<tr>
<td>Cephalosporin-c</td>
<td>1.202 X 10$^3$</td>
<td>3.74 X10$^{-9}$</td>
</tr>
<tr>
<td>7-ACA</td>
<td>1.486 X 10$^3$</td>
<td>4.29 X10$^{-9}$</td>
</tr>
<tr>
<td>7-ADCA</td>
<td>1.035 X 10$^3$</td>
<td>4.54 X10$^{-9}$</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>1.205 X 10$^3$</td>
<td>3.742X10$^{-9}$</td>
</tr>
<tr>
<td>6-APA</td>
<td>1.188 X 10$^3$</td>
<td>6.026X10$^{-9}$</td>
</tr>
</tbody>
</table>
Figure 3.27: Semi-log plot of $\sigma_0 - \sigma$ versus $C_{QCl}$. $C_{Pl} = 1 \text{ mM}$; pH = 8 and 9.8 for cephalosporin-c.
3.4.5 Validation of kinetic model

3.4.5.1 Qualitative consideration

As discussed in section 3.4.2 and 3.4.3, the extraction mechanism appears to be dependent on the range of Aliquat-336 concentration in the aqueous phase. The results revealed that at low concentration i.e. below 2 mM, simple two film model describing the mass transfer across the liquid interface can be used to analyse the extraction kinetics. Such models had been used for analysis of extraction kinetic of salicylic acid by Amberlite LA-2 in xylene (Schlichtling et al., 1987), d-l phenylalamine with Aliquat-336 (Haensel et al., 1986) and penicillin G extraction with Amberlite LA-2, dioctylamine and / or tri-n-octylamine (Reschke and Schurgerl, 1984).

At higher Aliquat-336 concentration, the extraction mechanism seems to be different considering, the surfactant properties of the carrier, it is reasonable to presume that the role of the interfacial chemical reaction is important. The interfacial chemical reaction control mechanism was reported for extraction of phenylalamine with Aliquat-336 (Chan and Wang, 1993), citric acid with tri-n-octylamine in xylene under certain conditions (Juang and Huang, 1994) and penicillin G extraction with Amberlite LA-2. Both film diffusion and interfacial reaction was found to control the extraction of organic acids such as acetic, propionic, crotonic acids, etc. with Trioctyolphosphine oxide (TOPO) as the extractant (Matsumoto et al., 1996). In this work, the kinetic data will be analysed from both the two models considered independently over the range of Aliquat-336 and beta-lactam concentrations studied.

3.4.5.2 Two- film model

The two film model has been examined with the data on Aliquat-336 extraction of 6-APA and 7-ACA only. The basic aim is to compare the change in beta-lactam concentration with time (concentration profiles) in stirred cell experiments under specific set of conditions with the theoretical profiles predicted from equation 3.6 representing the kinetic model. Figures 3.28 and 3.29 shows the concentration profiles for 6-APA and
Figure 3.28: Comparison of experimental and theoretical dimensionless 6-APA concentration profile. pH = 8; $C_{\text{Pi}} = 1 \text{ mM}$; Symbol: experimental points; Curve: theoretical.
Figure 3.29: Comparison of experimental and theoretical dimensionless 7-ACA concentration profile. pH = 8; \( C_{P_i} = 1 \text{ mM} \); Symbol: experimental and Curve: theoretical.
7-ACA, respectively at two Aliquat-336 concentrations. As expected, the extraction rate is enhanced with increasing carrier concentration. Equation 3.6 was numerically integrated using a program developed in FORTAN and executed in a Pentium PC Machine (refer Appendix 2B for the complete program). The three mass transfer coefficients \( k_{QCL} \), \( k_{F} \) and \( k_{QF} \) and the associated diffusion coefficient were estimated following procedures discussed in section 3.4.2, 3.4.3 and the values are listed in Table 3.2. These values of the mass transfer coefficients are comparable to those reported in literature (Table 3.3) but evaluated through an identification procedure by fitting the calculated concentration profiles to the measured one. The values of the equilibrium constants of the extractive reactions are 0.17 and 0.21 for 6-APA and 7-ACA, respectively and the specific interfacial area, \( S \) of the stirred cell used is 19.2 cm\(^2\). It should however, be noted that the use of these mass transfer coefficients may be somewhat conservative in-as-much as their values can be considered to change with time of extraction. With these mass transfer coefficients, \( K_{F} \) and \( S \) values, the theoretical concentration profiles have been computed and shown as the smoothed curves along with the experimental data points (symbols) in Figures 3.28 and 3.29 which pertain to 6-APA and 7-ACA, respectively. The experimental and theoretical profiles agree fairly well when the carrier and solute concentrations are low.

However, deviation could be observed at high carrier concentration which may at first instance be attributed to probable error in the values of the mass transfer coefficients which appear to be in the lower side. However, since any enhancement in their values by further increasing the stirring speed (leading to phase dispersion) cannot be anticipated, it is presumed that some other physico-chemical processes occurring at the interface controls the extraction. This is also consistent with the results presented in the previous sections.

### 3.4.5.3 Model with diffusion and interfacial reaction

Equations 3.48 and 3.49 were used to analyse the experimental data. In order to estimate the model parameters, plots of \( 1/J_{i} \) versus \( 1/C_{QCH} \) (equation 3.50) were used. Figure 3.30 shows such plots for all the beta-lactams studied in this work and the values
### Table 3.2 Values of the estimated mass transfer and diffusion coefficient.

<table>
<thead>
<tr>
<th>Beta-lactam</th>
<th>$k_{Qc1}$ (cm/s)</th>
<th>$k_P$ (cm/s)</th>
<th>$k_{QP}$ (Cm/s)</th>
<th>$D_{QP}$ (cm²/s)</th>
<th>$D_{Qc1}$ (cm²/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-APA</td>
<td>$3.4 \times 10^{-4}$</td>
<td>$4.6 \times 10^{-4}$</td>
<td>$2.79 \times 10^{-4}$</td>
<td>$1.1 \times 10^{-4}$</td>
<td>$1.3 \times 10^{-4}$</td>
</tr>
<tr>
<td>7-ACA</td>
<td>$3.5 \times 10^{-4}$</td>
<td>$8.6 \times 10^{-4}$</td>
<td>$2.98 \times 10^{-4}$</td>
<td>$6.46 \times 10^{-4}$</td>
<td>$7.58 \times 10^{-4}$</td>
</tr>
</tbody>
</table>

### Table 3.3 Reported mass transfer coefficients of two-film model evaluated in stirring for various systems.

<table>
<thead>
<tr>
<th>System</th>
<th>Solute (in aq.)</th>
<th>Coefficient based on</th>
<th>Coefficient based on</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>carrier (in solvent)</td>
<td>Solute $k_a$ (cm/s)</td>
<td>carrier complex $k_o$ cm/s $k_c$ cm/s</td>
</tr>
<tr>
<td>Penicillin-G</td>
<td>Amberlite LA-2/ n-butylacetate</td>
<td>$4.5 \times 10^{-4}$</td>
<td>$1.0 \times 10^{-3}$</td>
</tr>
<tr>
<td>dl-phenyl-alanine</td>
<td>Aliquat-336/ Xylene</td>
<td>$6.4 \times 10^{-4}$</td>
<td>$5.6 \times 10^{-4}$</td>
</tr>
<tr>
<td>Organic acids i.e Lactic, malic, citric, crotonic etc.</td>
<td>Trioctylphosp/ Heaxne</td>
<td>$0.8 \times 10^{-3}$</td>
<td>$1.5 \times 10^{-3}$</td>
</tr>
</tbody>
</table>
Figure 3.30: Plot of $1/J_1$ versus $1/C_{QCl}$. pH = 8; pH = 9.8 for cephalosporin-c.
of the parameters are listed in Table 3.4. The values of the equilibrium constants for the beta-lactam are taken from section 2.4.2 (page no.76). With the above parameter values theoretical concentration profiles have been generated at two levels of carrier concentration using equation 3.48 which has been numerically integrated with the help of a computer program in FORTRAN and executed in a PC 486. (Annexure 2A and 2C for program). These theoretical profiles (curves) alongwith experimental data points (represented by symbols) are shown in Figures 3.31 to 3.35 for 7-ACA, 6-APA, cephalaxin, 7-ADCA and CPC, respectively. It is apparent from these figures that the agreement between theoretical and experimental concentration profiles obtained for all the studied beta-lactams is reasonably good at high carrier concentration i.e stoichiometrically excess for the extractive reaction. However, deviation occurs at low concentrations (but stoichiometrically equivalent to the solute) an observation which apparently implies a different extraction mechanism and is consistent with that interpreted from the two-film model too.

3.5 Conclusion

The rate of extraction of beta-lactam antibiotics by Aliquat-336 (carrier) from aqueous phosphate and carbonate buffer solution to an organic phase of n-butylacetate and carrier increases with increase of carrier concentration in the organic phase upto 5 mM beyond which the rate tends to reach an asymptote. The extraction rate decrease with an increase of beta-lactam concentration in the aqueous phase in the range of 1.5-2 mM . An increase of the aqueous phase pH (from 4 to 9.8) increases the extraction rate probably through favorable extraction equilibrium relationship.

The extraction mechanism seems to be dependent on the solute-carrier concentration. In the lower range of carrier concentration, a simple mass transfer model based on two film theories proposed to describe the extraction kinetics predicts fairly well the experimental concentration versus time profile.

However, over the entire concentration range, a kinetics model proposed from interfacial reaction controlled mechanism provides a better prediction of the concentration profile for the beta-lactams considered in the work.
Table 3.4 Parameter value of the interfacial reaction model for extraction kinetics of various beta-lactam.

<table>
<thead>
<tr>
<th>Beta-lactam</th>
<th>$K_1$ (l/mol)</th>
<th>$K_2$ (l/mol)</th>
<th>$K_3$ (l/mol)</th>
<th>$k_2$ (cm/sec)</th>
<th>$k_{-2}$ (cm/sec)</th>
<th>$K_P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-APA</td>
<td>426.66</td>
<td>9.02 x10^{-2}</td>
<td>167.47</td>
<td>1.55 x10^{-3}</td>
<td>1.73 x10^{2}</td>
<td>0.23</td>
</tr>
<tr>
<td>7-ACA</td>
<td>1205.67</td>
<td>1.176 x10^{2}</td>
<td>70.92</td>
<td>1.176 x10^{-3}</td>
<td>9.99 x10^{2}</td>
<td>0.20</td>
</tr>
<tr>
<td>7-ADCA</td>
<td>814.39</td>
<td>3.92 x10^{2}</td>
<td>106.41</td>
<td>9.302 x10^{-4}</td>
<td>2.37 x10^{2}</td>
<td>0.30</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>884.99</td>
<td>2.908 x10^{2}</td>
<td>34.31</td>
<td>9.99 x10^{-4}</td>
<td>3.438 x10^{2}</td>
<td>0.75</td>
</tr>
<tr>
<td>CPC</td>
<td>843.37</td>
<td>7.648 x10^{2}</td>
<td>72.48</td>
<td>1.428 x10^{-3}</td>
<td>1.867 x10^{2}</td>
<td>0.89</td>
</tr>
</tbody>
</table>
Figure 3.31: Comparison of experimental and theoretical dimensionless 7-ACA concentration profile. pH = 8; $C_{P_i} = 1$ mM; Symbol: experimental and Curve: theoretical.
Figure 3.32: Comparison of experimental and theoretical dimensionless 6-APA concentration profile. pH = 8; \( C_{pi} = 1 \) mM; Symbol: experimental and Curve: theoretical.
Figure 3.33: Comparison of experimental and theoretical dimensionless cephalexin concentration profile. pH = 8; $C_{Pi} = 1$ mM; Symbol: experimental points; Curve: theoretical.
Figure 3.34: Comparison of experimental and theoretical dimensionless 7-ADCA concentration profile. pH = 8; $C_{pl} = 1$ mM; Symbol: experimental and Curve: theoretical.
Figure 3.35: Comparison of experimental and theoretical dimensionless cephalosporin-c concentration profile. pH = 9.8; \( C_{pi} = 1 \text{ mM} \); Symbol: experimental points; Curve: theoretical.
### 3.6 Nomenclature

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Amine (carrier), (mM)</td>
</tr>
<tr>
<td>7-ACA</td>
<td>7-Aminocephalosporanic acid</td>
</tr>
<tr>
<td>7-ADCA</td>
<td>7-Aminodexocephalosporanic acid</td>
</tr>
<tr>
<td>AHP</td>
<td>solute-amine complex</td>
</tr>
<tr>
<td>6-APA</td>
<td>6-Aminopenicillanic Acid</td>
</tr>
<tr>
<td>a</td>
<td>constant by equation (3.32) and (3.39)</td>
</tr>
<tr>
<td>b</td>
<td>constant by equation (3.32) and (3.39)</td>
</tr>
<tr>
<td>B</td>
<td>parameter defined in equation (3.6)</td>
</tr>
<tr>
<td>c</td>
<td>constant by equation (3.32) and (3.39)</td>
</tr>
<tr>
<td>C</td>
<td>concentration (mM)</td>
</tr>
<tr>
<td>Cl^-</td>
<td>Chloride ion</td>
</tr>
<tr>
<td>D</td>
<td>diffusivity, (cm²/sec).</td>
</tr>
<tr>
<td>H^+</td>
<td>proton.</td>
</tr>
<tr>
<td>HP</td>
<td>beta-lactam</td>
</tr>
<tr>
<td>J</td>
<td>extraction flux, (mol/cm²-Sec)</td>
</tr>
<tr>
<td>Jp, JQCL, JQP</td>
<td>mass transfer rate (flux) of beta-lactam, Aliquat-336 and complex with beta-lactam with Aliquat-336, respectively.</td>
</tr>
<tr>
<td>k</td>
<td>constant by equation (3.55) and (3.56).</td>
</tr>
<tr>
<td>kCl</td>
<td>aqueous phase interfacial mass transfer coefficient of Cl^-, (cm/s)</td>
</tr>
<tr>
<td>kL</td>
<td>aqueous phase interfacial mass transfer coefficient of P^-, (cm/s)</td>
</tr>
<tr>
<td>kP</td>
<td>mass transfer coefficient of beta-lactam</td>
</tr>
<tr>
<td>kQCl</td>
<td>mass transfer coefficient of Aliquat-336.</td>
</tr>
<tr>
<td>kQP</td>
<td>mass transfer coefficient of Aliquat-336-beta-lactam ion.</td>
</tr>
<tr>
<td>k_{1,2,3}</td>
<td>forward rate constant defined.</td>
</tr>
<tr>
<td>k_{-1,2,3}</td>
<td>reversed rate constant defined.</td>
</tr>
<tr>
<td>K_1, K_2, K_3</td>
<td>equilibrium constant.</td>
</tr>
<tr>
<td>K_{d1, d2}</td>
<td>dissociation equilibrium constant defined by equations (3.11) and (3.12), [-]</td>
</tr>
<tr>
<td>K_P</td>
<td>equilibrium constant, [-]</td>
</tr>
<tr>
<td>J_{s1}</td>
<td>specific initial extraction rate, (mol/sec)</td>
</tr>
</tbody>
</table>
N  stirring speed, (rpm)
P+ beta-lactam
P' beta-lactam anion
QA buffer anion-carrier complex
QCl Aliquat-336
QP quaternary amine-beta-lactam complex

ω1, ω2, ω3 adsorption interfacial chemical reaction, desorption, (mol/cm²-sec)

R  parameter defined in equation (3.6)
R  universal constant in equation (3.56)
S  interfacial area, (cm²)
t  time of extraction, (sec.)
T  absolute temperature
V  volume of solution, (lt)

σ0  interfacial tension of pure solvent (mN/m)
σ  interfacial tension between aqueous beta-lactam solution and organic phase,
   (mN/m)
σs  interfacial tension between saturated aqueous beta-lactam solution and organic
    phase
σu  interfacial tension between unsaturated aqueous beta-lactam solution and
    organic phase
Δσ  difference of interfacial tension between organic phase saturated and unsaturated
    solution, (mN/m)
θθ  fraction of interfacial area unoccupied, [-]
θQCl fraction of interfacial area occupied by QCl, [-]
θQP fraction of interfacial area occupied by QP, [-]
γ.1 constant defined in equation (3.15)
⊗ interfacial vacant site
Γ  interface excess concentration (mol/m²)
Γα saturated interface excess concentration (mol/m²)
Subscript/superscript

aq.   aqueous phase
i     initial
in    interfacial concentration
org.  organic (solvent) phase
u     unsaturated
s     saturated
3.7 REFERENCES


Langmuir I, (1917), Constitution and Fundamental properties of solids and liquids

