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Review Article

Dispersive Liquid-Liquid Microextraction Analysis, Dynamics in Non-Steady-State Mass Transfer: Naproxen for Sample

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Abstract

Mass transfer correlations have been obtained for the past eight decades by the Wilson-plot method which has proved to be suitable for systems operating in steady-state conditions and where the only variable is the fluid velocity. In reality, a steady-state mass transfer may not be established at the initial stage of extracted phase DLLME, which involves mass transfer across two interfaces. The rate of analyte transfer at the balk solution/tangent layer interface may not be equal to the extraction rate at the tangent layer/ Dispersive solvent interface. An improved model is proposed in this report to handle the situation of the non-steadystate mass transfer for the tangent layer. A mathematical solution is obtained for the dynamic process of the non-steady-state mass transfer by correlating the variation of the analyte concentration in the tangent layer with the analyte extraction rate. The difference in dispersive solvent shows that mass transfer in the methanol is faster than in the acetonitrile.

Keywords: mass transfer; Dispersive liquid-liquid microextraction; Naproxen; HPLC

Introduction

The rate at which a component is transferred between two different phases depends on the mass transfer coefficient, the interfacial area and on the degree of departure of the component from its partitioning equilibrium [1-3]. Evaluation of mass transfer coefficients is of most importance since they determine the rate at which equilibrium is approached, control the time required for a given separation and therefore the size and cost of the equipment to be used [4-6]. In order to estimate mass transfer coefficient necessary for engineering analyses and design, resort is made to conceptual models, to analogies and to correlative methods [4,7,8]. The Chilton and Colburn analogy (based on experimental data), between momentum, heat, and mass transfer, has been one of the most extensively and successfully applied and a large variety of correlations for different geometries and hydrodynamic conditions have been proposed [9]. Alonso reported the mass transfer analysis and modeling of the hollow fiber non-dispersive liquid-liquid extraction of Cr with Aliquat 336 [10]. Chen and lee studied effects of surfactants on the mass transfer in liquid- liquid extraction [11]. Dekker studied the rate of mass transfer in the liquid-liquid extraction of the enzyme Ix-amylase between an aqueous phase and a reversed micellar phase [12]. Dispersive Liquid-Liquid Extraction (DLLME) is a mode of liquid-liquid extraction in smaller level. DLLME employs a mixture of an extracting solvent and water miscible polar disperser solvent. DLLME has great advantages for analyzing organic chemicals in the extracted phase over an extracted phase [13]. During a static extracted phase analysis, chemicals with high affinity toward the dispersive solvent are concentrated in the extraction phase and the extraction results in a higher sensitivity than conventional static extracted phase analysis. In this work we want to analyze mass transfer in DLLME.

Theoretical Treatment

DLLME is a partition process [14]. Once the partition equilibrium is attained, the extracted amount of analyte can be expressed as follows:

$$n^{\infty} = \frac{k_{fh}k_{hs}v_f v_s}{k_{fh}k_{hs}v_f + k_{hs}v_h + v_s}c_0 \quad (1)$$

Here n^{∞} is the amount of analyte extracted by the Dispersive solvent when partition equilibrium is attained. k_{fh} and k_{hs} are

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equilibrium partition constants for the analyte between the balk solution and the tangent layer(layer between dispersive solvent and balk solution) and between the dispersive solvent and tangent layer, respectively. v_f, v_h, and v_s are volumes of the dispersive solvent, the tangent layer, and the initial phase (balk solution). c_0 is the initial concentration of the analyte in the initial phase or aqueous phase. Based on the boundary conditions of DLLME, the analytical solution is very complicated. Direct application of the model to the experimental results is a difficult task. A simple dynamic model with the focus on the mass transfer at the two interfaces was proposed to deal the dynamic process of extracted phase DLLME. This model avoided the mathematical treatment for the second-order partial differential equation, and a simple analytical solution was obtained:

$$n = n^{\infty}[1 - e^{(-a_h t)}] \qquad (2)$$

Here n is the amount of analyte extracted by the dispersive solvent before partition equilibrium, t is the extraction time, and a_h is a complicated parameter that determines how fast the equilibrium can be reached. The extracted amount before partition equilibrium is proportional to the amount that can be extracted at equilibrium. There is an exponential term between them. As time goes to infinity, this term vanishes. The above model is derived on the basis of a steady-state kinetics that assumes that the mass-transfer rate at the tangent layer/initial phase interface is equal to the mass-transfer rate at the tangent layer/disperser solvent interface. Analyte concentration in the tangent layer, c_h, remains at a constant level. This assumption may not describe the tangent layer process precisely. Once the dispersive solvent is exposed to the tangent layer over an initial phase, analyte concentration in the tangent layer is disturbed since the mass transfer from the initial phase to the tangent layer is not an instant process. In this report, an improved theoretical model is built to deal with the situation where the steady-state mass transfer between the two interfaces is not established. The analyte concentration in the tangent layer varies as the tangent layer extraction starts. The rate of variation of the analyte concentration in the tangent layer is the difference between the rate of analyte transfer from the initial phase and the rate of analyte extraction by the dispersive solvent [13-15]. By correlating the rate of analyte extraction and its rate of variation in the extracted phase, an expression for extracted amount n can be obtained as a function of extraction time t. Unlike eq 2, it contains two exponential terms, with each one similar to eq 2. The new model fits experimental data better than eq 2 and it also provides an explanation for quantitative tangent layer dispersive solvent in a non-steady-state mass-transfer process. Extracted phase DLLME involves mass transfer in three phases and across two interfaces. The dynamics at the two interfaces (initial phase/ tangent layer and tangent layer/dispersive is the focus of the study. At the extracted phase/dispersive solvent interface, the rate of analyte extraction can be expressed according to Fick's first law of diffusion from the Dispersive solvent surface to its inner layers.

$$\frac{1}{a_f}\frac{dn}{dt} = -d_f\left(\frac{\partial c_f}{\partial x}\right)|_{x=0} = m_f(c_f|_{x=0} - c_f|_{x=\delta}) \qquad (3)$$

a_f is the surface area of the dispersive solvent, d_f is the diffusion constant of the analyte inside the dispersive solvent, c_f is the analyte concentration in the dispersive solvent, and m_f is the mass transfer coefficient of the analyte,. . $m_f = \frac{d_f}{\delta}$ δ is the thickness of the dispersive solvent. Figure 1 shows a schematic description of the tangent layer/dispersive solvent interface. As shown in Figure 1, the analyte concentration profile inside the dispersive solvent can be simulated with a parabolic function. The average concentration of the analyte in the dispersive solvent is thus $\frac{(c_f|_{x=0} + 2c_f|_{x=\delta})}{3}$ following the parabolic approximation. Therefore, the extracted amount of analyte is the average concentration times the volume of the dispersive solvent:

$$n \approx v_f \frac{c_f|_{x=0} + 2c_f|_{x=\delta}}{3} \qquad (4)$$

On the basis of eq 4, $m_f(c_f|_{x=0} - c_f|_{x=\delta})$ in eq 3 can be written as a function of $c_f|_{x=0}$ and n:

$$m_f(c_f|_{x=0} - c_f|_{x=\delta}) = \frac{3}{2}m_f(c_f|_{x=0} - \frac{n}{v_f}) \qquad (5)$$

At the dispersive solvent surface with the tangent layer, the partition equilibrium exists for the analyte. Therefore, we have:

$$c_f|_{x=0} = k_{fh}c_h \qquad (6)$$

c_h is the analyte concentration in the tangent layer. Substituting eqs 5 and 6 into eq 3, we have

$$\frac{dn}{dt} + \frac{3a_f m_f}{2v_f}n = \frac{3}{2}a_f m_f k_{fh}c_h \qquad (7)$$

Equation 7 correlates the extracted analyte n with its concentration in the tangent layer c_h. We can express c_h in terms of n and $\frac{dn}{dt}$ using this equation. Differentiating eq 7, we have

$$\frac{dc_h}{dt} = \frac{2}{3a_f m_f k_{fh}}\frac{d^2n}{dt^2} + \frac{1}{k_{fh}v_f}\frac{dn}{dt} \qquad (8)$$

At the balk solution (aqueous solution) /tangent layer, the transfer rate of the analyte from the balk solution (aqueous solution) to tangent layer between initial phase and dispersive solvent is assumed to be proportional to the deviation of initial phase concentration from the equilibrium value. Therefore, we have

$$r = k\left(c_h^0 - c_h\right) = k(k_{hs}c_s - c_h) \qquad (9)$$

r is the transfer rate of the analyte and k is the transfer rate constant. c_h^0 c_h^0 is the tangent layer concentration of the analyte at equilibrium. It is equal to $k_{hs}c_s$, and c_s is the analyte concentration in the balk solution (aqueous solution) . c_s can be expressed as follows:

$$c_s = c_0 - \frac{v_h c_h}{v_s} - \frac{n}{v_s} \qquad (10)$$

Therefore, eq 9 can be rewritten in terms of n and c_h:

$$r = kk_{hs}c_0 - \frac{kk_{hs}}{v_s}n - k(\frac{k_{hs}v_h + v_s}{v_s})c_h \qquad (11)$$

it is assumed that the transfer rate r is equal to the extraction rate described in eq 3. If a steady-state mass transfer from the initial phase to the dispersive solvent is established through the extracted phase, the assumption is true and the analyte concentration in the tangent layer is a constant. But, before the steady-state mass transfer is established, the analyte concentration in the tangent layer varies with time. The variation rate of this layer concentration is the difference between the transfer rate and the extraction rate:

$$\frac{dc_h}{dt} = r - \frac{1}{v_h}\frac{dn}{dt} \qquad (12)$$

The first term in eq 12 is the analyte transfer rate from the balk soluion. It has a positive sign since analyte transfer increases the extracted phase concentration. The second term is the DLLME extraction rate expressed as the depletion rate of the analyte in the dispersive solvent with a negative sign. The variation rate as described in eq 12 is not equal to zero. Substitute eq 11 into eq 12, we have

$$\frac{dc_h}{dt} = kk_{ks}c_0 - \left(\frac{k_{hs}v_h + v_s}{v_s}\right)c_h - \frac{kk_{hs}}{v_s}n - \frac{1}{v_h}\frac{dn}{dt} \qquad (13)$$

Substitute c_h from eq 7 and $\frac{dc_h}{dt}$ from eq 8 into eq 13, we have

$$\frac{d^2n}{dt^2} + p\frac{dn}{dt} + qn = \frac{3}{2}a_f m_f k k_{fh} k_{hs} c_0 \quad (14)$$

with

$$p = k\left(\frac{k_{hs}v_h + v_s}{v_s}\right) + \frac{3}{2}a_f m_f \left(\frac{k_{fh}v_f + v_h}{v_f v_h}\right) \quad (15)$$

and

$$q = \frac{3}{2}a_f m_f k \frac{k_{fh}k_{hs}v_f + k_{hs}v_h + v_s}{v_f v_s} \quad (16)$$

Equation 14 is a second-order nonhomogeneous linear differential equation. Its general solution is

$$n = c_1 e^{-at} + c_2 e^{-bt} + \frac{k_{fh}k_{hs}v_f v_s}{k_{fh}k_{hs}v_f + k_{hs}v_h + v_s} c_0 \quad (17)$$

With

$$a = \frac{1}{2}(p + \sqrt{p^2 - 4q}) \quad (18)$$

and

$$a = \frac{1}{2}(p - \sqrt{p^2 - 4q}) \quad (19)$$

c_1 and c_2 are integration constants. Apply the initial condition $n|_{t=0} = 0$, $n|_{t=0} = 0$ we have

$$c_1 + c_2 + \frac{k_{fh}k_{hs}v_f v_s}{k_{fh}k_{hs}v_f + k_{hs}v_h + v_s} c_0 = 0$$

or

$$\propto + \beta = \frac{k_{fh}k_{hs}v_f v_s}{k_{fh}k_{hs}v_f + k_{hs}v_h + v_s} c_0 = n^{\infty} \quad (20)$$

with $\alpha = -c_1$ and $\beta = -c_2$. Equation 17 can be rewritten as

$$n = \propto \left[1 - e^{(-at)}\right] + \beta\left[1 - e^{(-bt)}\right] \quad (21)$$

The amount of extracted analyte n can be expressed as a function of extraction time t in a form with two exponential terms. According to eq 20, α and β should be proportional to c_0. Therefore, we have $n \propto c_0$ in eq 21 once t is held constant. The $n \propto c_0$ relation meets the key requirement for quantitative analysis. The amount of sample extracted by DLLME is proportional to the initial concentration of the material in the sample matrix. As extraction time goes to infinity, n is equal to $\alpha + \beta$ and eq 21 becomes eq 1, which is derived from the thermodynamic partition process.

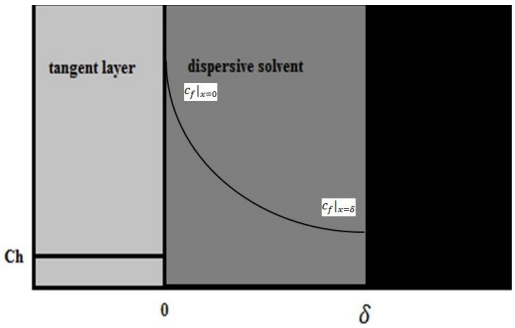

Figure 1: Schematics of the disperser solvent and tangent interface. The concentration profile of the analyte inside the disperser solvent follows a parabolic simulation.

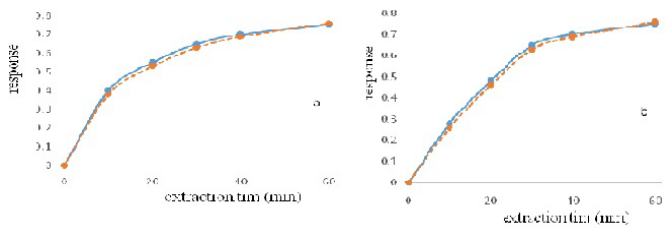

Figure 2: DLLME extraction time profiles of methanol **(a)** and acetonitrile **(b).** The initial phase was 10mL of sample solution containing 10ng mL^{-1} of naproxen and its temperature was 22°C. The solid lines are eq 2 fit, and dotted lines are eq 21 fit.

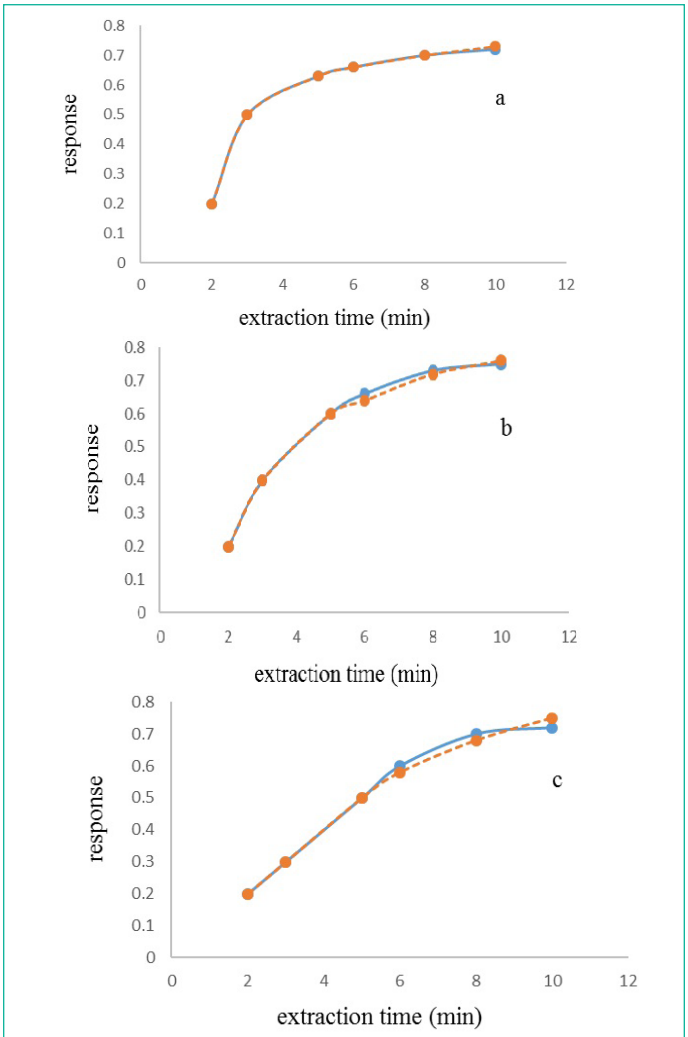

Figure 3: DLLME extraction time profiles of methanol with three different solution temperatures: **(a)** 5, **(b)** 22, and **(c)** 45 °C. The solid and dotted lines are regressions with eq 2 and eq 21, respectively.

Experimental

Chemicals and stock solutions: Naproxen was purchased from Cipla pharmacy (Mumbai, India). HPLC grade (Methanol, acetonitrile), was obtained from Merck (Darmstadt, Germany). dodecane was obtained from Aldrich (Milwaukee, WI, USA). Water used was double distilled deionized. Stock solution of naproxen (1.0mg/L) was prepared in methanol and stored in the dark at 4°C. Working standard solutions were diluted with double distilled deionized water at concentration of 10.0ng mL^{-1} when ever needed.

Instrumentation and operating condition: Chromatographic measurements were carried out using a HPLC system equipped with a series 10-LC pump, UV detector model LC-95

Table 1: List of Parameters p and q Derived from the Regression of Experimental Data with Eq 21 for DLLME with aqueous phase at Different Temperatures and Different disperser solvent.

Disperser solvent	temp (°C)	p (s-1)	q (s-2)
Methanol	5	0.0074	3.6×10-6
Methanol	22	0.028	1.0×0-4
Methanol	30	0.05	4.3×10-4
Methanol	45	0.56	9.0×10-3
Acetonitrile	15	0.031	1.9×10-5

set at 270 nm and model 7725i manual injector with a 20µL sample loop (Perkin-Elmer, Norwalk, CT, USA). Column used was C_{18} (250×4.6mm, 10µm particle size) from Dr. Maisch GmbH (Ammerbuch-Entringen, Germany). In order to select the composition of mobile phase, several mobile phases with different percents of methanol in water (40, 50, 60 and 70 % v/v) were tested and the best mobile phase was 60 percent methanol based on peak shape, retention time and resolution at flow rate of 1.0 mL/min at room temperature.

Ddispersive liquid–liquid microextraction procedure: For DLLME, 10mL of sample solution containing 10ng mL^{-1} of naproxen was placed in a handmade centrifuge tube with narrow neck (~4mm i.d.) which was specifically designed for ease of taking supernatant phase. A mixture of 100µL dodecane (as extraction solvent) and 350µL methanol (as disperser solvent) was rapidly injected into the sample solution using 1.0mL syringe and mixed by vortex agitator at 500 rpm stirring rate to obtain a cloudy solution. The cloudy solution was centrifuged for 5 min at 3500rpm and the extraction product (supernatant phase) collected in the neck of the tube (about 80±2µL) [16]. This supernatant phase was injected in to the HPLC.

Results and Discussion

A linear proportional relationship between n and C_0 was observed when the sampling time was far shorter than that required to reach a partition equilibrium [17]. In this report, eq 21 is theoretically derived from the dynamic process of tangent layer. Figure 2 shows both eqs 2 and 21 fitting the experimental data of extracted phase of DLLME at room temperature (22°C). It is obvious that eq 21 describes the experimental measurements dodecane (extraction solvent) and methanol (dispersive solvent). This is an expected result because eq 21 is derived under a situation closer to the reality during an extracted phase. Through the regression using eq 21, two parameters a and b are obtained. According to eqs 18 and 19, we have $p = a + b$ and $q = a \times b$. Therefore, the values of two important parameters p and q are obtained. Parameter p has two terms (eq 15) corresponding to the mass transfer at the two interfaces balk solution (aqueous solution) /tangent layer and tangent layer/ dispersive solvent, respectively. The first term of p is proportional to k, which is the rate constant of analyte transfer from the balk solution (aqueous solution) to tangent layer. It is also dependent on the k_{hs}, the partition constant of the analyte between the balk solution (aqueous solution) and tangent layer. Both k and k_{hs} are expected to be highly dependent on the temperature of the condensed phase. The second term of p is proportional to m_f, the mass-transfer coefficient of the analyte inside the dispersive solvent. It is expected to be dependent on the nature of dispersive solvent. Parameter q is proportional to both k and m_f and is also related to k_{hs} as described in eq 16. If the temperature of the tangent layer is raised, both k and k_{hs} values will increase and we would expect to see larger p and q. Table 1 lists the parameters p and q obtained from the regressions using eq 21. As expected, both p and q values increase as the temperature of the aqueous phase increases. As temperature was increased from 5 to 22 °C, the q value increased about 2 orders of magnitude. If the transfer rate constant follows an Ahrrenius' form, $k = k_0 e^{\frac{-Ea}{RT}}$ for every temperature increase of 10 °C, k will increase 2-3-fold. K_{hs} is also expected to increase as temperature increases, following a similar form $k_{hs} = k_0 e$. A 2-3-fold increase of k_{hs} is also expected for every 10 °C temperature increase. Therefore, a 2 orders of magnitude increase in q is reasonable for a temperature increase from 5 to 22 °C combining the increases of k and k_{hs}. As for parameter p (eq 15), only the first term of p is proportional to k, which will make the p value increase relatively small as the temperature of the condensed phase increases. Since parameter q is proportional to m_f according to eq 16, different dispersive solvent should have different q values when the same experimental conditions are applied. Table 1 shows that the q value for methanol is more than 5 times larger than that of acetonitrile during a room-temperature tangent layer. Mass transfer inside the methanol is expected to be easier than in the acetonitrile. The larger q methanol compared to acetonitrile is seen as predicted. The difference between the previous model (eq 2) and the new model (eq 21) is dependent upon how fast the analyte molecules can transfer from the balk solution (aqueous solution) to tangent layer. If the analyte transfer is a fast process, a steady-state mass transfer at the two interfaces can be quickly reached. In this case, eq 21 will reduce to eq 2, which describes the dynamic process of tangent layer with a steady-state mass transfer. As the temperature of the balk solution (aqueous solution) increases, the transfer rate of analyte increases, and there should be less difference between eq 21 and eq 2. Figure 3 shows the experimental data fitted with both eq 2 and eq 21. At low balk solution (aqueous solution) temperature, the difference between these two models is large (Figure 3a). As the temperature of the balk solution (aqueous solution) increased to 45°C, there is a very small difference between these two models (Figure 3c). Equation 21 also has the $n \propto c_0$ relationship. This relationship indicates that quantification is feasible using dispersive solvent for tangent layer analysis even before a steady state of mass transfer is reached. This study provides the theoretical base for fast quantitative tangent layer analysis.

Conclusion

the new model provides a good description of the experimental measurements, especially when the transfer rate of analyte from the balk solution (aqueous solution) to tangent layer is slow. As is predicted by the new model, the parameters (p and q) derived from the experimental data vary as the temperature of the balk solution (aqueous solution) changes. As the temperature of the balk solution increases and the transfer rate of analyte molecules increases, the new model also reduces to the previous proposed model, as predicted. The difference in dispersive solvent shows that mass transfer in the methanol is faster than in the acetonitrile.

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