

An experimental method to estimate the mass transfer through the interfacial region of liquid membrane systems

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Abstract

A simple and reliable experimental method is reported to measure the mass transfer resistance through a liquid membrane as found in multiple emulsions for drug controlled release. A straightforward data analysis leads to calculate the mass transfer coefficient corresponding to the crossing of the interfacial region. The method is used to discuss some typical results with both oil and water soluble tracers.

Key words: Controlled release; liquid membrane; mass transfer; multiple emulsion.

Un método experimental para estimar la transferencia de masa a través de la región interfacial de membranas líquidas

Resumen

Se reporta un método experimental para determinar la resistencia en la transferencia de masa a través de una membrana líquida, tal como se encuentra en emulsiones múltiples utilizadas en el suministro controlado de medicamentos. El análisis de los datos permite calcular el coeficiente de transferencia de masa para cruzar la región cercana a la interfase. Se usa el método para discutir algunos resultados con trazadores hidro o liposolubles.

Palabras clave: Emulsión múltiple; liberación controlada; membranas líquidas; transferencia de masa.

Introduction

According to Matsumoto and collaborators (1) the first paper dealing with multiple emulsions may be attributed to Seifriz, back in 1925. The interest in multiple emulsions is relatively recent, particularly because of the potential of such systems to carry out a mass transfer process between two compatible phases through an insoluble

liquid membrane. This has found applications in the controlled release of drugs (2, 3), the separation of hydrocarbons (4, 5), the extraction of metallic ions against the concentration gradient (6, 7) and others (2, 8).

Multiple emulsions involve quite different problems to be dealt with. First their preparation, that is the way to make it (2, 8-10). They were initially found to occur

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when the emulsion so-called catastrophic inversion (11) was driven by a continuous change in composition, generally by excessive addition of the internal phase, as recently documented (12). It was also found that they spontaneously form when emulsifying surfactant-oil-water preequilibrated systems whenever the water-to-oil ratio and formulation compel opposite tendencies, so that both antagonistic requirements are satisfied (13). Of course, they may be prepared by using a sequential addition technique such as first preparing a W/O emulsion, then using it as the internal phase to prepare a O/W emulsion (14)

A problem to be dealt with is that no surfactant is able to stabilize both internal drop and external drop curvatures, since they have opposite signs. A non-equilibrium mechanism has to be provided at one of the interfaces, such as the adsorption of a polymeric surfactant (15). Another way is to increase the viscosity of the external phase using thickener such as carboxymethyl cellulose (16).

Provided that the previously mentioned problems are tackled, the mass transfer of a solute through the liquid membrane has to be controlled. The transfer generally includes the crossing of the first interface from initial phase "i" to liquid membrane phase "m", then the transport through the liquid membrane bulk, then the crossing of the second interface, and finally the transport to the final phase "f" bulk. In this paper, the interfacial region includes the interface and adjacent diffusive layers that are kept to a minimum thickness thanks to appropriate experimental conditions. Transport through the bulk phases, which is ruled out in the present study, may be easily modeled and predicted by diffusive or convective mechanisms (17,18). The mass transfer flux J through an interface area A is driven by a chemical potential difference $\Delta\mu$, which is often written as a concentration gradient or a concentration departure from equilibrium

ΔC . This flux is also written to be proportional to an interfacial transfer coefficient k .

$$J/A = \kappa \Delta\mu$$

$$\text{generally written as } J/A = \kappa \Delta C \quad [1]$$

The gradient ΔC depends upon the equilibrium partitioning between the two phases. If activity coefficients are assumed to be unity, the chemical potential of the solute in the "i" and "m" phase is written as:

$$\mu_i = \mu_i^\circ + RT \ln C_i$$

$$\text{and } \mu_m = \mu_m^\circ + RT \ln C_m \quad [2]$$

$$\text{at equilibrium } \mu_i = \mu_m \quad [3]$$

if the partition equilibrium constant is defined as $K_{eq} = C_m/C_i$, then

$$RT \ln K_{eq} = \mu_i^\circ - \mu_m^\circ \quad [4]$$

K_{eq} depends upon the formulation, i.e. the nature of the "i" and "m" phases and of the solute, as extensively discussed in a recent paper on amphiphile partitioning (19).

When there is a departure from equilibrium, the driving force $\Delta\mu = \mu_i - \mu_m$ may be written as:

$$\Delta\mu = \mu_i^\circ + RT \ln C_i - \mu_m^\circ - RT \ln C_m =$$

$$RT (\ln C_i - \ln C_m/K_{eq}) \quad [5]$$

which by first order expansion in the vicinity of equilibrium, leads to

$$\frac{\Delta\mu}{RT} = \frac{\Delta C}{C} = \frac{(C_i - C_m/K_{eq})}{C_m/K_{eq}} \quad [6]$$

ΔC is thus taken as $C_i - C_m/K_{eq}$, as often done without justification in the literature (17). This implicitly means that the K_{eq}/C_m contribution is included somehow in the transfer coefficient k in equation (1).

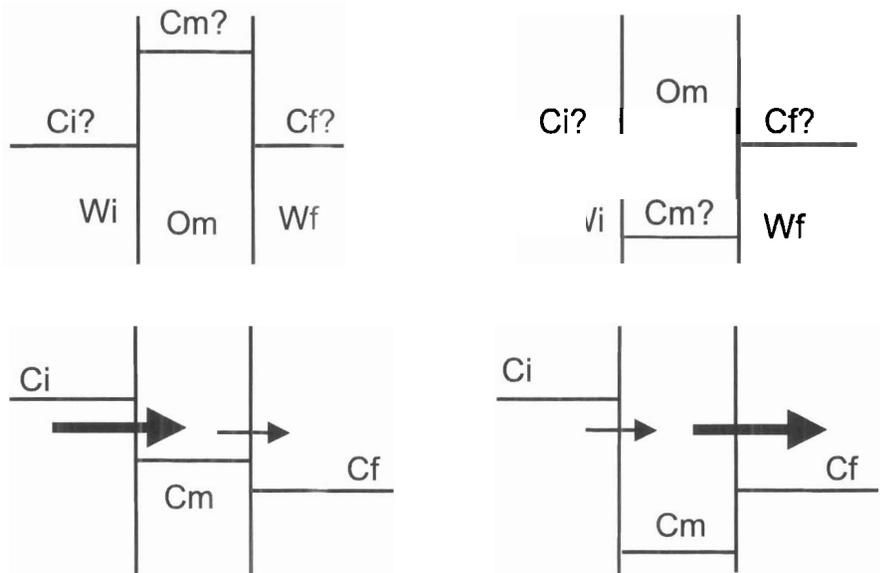


Figure 1. Concentration values in the two extreme cases.

Thus, the unknown in equation (1) is the interfacial transfer coefficient, which will be shown to change drastically from one system to another. The present paper reports on an experimental method to attain an estimate of such coefficient.

Mathematical Model for Mass Transfer

The discussion is carried out on a $W_i/O/W_f$ or a $W_f/O/W_i$ multiple emulsion, which is no restraining as far as the generality of the result is concerned. Both W_i and W_f phases have the same composition, unless otherwise mentioned, with exception of the tracer solute that is located in phase W_i at time zero (initial phase) and is allowed to transfer to phase W_f (final phase) through the liquid membrane phase O_m . A proper stirring process allows to keep all phases homogeneous so that the sole driving forces take place at both interface crossings. In particular this means that the concentration of solute is constant in each phase as shown in Figure 1.

Since phases "i" and "f" are identical, the only driving force is the solute concen-

tration gradient. The solute transfer proceeds from the high concentration C_i , which is $C_i(0)$ at time zero, to the lower C_f , which is zero at time zero. After an infinite time, the two concentrations will reach an equal value so-called $C_{i\infty}$ or $C_{f\infty}$.

Figure 1 upper graphs indicate the two extreme cases in which the solute is more (Figure 1, left) or less (Figure 1, right) soluble in the oil liquid membrane phase (O_m) than in the outside water phases W_i and W_f . In the lower graphs, the bold arrow indicates the easy or rapid interfacial mass transfer in the corresponding upper graph case, while the thin arrow corresponds to the limiting transfer.

The driving force to cross the interface is the departure from the equilibrium concentration. Flux densities per unit interfacial area are written as

$$J_{im}/A_{im} = k_{im} (C_i - C_{ieq}) = k_{im} (C_i - C_m/K_{eq}) \quad [7]$$

$$J_{fm}/A_{mf} = k_{fm} (C_f - C_{feq}) = k_{fm} (C_f - C_m/K_{eq}) \quad [8]$$

where the subscript indicates the direction of transfer. For instance J_{im} is the flux from phase "i" to phase "m". Since C_f will increase from an initial zero value, J_{fm} is negative, which means that the transfer takes place from phase "m" to phase "f". In the present case both transfer areas are equal and noted A, for the sake of simplicity.

During the initial instants $C_i \gg C_{ieq}$ and $C_f \ll C_{feq}$, so that equations [7] and [8] become

$$J_{im} = k_{im} A C_i \quad [9]$$

$$J_{mf} = -J_{fm} \approx -k_{fm} A C_m / K_{eq} \quad [10]$$

The mass balance in phase "f" (with volume V_f) requires that

$$\text{Minimum of } (J_{im} \text{ or } J_{mf}) = V_f \frac{dC_f}{dt} \quad [11]$$

One of the two fluxes is limiting. If the solute is not very soluble in phase "m", then $K_{eq} \ll 1$ and the limiting flux is J_{im} . If the solute is much more soluble in "m" than in phase "i" ($K_{eq} \gg 1$), then a quasi steady state is assumed, i. e., $C_i = C_m / K_{eq}$, and the limiting flux is J_{mf} .

$$J_{mf} \approx -k_{fm} A C_m / K_{eq} \approx -k_{fm} A C_i \quad [12]$$

Equations [9] and [12] indicate that the initial trend is such that

$$\frac{dC_f}{dt} = k_{lim} C_i(0) \frac{A}{V_f} \quad [13]$$

where $C_i(0)$ is the initial value of C_i , and k_{lim} , the interfacial transfer coefficient of the limiting flux, which is k_{im} (respectively k_{fm}) if the solute is less (respectively more) soluble in phase "m" than in the outside phases.

By integrating equation [13], the initial variation of C_f is found to be:

$$C_f = k_{lim} C_i(0) \frac{A}{V_f} t \quad [14]$$

C_f is expected to increase linearly with time, and the proportionality factor includes

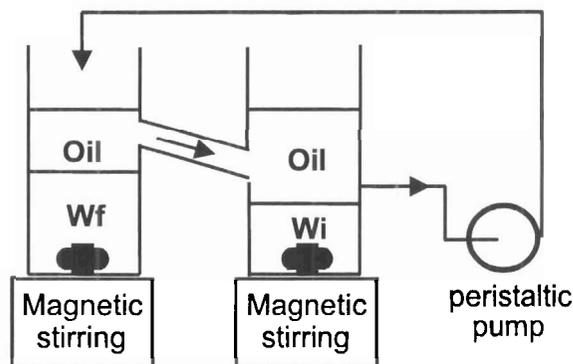


Figure 2. Practical experimental set up.

the initial concentration in phase "i", the limiting interfacial transfer coefficient, and a geometric ratio A/V_f . This initial linear variation of C_f vs. time may be used to estimate the limiting interfacial transfer coefficient.

Experimental Set Up

The mass transfer experiences are carried out in the experimental set up shown in Figure 2. The apparatus essentially consists in two beakers and a communicating tubing which allows the oil phase to overflow by gravity. The oil return to the higher beaker is driven by a peristaltic pump (Masterflex).

There are three different phases: the "initial" water phase (W_i) that contains the tracer at time zero. The (membrane) oil phase (O_m) through which the tracer should cross to attain the "final" water phase (W_f) which initially does not contain any tracer. As shown in Figure 2, the water phases are located at the bottom of the beakers and the oil phase at the top. The two water phases are kept homogeneous by a gentle magnetic stirring. The oil phase is mixed by pumping it from one beaker to the other. Tangential entries are used to minimize the eventuality of emulsification. All three phases are homogeneous at all times. Typical volumes are 200, 180 and 300 mL for phases W_i , O_m and W_f respectively. The experiences are carried out at constant temperature by locating the

two beakers in a isothermal water bath slightly above ambient temperature.

The water and oil phases may contain surfactant and/or electrolyte in variable nature and amount in order to adjust the physicochemical formulation. In a typical experience, the water phase is split between W_i and W_f , then the tracer solute is added to W_i so that its initial concentration $C_i(0)$ is 5000 ppm unless otherwise stated. Then, the oil phase is gently poured over W_f until it overflows above W_i . Immediately, the stirrers and the peristaltic pump are put to work, as the experience begins. Such a start up process takes typically 3 to 5 min. Sampling of the different phases, particularly the receiving water phase W_f , is typically carried out every 15 min, and the tracer concentration is determined by UV absorbance with a spectrophotometer set to detect the benzene ring contained in the tracer.

Two kinds of systems are studied. In the first kind, toluene sulfonate (p-toluene sulfonic acid, sodium salt, p. a. from Fluka), noted TSNa, is selected as a water soluble tracer. The effect of the oil phase polarity is investigated by selecting either n-octane or 1-octanol. In some experiments, the oil phase contains 5 wt.% of a lipophilic non-ionic surfactant of the sorbitan ester type (SPAN-80 from ICI).

In the second kind of systems, phenol (p.a. from Merck) is selected as the solute tracer. It is much more soluble in the oil phase than TSNa, but it is also soluble in the water phase. The oil phase is n-heptane. Two systems are studied. One contains a mixture of surfactants: hexadecyl-octadecyl, HSS (25%) and dodecyl, DDSS (75%) sulfate sodium salts (0.06 wt.%) and 2-butanol (2 vol.%). The salinity of the water phase ranges from 0 to 19 wt.% NaCl. The other system contains a tetradecyl trimethyl ammonium bromide, TTAB, (0.03 wt.%) and 2-butanol (50%) and n-pentanol (50%), with a salinity range in the water phase from 0 to 14 wt.% NaCl, in order to vary the physico-

chemical formulation. The oil-water system is contacted and left to pre-equilibrate for 48 h before pouring the water and oil phases in the apparatus. Phenol is added to water phase W_i just before performing the experiment.

Experimental Results and Data Processing

The mass transfer experiments are carried out in the same way for all systems. Figure 3 shows the variation of C_i and C_f with time for either anionic or cationic surfactant systems containing phenol as tracer. In both cases the physicochemical formulation is such that the phenol preferably partitions into the oil phase (m), so that the case corresponds to $K_{e,q} > 1$ (Figure 1 left).

The data indicate that there is a transfer from "i" to "f", until both C_i and C_f reach an asymptotic equilibrium value after a few hours. It is worth noting that the initial variation of C_f with time is quite linear, which corroborates the model prediction, not only for the first instants but during a few hours.

In both cases C_i decreases more rapidly than C_f increases, because there is a phenol accumulation in the oil phase according to the partition equilibrium. The asymptotic value is essentially attained after 150 min in Figure 3 right case, while it takes about twice this time in Figure 3 left case. It may be conjectured that the transfer is quicker in Figure 3 left case. It is worth noting that a similar conclusion may be also deduced by comparing the early variation of either C_f or C_i , i.e., the tangent slope near origin of time. For now it is just a qualitative comment. A closer analysis of the measurement criterion will be presented later.

Figure 4 left plot indicates several cases in which the solute to be transferred is TSNa, which is much more soluble in water than in oil ($K_{e,q} \ll 1$). The situation corresponds to Figure 1 right case. Because of the

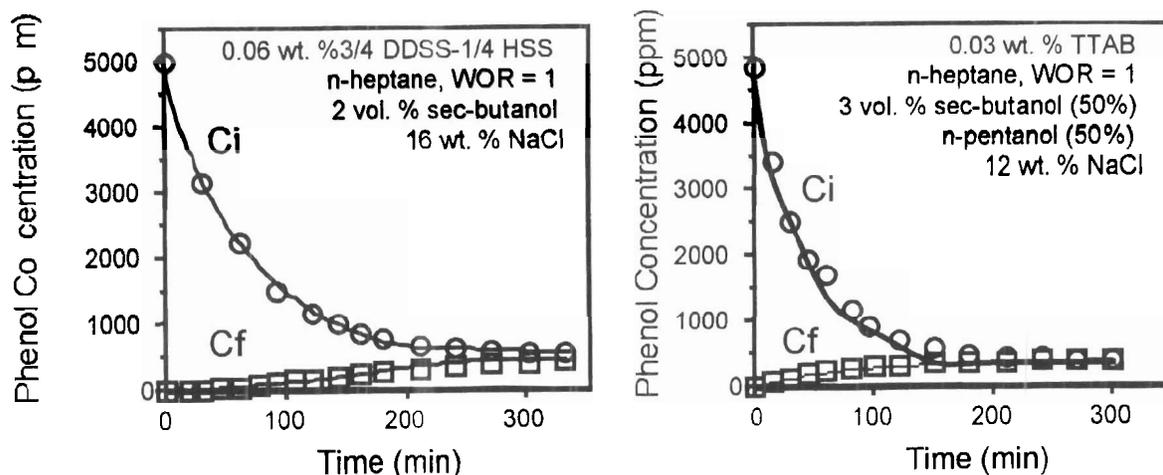


Figure 3. Variation of tracer concentrations C_f and C_i , respectively in W_f and W_i water phases as times elapses.

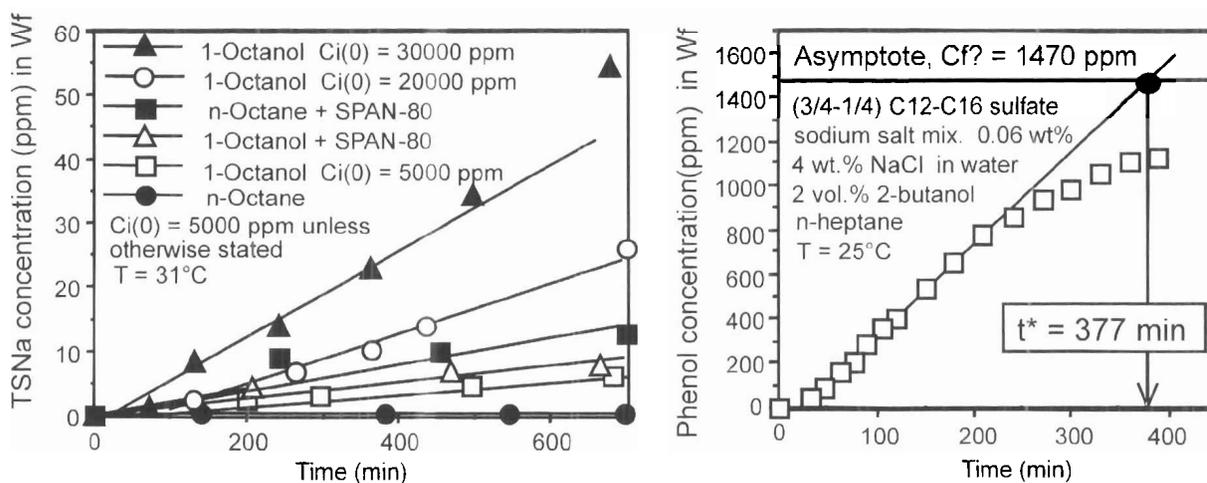


Figure 4. Early variation of C_f in several cases.

very low solubility of TSNa in the oil phase, the transfer proceeds very slowly, and there is essentially no significant decrease in C_i during the span of the reported experiments. Thus only C_f is plotted versus time. As before it is seen that C_f initial variation is linear, but it takes place at a much lower rate than in the phenol case.

A straightforward comparison based upon the early trend slope indicates that the interfacial transfer considerably varies with the nature of the oil phase.

When the oil phase changes from pure octane to octanol, the transfer rate is increased several times. A similar augmentation occurs if a lipophilic surfactant (SPAN-80) is added to octane. In both cases the TSNa partitioning becomes less unfavorable to the "m" phase as this phase gets more polar, a situation that increases the transfer towards oil according to equations [1] and [6]. Adding the same surfactant to octanol does not produce a major change, probably because it does not significantly affect the polarity of the oil phase.

As a matter of fact all such changes result in an interfacial tension reduction that seems to be the fundamental reason for the transfer increase (20).

By comparing the plots for systems originally containing octanol oil phase and 5000, 20000 and 30000 ppm of TSNa in W_i , it is verified that the slope is proportional to the original concentration $C_i(0)$, as expected from equation (14). This corroborates that k_{lim} does not depend upon initial tracer concentration.

Figure 4 right plot is a blow up of the initial C_f variation in a case in which the phenol solute is just slightly more soluble in water than in oil, i. e., where K_{eq} is close to unity. In this case the linearity extends to almost four hours, a time at which a considerable amount of tracer has been transferred. In such cases both interface crossings could limit the overall transfer. Fortunately, if both transfers are linearly depending upon C_i , then the overall transfer would be too.

Note that there is a short initial lag time before C_f starts increasing. This is presumably due to some initial delay in interfacial equilibration and convective transport of the oil phase from one W/O interface to the other. In other words it is just a slight shift in time origin, which is neglected in practice.

Criteria to Estimate the Interfacial Transfer

The previous discussion has shown that the initial dC_f/dt slope is a measurement of the limiting interfacial transfer rate. Equation [14] indicates that the transfer is proportional to the solute concentration $C_i(0)$, which also means that it is proportional to the concentration in any phase at equilibrium, in particular the asymptotic value $C_{f\infty}$. In effect, a straightforward mass balance of solute leads to the following proportionality between $C_{f\infty}$ and $C_i(0)$:

$$\frac{C_{f\infty}}{C_i(0)} = \frac{V_i}{(V_i + V_f + K_{eq} V_m)} \quad [15]$$

The initial dC_f/dt slope divided by $C_{f\infty}$ is thus preferred because it takes into account the fact that the solute is more or less soluble in the final water phase (K_{eq}), as well as the relative phase volumes. This criterion is proportional to k_{lim} , and the proportionality constant only depends upon geometric factors and equilibrium constant as indicated in equation [16].

It is worth noting that the slope dC_f/dt divided by $C_{f\infty}$ is the inverse of the time t^* at which the original tangent cuts the asymptote (Figure 4, right).

Because t^* is the time at which the final $C_{f\infty}$ value would be attained if the original transfer rate were maintained, it has a very significant meaning as far as the transfer rate is concerned.

$$\frac{dC_f / C_{f\infty}}{dt} = \frac{1}{t^*} = \frac{k_{lim} A C_i(0)}{C_{f\infty} V_f} = \frac{k_{lim} (V_i + V_f + K_{eq} V_m) A}{V_i V_f} \quad [16]$$

Using equation [16], k_{lim} was calculated for different systems. The corresponding values are shown in Table 1.

It is readily seen that the change of oil from octane to octanol increases the transfer rate of TSNa almost 30 times, a situation which is also attained by adding a lipophilic surfactant in the octane phase. No significant change is attained with such a surfactant if the oil phase is already polar, e.g., octanol. Phenol transfer through heptane is about ten thousand times faster than TSNa and it is found to depend upon the physico-chemical formulation.

Conclusions

A very simple experimental set up allows to estimate in a reliable way the limiting

Table 1
 k_{lim} value for different systems

Systems with TSNA tracer				
Oil phase	n-Octane	n-Octane + 5% SPAN80	1-Octanol	1-Octanol + 5% SPAN80
k_{lim} (m/s)	$8 \cdot 10^{-11}$	$4.5 \cdot 10^{-9}$	$2.3 \cdot 10^{-9}$	$2.8 \cdot 10^{-9}$

In the octane and octanol cases the receiving phase (W_r) is distilled water.

In the octane + SPAN and octanol + SPAN cases, the receiving water phase contains 1 wt.% TWEEN 20.

In all cases the initial water phase (W_i) contains 5000 ppm of TSNa.

Systems with phenol tracer					
Cationic Systems			Anionic Systems		
wt.% NaCl	2	12	14	4	16
k_{lim} (m/s)	$7.5 \cdot 10^{-7}$	$5 \cdot 10^{-7}$	$2.7 \cdot 10^{-7}$	$5.3 \cdot 10^{-7}$	$2.2 \cdot 10^{-7}$

Cationic systems contain tetradecyl trimethyl ammonium bromide TTAB, (0.03 wt.%) and 2-butanol (50%) and n-pentanol (50%).

Anionic systems contain a mixture of hexadecyl-octadecyl HSS (25%) and dodecyl DDSS (75%) sulfate sodium salts (0.06 wt.%) and 2-butanol (2 vol.%).

In all cases, the initial aqueous phase (W_i) contains 5000 ppm of phenol.

overall interfacial transfer coefficient in a W/O/W liquid membrane system, such as those found in multiple emulsions. Experimental evidence shows that this transfer coefficient could vary widely, depending on the nature of the oil/water system, the nature of the solute to be transferred, and the physico-chemical formulation, particularly the presence of surfactant.

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