Solubility and Partitioning Behavior of Surfactants and Additives Used in Bioprocesses

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For rapid development of initial solvent extraction processes, knowledge of the solubility and partition behavior of surfactants and solubility enhancers is required. Unfortunately, experimental solubility data for many common surfactants and solubility enhancers in aqueous and organic solvents have not been reported. There are also few references to the partitioning behavior of these additives between water and common extraction solvents. In this paper, the solubility and partition coefficients were measured at 293 K for a range of additives in solvent systems of varying polarities and classes: ethyl acetate, isobutyl alcohol, toluene, methyl ethyl ketone, methyl *tert*-butyl ether, and 0.2 mol·L^{-1} potassium phosphate buffer (pH 7). The additives chosen were based on common usage and represent a cross-section of the surfactant classes: UCON LB-625, P2000, Triton X-100, sodium dodecyl sulfate (SDS), Tween 20, Tween 80, hexadecyltrimethylammonium bromide (CTAB), ammonium sulfate, and methyl-β-cyclodextrin. The partition behavior of these additives (except Tween 20) was also investigated. The effect of ionic strength, pH, and cosolvents on the partition coefficient was also determined to provide a database for surfactant and solubility enhancer behavior in order to allow for rapid optimization of initial extraction processes. The solubility results showed that the antifoams were extremely soluble in the organic solvents but had limited solubility in water. The nonionic surfactants were soluble in all solvents tested. The anionic surfactant was soluble in all solvents tested, with the exception of toluene. The cationic surfactant and ammonium sulfate had limited solubility in most solvents. The methyl-β-cyclodextrin had varying degrees of solubility depending on polarity. The partition results can largely be predicted from the solubility data, with the exception of the nonionic surfactants. For all of the compounds that partitioned, the behavior could also be predicted based on solvent polarity, with larger partition coefficients for the more polar solvents. These data can be used to design initial extraction processes containing these additives and, by analogy, for other related additives as well.

Introduction

With the use of high throughput screening to identify discovery leads, the bottleneck for speed to market is process development, highlighting the need for rapid production of bioprocess intermediates for biocatalysis and fermentation. This in turn highlights the need for rapid development of purification processes for these intermediates. For many biocatalysis isolations, the initial step is solvent extraction to remove the product from the aqueous reaction mixture and into the organic solvent for further purification. Solvent extraction has been widely used in the chemical and process industries and is important for initial recovery of product from aqueous streams. It has been used for certain classical bioprocess applications such as penicillin extraction;[1] however, solvent extraction is less developed for biologically produced products. While the fundamental mechanisms are well understood, extraction performance for many practical systems of interest are still poorly characterized,[2] especially the extraction behavior of surfactants and antifoams. Surfactants and antifoams, if carried through the isolation, can foul filtration membranes,[3] decrease resin capacity, and be difficult to remove. Work has been done to understand the impact of biosurfactants in fermentation broths,[4] but there are few examples in the literature on the behavior of additives in free enzyme systems for bioconversions. Surfactants have been used in many aqueous systems to enhance the solubility of nonpolar solutes.[5] In bioconversions, the hydrophobic substrate is sequestered within aggregates of surfactant molecules, changing the effective concentration available for reaction.[6]

For rapid process development of initial solvent extraction processes for bioconversions, knowledge of the solubility and behavior of surfactants and solubility enhancers is required. Unfortunately, few experimental solubility data for many common surfactants and solubility enhancers in aqueous and organic solvents have not been reported. Also, there are few literature reports on the partitioning behavior of these additives between water and common extraction solvents. In this paper, the solubility and partition coefficients at 293 K were measured for a range of additives in solvent systems of varying polarities. The effect of ionic strength, pH, and cosolvents on the partition coefficient was also determined to provide a database for surfactant and solubility enhancer behavior. The purpose of this database is to accelerate process development by allowing for rapid optimization of initial extraction processes.

Experimental Section

Materials and Methods. Eight additives were investigated. These additives were chosen to encapsulate a range of surfactant classes as well as to characterize the behavior of additives

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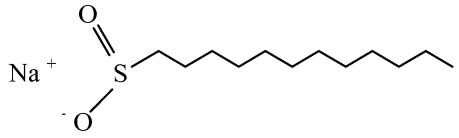
Table 1. Additive Manufacturer Data and Properties

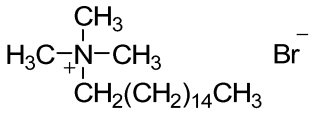
name	manufacturer (catalog no.)	class	MW
UCON LB-625	Union Carbide (Houston, TX)	antifoam	1500
P2000	Dow (Midland, MI)	antifoam	2000
hexadecyltrimethylammonium bromide (CTAB)	Fluka (Milwaukee, WI) (52370)	cationic	365
sodium dodecyl sulfate (SDS)	Biorad (Hercules, CA) (161-0418)	anionic	289
tert-octylphenoxypoly ethoxyethanol (Triton X-100)	Sigma (St. Louis, MO) (X-100)	nonionic	625
polyoxyethelyene sorbitan monolaurate (Tween 20)	Sigma (St. Louis, MO) (P-1379)	nonionic	1310
polyoxyethelyene sorbitan monooleate (Tween 80)	Croda (East Yorkshire, UK)	nonionic	1310
ammonium sulfate	Fisher (Hampton, NH) (BP212R-1)	solubility enhancer	132
methyl-β-cyclodextrin (Cavasol W7 M Pharma)	Wacker Biochem (Adrian, MI)	solubility enhancer	1310
potassium phosphate	Fisher (Hampton, NH) (P285-3)	salt	136

commonly used in biocatalysis and fermentation. Their basic properties, including manufacturer information, are summarized in Table 1, and their chemical structures are given in Figure 1.

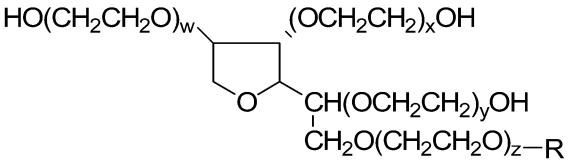
Solubility Measurements. All experimental studies employed solvents of HPLC grade from Fisher Scientific (Pittsburgh, PA) or EM Science (Gibbstown, NJ). For the solubility measurements of the various additives, each was added to 5 mL of solvent by volume until the saturation point was reached, where saturation was defined as incidence of a second phase (solid or liquid). Excess amounts of additive were added to ensure maximum solubility where appropriate. The solutions were kept at 292 to 293 K while being shaken until equilibrium was approached. Solutions were sampled after 4 h and 16 h to compare concentrations and ensure that enough time had elapsed to approach equilibrium. Additives with limited solubility in the solvent were centrifuged at 4000 rpm for 5 min to ensure complete separation of the two phases. For additives with high solubility in the solvent, experimentation was discontinued upon reaching 6 mL of additive for 5 mL of solvent, which corresponds to approximately 500 g·L^{-1}. Samples were analyzed by reversed-phase HPLC and total solids measurements.



Sodium dodecyl sulfate (SDS).
Anionic surfactant



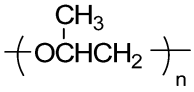
Hexadecyltrimethylammonium bromide (CTAB)
Cationic surfactant



Sum of w+x+y+z = 20

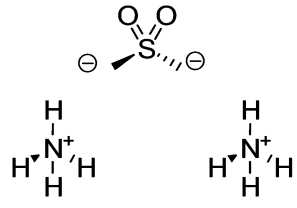
Tween 20 (monolaurate) R = $C_{11}H_{23}CO_2^-$
Tween 80 (monooleate) R = $C_{17}H_{33}CO_2^-$

Polyoxyethlyene sorbitan (Tween®)
Nonionic surfactant

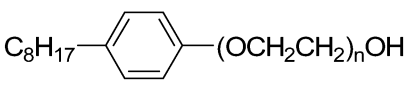


P2000 (MW=2000)
UCON LB-625 (MW=1500)

UCON® and P2000®
Antifoams

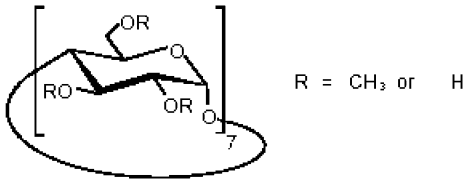


Ammonium Sulfate $(NH_4^+)_2SO_4^{2-}$
Solubility enhancer



n = 10

t-octylphenoxypoly ethoxyethanol (Triton® X-100)
Nonionic surfactant



Methyl-β-cyclodextrin (Cavasol®)
Solubility enhancer

Figure 1. Structures of additives in bioprocesses.

Partitioning Experiments. At equilibrium, $[X]_{aq} \leftrightarrow [X]_{org}$, the distribution of the solute between the two phases is given by the partition coefficient (K_p):

$$K_p = \frac{[X]_{org}}{[X]_{aq}} \quad (1)$$

where $[X]_{org}$ and $[X]_{aq}$ are the concentrations of the solute in the organic and aqueous phases, respectively. For this study, we are measuring a simple partition coefficient at constant temperature and pressure, not attempting a more complex analysis of partitioning behavior. A 3 g·L^{-1} additive solution was prepared in 50 mL of 2 × 10^{-3} mol·L^{-1} potassium phosphate buffer using a 150 mL glass bottle. Adjustments of the pH and salt concentration of the aqueous phase were performed prior to the addition of solvent. The additive in buffer was then extracted with an equal volume of organic solvent. Cosolvents were added to the two-phase mixture where necessary. The mixture was agitated and separated with a separation funnel. The organic and aqueous layers were collected and analyzed by HPLC with ELS detection (Sedex 55) and by total solids. If the pH was adjusted before extraction, it was measured again after extraction. In all cases, the post-extraction pH remained unchanged. Only glass vessels were used due to possible adsorption of the additives to plastic. CTAB and ammonium sulfate were analyzed only by total solids as these compounds were not retained on the reversed-phase column.

Analytical Methods

HPLC Analysis. The concentrations of the following additives were determined by reversed-phase HPLC with ELS detection: P2000, UCON LB-625, Triton X-100, Tween 20, Tween 80, SDS, and methyl-β-cyclodextrin. Analytical measurements were performed on a Hewlett-Packard HP-1100 HPLC system (Hewlett-Packard, Palo Alto, CA) composed of a quaternary pump, column thermostat, and evaporative light scattering detector. The data analyses were performed using ChemStation Software Rev. A.05.04 and a Windows 95 (Microsoft, Eugene, OR) operating system. The Evaporative Light Scattering Detector, Sedex 55 ELSD (Sedere, Lawrenceville, NJ), was connected to the HPLC to allow for detection of nonvolatile solutes without chromaphores. The ELS detector measured the amount of light scattered by nonvolatile particles in the effluent stream that had been dried through evaporation. The three stages common to all ELS detectors are nebulization, effluent evaporation, and detection (Figure 2).[7]

The HPLC method employs a PLRP-S column (Phenomenex, Torrance, CA) with a particle size of 5 μm and a pore size of 100 Å. This packing was selected as it has been successfully used with polysorbates and other detergents.[8] The column had dimensions of 150 × 4.6 mm i.d. and was maintained at 298 K. The two mobile phases were HPLC-grade water (A) and acetonitrile (B). An elution gradient from 90% A and 10% B to 10% A and 90% B over 30 min was used as the base assay. The gradient and time were adjusted depending on the retention time of the various additives in an attempt to minimize assay time. The ELS detector parameters were set at 333 K, 2.5 bar, and gain 10 or 11. The samples were dried down under nitrogen and re-suspended in an appropriate volume of methanol prior to injection in order to ensure that the sample fell within the range of the calibration curve. Calibration curves were prepared by serial dilution from a stock solution of 2 g·L^{-1} additive in methanol. The calibration range of 0.5 to 2 g·L^{-1} was chosen based on the saturation of the ELS detector. Calibration curves

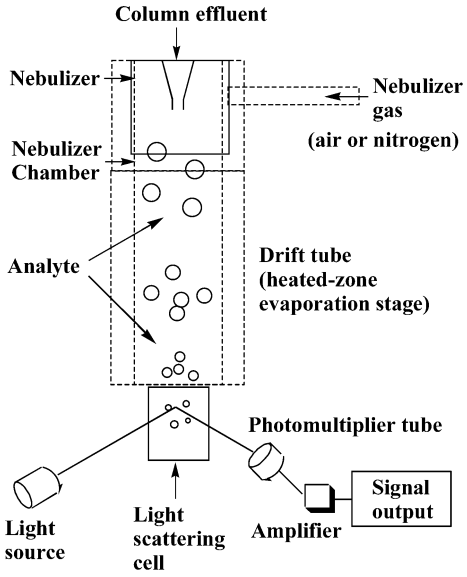


Figure 2. Schematic of evaporative light scattering detector.[7]

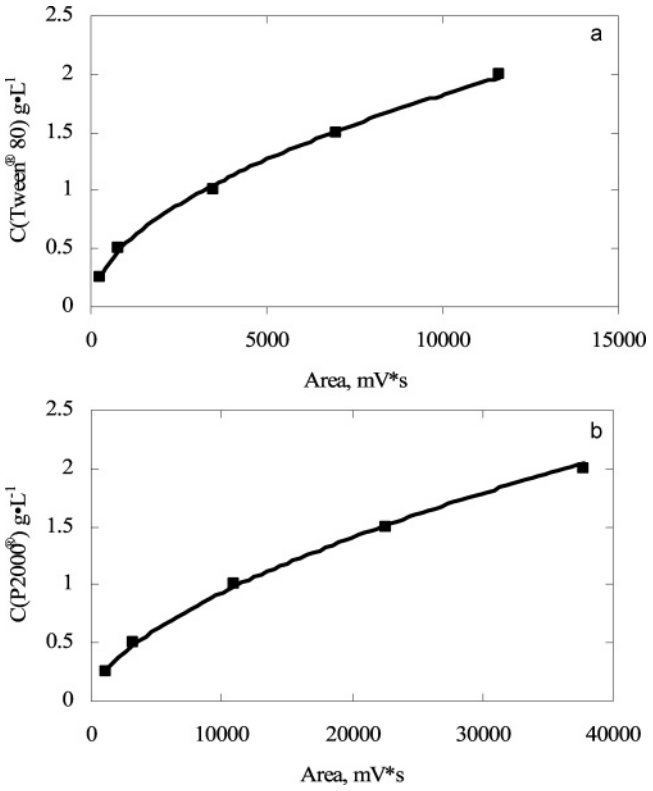


Figure 3. ELSD calibration curves of P2000 and Tween 80 using a power law function. (a) The P2000 fit was $C = 0.0039 \times \text{area}^{0.5935}$ with $\sigma^2 = 0.97$. (b) The Tween 80 fit was $C = 0.0143 \times \text{area}^{0.5265}$ with $\sigma^2 = 0.97$.

were constructed using a power law fit for each compound; examples for P2000 and Tween 80 are shown in Figure 3. The estimated limit of quantification for the HPLC method was 0.25 g·L^{-1} for all additives. The measurements of additive concentration by HPLC with ELS detection had an uncertainty of 3%.

Total Solids Analysis. The concentration of CTAB and ammonium sulfate was determined by the total solids method as these compounds were not retained on the reversed-phase column. The total solids concentration measurement was performed by evaporating the solvent from a previously weighed sample of solution (5 mL) in a convection oven at 333 K for 12 h or until a constant mass was obtained. The total solids measurement was calculated by dividing the mass difference

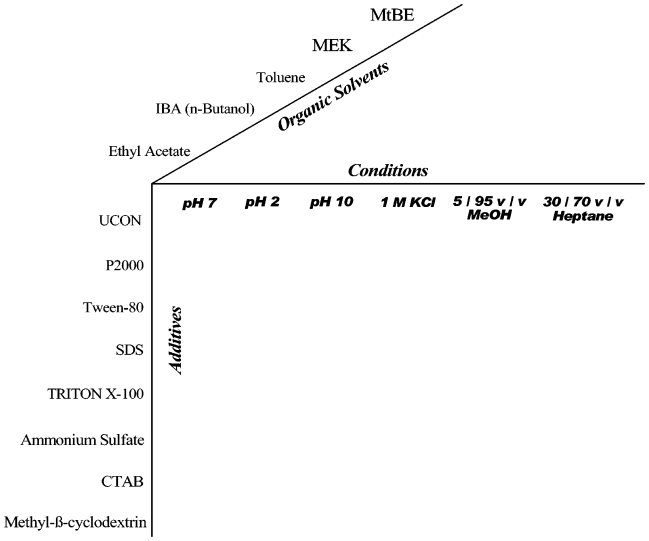


Figure 4. Experimental design of additive partitioning study.

by the sample volume and had an uncertainty of 1%. The estimated limit of quantification for the total solids method was 0.5 $g \cdot L^{-1}$.

Results and Discussion

This work was carried out to evaluate the solubility and partitioning behavior of common additives with respect to solvent system, extraction conditions, and additive type. The study followed a matrix approach using representative additives and solvents, which is shown in Figure 4. The solvents were chosen to represent a range of polarity and solvent class. The solvents used were ethyl acetate (EtOAc), isobutyl alcohol (IBA), toluene, methyl ethyl ketone (MEK), methyl *tert*-butyl ether (MTBE), and 2×10^{-3} $mol \cdot L^{-1}$ potassium phosphate buffer (pH 7). The additives chosen were based on common usage and represent a cross-section of the surfactant classes.

The solubility was determined for nine additives: UCON LB-625, P2000, Triton X-100, sodium dodecyl sulfate (SDS), Tween 20, Tween 80, hexadecyltrimethylammonium bromide (CTAB), ammonium sulfate, and methyl-β-cyclodextrin. The partition behavior of eight of these additives (except Tween 20) was also investigated, varying the extraction parameters to examine the effect of pH, ionic strength, and addition of cosolvents. The partition coefficient was determined in the same organic solvents extracting from a 2×10^{-3} $mol \cdot L^{-1}$ potassium phosphate buffer under six extraction conditions: pH 7, pH 2, pH 10, and with the addition of 1 $mol \cdot L^{-1}$ KCl, 5/95 v/v methanol in organic solvent, or 30/70 v/v heptane in organic solvent. The latter three conditions were all investigated at pH 7.

Solubility Results. Experimental solubility data for the range of additives in organic solvent at room temperature (292 to 293 K) are presented in Table 2. The antifoams (UCON LB-625 and P2000) were extremely soluble in the organic solvents (>500 $g \cdot L^{-1}$) but had limited solubility in water from 3 to 15 $g \cdot L^{-1}$. Both antifoams have the same structure but differ by chain length. The water insolubility is due to their many hydrocarbons and their limited capacity for hydrogen bonding (a single terminal alcohol). However, the oxygen in the repeating oxypropylene groups gives them some limited solubility in aqueous solutions acting as a hydrogen bond acceptor. Therefore, P2000 (MW 2000), which has more repeats than UCON LB-625 (MW 1500), has five times the aqueous solubility.

The nonionic surfactants (Triton X-100, Tween 80, and Tween 20) were extremely soluble in all solvents due to the ability to act as both hydrogen bond donors and acceptors. The anionic surfactant (SDS) was very soluble in all solvents, except toluene due to the polarity of its headgroup. In toluene, the SDS self-associated and solidified. The cationic surfactant (CTAB) had a low solubility in the less polar solvents due to its ionic nature but had limited solubility in the more polar solvents with a maximum of 30 $g \cdot L^{-1}$ in IBA. Ammonium sulfate was not soluble in organic solvents due to its ionic nature. Cyclodextrin has a very high solubility in both IBA and water (>1500 $g \cdot L^{-1}$) due to its ability to hydrogen bond but had more limited solubility in the other solvents, which is consistent with the manufacturer's data.

Partitioning Results. For the purposes of this discussion, the polarity of a solvent is defined as its overall solvation ability, which depends on all specific and nonspecific interactions. While solvent polarity is usually expressed as a physical property such as dielectric constant and dipole moment, this approach is inadequate as it does not account for the specific interactions between solvent and solute molecules such as hydrogen bonding and electron pair donor/acceptor interactions.[9] These experiments were designed by defining solvent polarity using the solvent polarity parameter (E_T^N) proposed by Reichardt and Dimroth, which takes into account the various interactions.[10] This parameter is based on the normalized solvent-induced shifts of the lowest energy absorption bands of certain solvatochromic indicators in the ultraviolet−visible spectral region.[11] The polarity parameter as well as the dielectric constant at 293 K and the dipole moment are given for common solvents in Table 3.[10]

The partition behavior of the eight additives was investigated, varying the extraction parameters to examine the effect of pH, ionic strength, and addition of cosolvents (methanol and heptane). The partition behavior in the five organic solvent extraction systems was examined at the following conditions: pH 7, pH 2, pH 10, 1 $mol \cdot L^{-1}$ KCl, 5/95 v/v methanol in organic solvent, and 30/70 v/v heptane in organic solvent. The pH adjustments were performed using 50% sulfuric acid and 50% sodium hydroxide prior to the addition of solvent. The pH of each system was also confirmed after the extraction. All extractions were two-phase systems.

Values of K_p for all additives and extraction conditions measured are reported in Table 4 for nonionic surfactants, in Table 5 for methyl-β-cyclodextrin, and in Table 6 for charged surfactants. The antifoams (UCON LB-625 and P2000) parti-

Table 2. Solubility of Additives in Toluene, Methyl *tert*-Butyl Ether (MtBE), Ethyl Acetate (EtOAc), Methyl Ethyl Ketone (MEK), Isobutyl Alcohol (IBA), and Water from T = 292 to 293 K

	solubility/$g \cdot L^{-1}$ in additive								
solvent	UCON LB625	P2000	Triton X-100	Tween 80	Tween 20	SDS	ammonium sulfate	CTAB	methyl-β-cyclodextrin
toluene	>581	>617	>649	>648	>671	0.3	0.8	0.0	0.6
MtBE	>581	>617	>649	>648	>671	>588	0.4	0.0	1.6
EtOAc	>581	>617	>649	>648	>671	>588	0.8	0.0	21.0
MEK	>581	>617	>649	>648	>671	>588	0.2	1.3	574
IBA	>581	>617	>649	>648	>671	>588	0.6	30.7	>1500
water	3.4	15.5	>865	>1080	>671	>588	532	3.1	>1500

Table 3. Polarity Parameters for Common Solvents.[10] [a]

solvent	polarity parameter, $E_T^N \times 100$	relative permittivity (293 K)	dipole moment, *D*
heptane	1.2	1.924	0.0
toluene	9.9	2.38	0.4
MtBE	14.8	4.5	1.2
EtOAc	23	6.02	1.7
MEK	32.7	18.5	2.8
acetone	35.5	20.6	2.9
acetonitile	46	37.5	3.2
IBA	55.2	17.7	1.7
methanol	76.2	32.6	1.7
water	100	79.7	1.9

[a] The polarity parameter (E_T) is obtained from the peak wavenumber of the longest wavelength charge transfer adsorption band of the betaine indication 2,6,-diphenyl-4-(2,4,6-triphenyl-1-pyridine)phenoxide in dilute solution of the solvent. This parameter is normalized by the following equation: $E_N^T[E_T(\text{solvent}) - E_T(\text{tetramethylsilane})]/[E_T(\text{water}) - E_T(\text{tetramethylsilane})]$.[11]

tioned into the organic for all solvents under all conditions ($K_p \approx \infty$) due to their low solubility in water. Ammonium sulfate remained in the aqueous phase for all solvents under all conditions ($K_p = 0$); therefore, these additives are not included in the tables.

The uniform high solubility of the nonionic surfactants in both aqueous and organic solvents makes it difficult to anticipate their partitioning behavior. As shown in Table 4, the values of the partition coefficients for the two nonionic surfactants (Triton X-100 and Tween 80) differed under the same conditions, but their overall behavior was similar. The nonionic surfactants favored the more polar organics due to their ability to participate in hydrogen bonding as acceptors. This effect could also be due to the higher water content in MEK (12 mass fraction) and IBA (15 mass fraction). At 30/70 v/v heptane added to the organic phase, both partition coefficients are significantly reduced as the organic phase is dewatered and becomes more nonpolar. Triton X-100 partitioned to a greater degree into the polar solvents given the magnitude of the coefficients, as shown in Figure 5. This is due to the greater number of alcohol groups and therefore stronger polarity of Tween 80, which favors the aqueous phase, as well as the hydrophobic tail of Triton X-100, which will favor the organic phase. While the overall trend was toward an increase in the partition coefficient as the organic solvent polarity increased, an increase was also observed in methyl *tert*-butyl ether relative to the other nonpolar solvents. This is possibly due to the ether−ether interactions between the oxypropylene chains and the solvent. For the nonpolar solvents, there were no substantial effects from the pH change or from the additions of salt and cosolvents, respectively. The deviations from the K_p at pH 7 (0.62) for the other pH values (K_p values of 0.20 and 0.10 for pH 2 and pH 10, respectively) are comparable to the partition behavior seen with the addition of 1 mol·L^{-1} KCl (K_p 0.21), which suggests that these differences are a salt effect.

Table 5 shows the partition coefficients determined for methyl-β-cyclodextrin under the various conditions; the data are plotted as a function of the polarity parameter (E_T^N) in Figure 6. Cyclodextrin has a closed circular structure of glucose molecules. The glycoside oxygen forming the bond between the adjacent glucose monomers and the hydrogen atoms lining the cavity give it its characteristic hydrophobic core. The methyl-β-cyclodextrin partition coefficient increases as a function of solvent polarity under all conditions. While pH does not significantly affect the partitioning as a function of polarity with the exception of IBA, both salt addition and heptane addition

Table 4. Partition Coefficients for the Extraction of Nonionic Surfactants Tween 80 and Triton X-100 with Organic Solvents under Various Conditions at $T = 294$ K

		partition coefficient, K_p, in solvent				
additive	extraction condition	toluene	methyl *tert*-butyl ether	ethyl acetate	methyl ethyl ketone	isobutyl alcohol
Tween 80	pH 2	0.00	0.00	0.19	1.01	1.92
	pH 7	0.11	1.03	0.22	1.11	3.41
	pH 10	0.00	0.62	0.18	2.00	0.26
	1 M KCl	0.00	0.00	0.00	1.20	0.41
	5/95 v/v MeOH[a]	0.00	0.00	0.17	1.17	2.71
	30/70 v/v heptane[b]	0.00	0.00	0.00	0.00	0.45
Triton X-100	pH 2	0.20	1.86	0.42	28.40	4.95
	pH 7	0.62	4.89	0.67	42.84	6.49
	pH 10	0.10	1.36	0.33	0.69	24.28
	1 M KCl	0.21	1.37	0.14	19.91	57.98
	5/95 v/v MeOH[a]	0.16	1.67	0.74	27.02	94.34
	30/70 v/v heptane[b]	0.17	0.46	0.36	2.92	1.01

[a] Solvent ratio of 5/95 methanol in organic phase. [b] Solvent ratio of 30/70 heptane in organic phase.

Table 5. Partition Coefficients for the Extraction of Methyl-β-cyclodextrin (Cavasol W7 M Pharma) with Organic Solvents under Various Conditions at $T = 294$ K

		partition coefficient, K_p, in solvent				
additive	extraction condition	toluene	methyl *tert*-butyl ether	ethyl acetate	methyl ethyl ketone	isobutyl alcohol
methyl-β-cyclodextrin	pH 2	0.77	0.90	1.14	1.45	2.09
	pH 7	0.13	0.16	0.65	0.90	1.52
	pH 10	1.18	1.23	1.34	1.66	5.31
	1 M KCl	1.31	1.32	1.64	1.73	3.52
	5/95 v/v MeOH[a]	0.92	0.88	0.54	0.38	0.32
	30/70 v/v heptane[b]	0.94	1.00	2.23	3.82	5.10

[a] Solvent ratio of 5/95 methanol in organic phase. [b] Solvent ratio of 30/70 heptane in organic phase.

Table 6. Partition Coefficients for the Extraction of Charged Surfactants SDS and CTAB with Organic Solvents under Various Conditions at T = 294 K

		partition coefficient, K_p, in solvent				
additive	extraction condition	toluene	methyl *tert*-butyl ether	ethyl acetate	methyl ethyl ketone	isobutyl alcohol
SDS	pH 2	0.00	0.18	8.49	5.40	13.36
	pH 7	0.00	0.33	15.89	7.88	22.03
	pH 10	0.00	0.51	3.40	11.39	17.28
	1 M KCl	0.00	3.13	13.96	10.26	14.42
	5/95 v/v MeOH[a]	0.00	0.52	11.07	9.34	43.44
	30/70 v/v heptane[b]	0.00	0.00	3.71	1.31	7.18
CTAB	pH 2	0.00	0.00	0.00	0.00	10.60
	pH 7	0.00	0.00	0.00	0.00	17.80
	pH 10	0.00	0.00	0.00	0.00	8.98
	1 M KCl	0.00	0.00	0.00	0.00	0.00
	5/95 v/v MeOH[a]	0.00	0.00	0.00	0.00	0.71
	30/70 v/v heptane[b]	0.00	0.00	0.00	0.00	0.00

[a] Solvent ratio of 5/95 methanol in organic phase. [b] Solvent ratio of 30/70 heptane in organic phase.

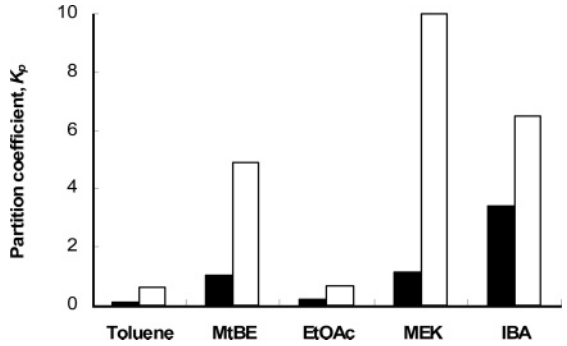


Figure 5. Partitioning behavior of nonionic surfactants at pH 7: ■, Tween 80; □, Trition X-100.

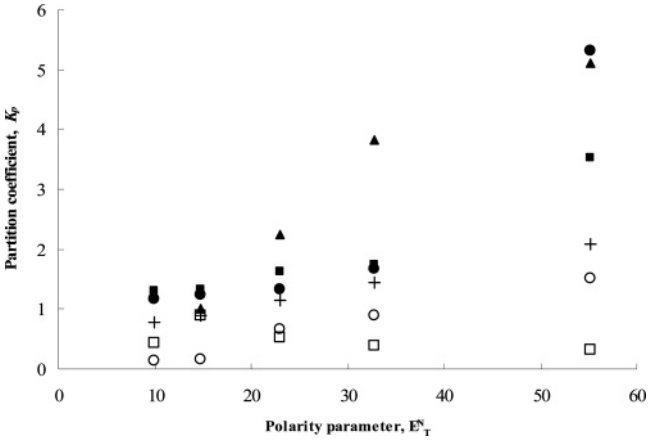


Figure 6. Partitioning behavior of methyl-β-cyclodextrin as a function of the solvent polarity parameter (E_T^N) at 294 K under various conditions: +, pH 2; ○, pH 7; ●, pH 10; ■, 1 M KCl; □, 5/95 v/v MeOH; ▲ 30/70 v/v heptane.

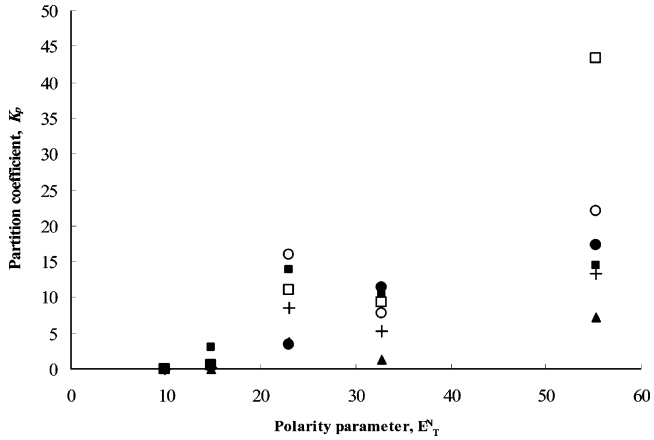


Figure 7. Partitioning behavior of sodium dodecyl sulfate (SDS) as a function of the solvent polarity parameter (E_T^N) at 294 K under various conditions: +, pH 2; ○, pH 7; ●, pH 10; ■, 1 M KCl; □, 5/95 v/v MeOH; ▲, 30/70 v/v heptane.

increase the coefficient by a factor of 3 to 5. The small variations in the partitioning at pH 2 and pH 10 could be due to a salt effect, as the coefficients are the same order of magnitude as for 1 mol·L^{-1} KCl addition. It is possible that the small amount of heptane is interacting with the hydrophobic core and the cyclodextrin is forming inclusion complexes, which could increase its organic concentration. While this is a surprising result since the heptane addition decreases the polarity of the organic phase, the trend is consistent for all solvents.

For the ionic surfactants, the partitioning behavior is more reflective of the solubility in the different solvents. Table 6 shows the partition coefficients determined for the charged surfactants. For the charged surfactants, SDS behaved like the nonionic surfactants, preferring the more polar environment. The partitioning behavior of SDS also had a proportional relationship with increasing solvent polarity at all conditions (Figure 7). The effect of pH on the partitioning behavior is more pronounced as would be expected when dealing with a charged compound. CTAB did not partition into any of the organic solvents, with the exception of IBA, and in that solvent favors the aqueous phase under half of the extraction conditions tested. This preference is likely due to the ionic nature of the compound and the negative ions being stabilized by hydrogen bonding.

Conclusions

Solubility measurements of common additives used in bioprocesses, including surfactants and antifoams, were performed in a range of solvents. The results showed that the antifoams were extremely soluble in the organic solvents but had limited solubility in water. The nonionic surfactants were soluble in all solvents tested. The anionic surfactant was soluble in all solvents tested, with the exception of toluene. The cationic surfactant and ammonium sulfate had limited solubility in most solvents. The solubility of methyl-β-cyclodextrin increased as the polarity of the solvent increased.

The partition coefficients for a subset of these surfactants were determined under a range of extraction conditions, varying ionic strength, pH, and cosolvents. The results can largely be predicted

from the solubility data. The antifoams partition strongly into the organic layer, regardless of solvent and conditions, which is likely due to their limited water solubility. The nonionic surfactant partition coefficients were low for the less polar solvents regardless of conditions. At the higher polarity solvents, the nonionic surfactants began to partition into the organic phase under some conditions. The charged surfactants only partitioned into the more polar solvents. These data can be used to design initial extraction processes containing these additives and, by analogy, for other related additives as well.

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