Natural Nontoxic Solvents for Recovery of Picolinic Acid by Reactive Extraction

ARTICLE *in* INDUSTRIAL & ENGINEERING CHEMISTRY RESEARCH · NOVEMBER 2011

Impact Factor: 2.59 · DOI: 10.1021/ie201228u

4 AUTHORS:

Mangesh D. Waghmare
Priyadarshini Institute of Engineering & Tech…
3 PUBLICATIONS **28** CITATIONS
SEE PROFILE

Kailas L. Wasewar
Visvesvaraya National Institute of Technology
125 PUBLICATIONS **1,530** CITATIONS
SEE PROFILE

Shriram Shaligram Sonawane
Visvesvaraya National Institute of Technology
41 PUBLICATIONS **204** CITATIONS
SEE PROFILE

Diwakar Shende
Visvesvaraya National Institute of Technology
26 PUBLICATIONS **184** CITATIONS
SEE PROFILE

I&EC research
Industrial & Engineering Chemistry Research

ARTICLE

pubs.acs.org/IECR

Natural Nontoxic Solvents for Recovery of Picolinic Acid by Reactive Extraction

Mangesh D. Waghmare,[†] Kailas L. Wasewar,[*,‡] Shriram S. Sonawane,[‡] and Diwakar Z. Shende[‡]

[†]Department of Chemical Engineering, Priyadarshini Institute of Engineering and Technology, Nagpur, 440019, India

[‡]Department of Chemical Engineering, Visvesvaraya National Institute of Technology, Nagpur, 440010, India

ABSTRACT: Pyridine carboxylic acids and their derivatives are attracting considerable attention for their presence in many natural products. 2-Pyridinecarboxylic acid, also known as picolinic acid is widely used in the pharmaceutical industries. Compared to chemical methods, enzymatic oxidation of 3-hydroxyanthranillic acid is an advantageous alternative for the production of picolinic acid. Reactive extraction is a promising method to recover carboxylic acid but suffers from toxicity problems of the diluent and extractant employed, therefore there is a need for a nontoxic extractant and diluent or a combination of less toxic extractants in a nontoxic diluent that can recover acid efficiently. The present paper focuses on the reactive extraction of picolinic acid using tri-*n*-butyl phosphate (TBP) in sunflower oil and castor oil. Results were presented in terms of distribution coefficients (0.0066 to 0.664 for sunflower oil and 0.0099 to 0.94 for castor oil), loading ratio (<0.5), degree of extraction (0.65 to 42.9% for sunflower oil and 0.9 to 74.6% for castor oil), and equilibrium complexation constants. Relative basicity, mass action law, and Langmuir models were used to represent the reactive extraction equilibrium for picolinic acid−TBP−diluent. Model results are close to experimental results.

1. INTRODUCTION

Picolinic acid (2-pyridine carboxylic acid) ($C_6H_5NO_2$) is a white colored crystalline solid with a carboxyl side chain at the 2-position. Being the isomer of nicotinic acid, picolinic acid acts as a chelating agent of elements like chromium, zinc, manganese, copper, iron, and molybdenum in the human body. Its utility is in the quantitative detection of calcium and in the production of phenylalanine, tryptophan, and alkaloid. Commercially available picolinic acid is used as an intermediate to produce pharmaceuticals (especially local anesthetics) and metal salts for the application of nutritional supplements.[1] Pyridine-derived carboxylic acids like picolinic acid are also important from the industrial point of view; for example, in nuclear reactor decontamination, where the low oxidation state metal ion (LOMI) decontamination process uses V(II)/V(III) picolinic acid complexes in the decontamination solutions.

Picolinic acid contains two active groups: a carboxyl group and a pyridinic nitrogen atom, therefore its aqueous solutions are weakly acidic.[2] Picolinic acid is produced via either chemical synthesis or by a fermentation route following enzymatic oxidation of 3-hydroxyanthranilic acid. It is also produced by the catabolism of tryptophan through kynurenine to 3-hydroxyanthranilic acid which is then further acted upon by the enzyme 3-hydroxyanthranilic acid oxygenase.[3] Because of the increased cost of petroleum products, it is preferred to produce the carboxylic acids by fermentation over chemical synthesis.[4] A major drawback in the use of fermentation to produce these acids is the difficulty in recovery from the dilute solutions in which they are produced. The main problem with fermentation technology is that, as the acid is generated, the pH of the system falls. The lowering of pH destroys the bacterial species which are responsible for the generation of acids. This leads to low acid product yield and concentration. The extractive fermentation, in situ application of the solvent extraction technique, keeps the product concentration in the broth at a desired level and suppresses product inhibition by continuously removing the product from the fermentation broth.

A number of methods are available, such as adsorption, precipitation, distillation, membranes, ion exchange, dialysis, reactive extraction etc., to recover carboxylic acids from fermentation broths or aqueous streams. Most of these methods have inherent drawbacks. Calcium hydroxide precipitation has a few shortcomings such as consumption of large quantities of reagents (H_2SO_4 and lime), a large amount of waste generation per ton of acid produced, disposal problems of waste, and very poor sustainability. Dialysis has good potential but has the drawbacks of a frequent cleaning requirement, membrane fouling, and a requirement of a larger dialysis unit as compared to a fermenter. Higher power consumption is the main problem with electrodialysis, although it allows simultaneous separation and concentration of the acid. Ion-exchange requires a large amount of chemicals and generates a large amount of waste. The distillation method is a well-established technology, but its drawbacks are formation of high-boiling internal esters, dimers and greater power consumption.[5−10] Reactive extraction with the proper selection of diluents and extractants can provide high selectivity and extraction but suffers from toxicity problems of solvents toward microbial strains. Selection of an extractant and diluent for reactive extraction should be on the basis of minimal toxicity and maximum capacity. The problem is more important when recovery is carried out in situ from the reactor, where extractant

Received: June 8, 2011
Accepted: October 10, 2011
Revised: October 10, 2011
Published: October 10, 2011

and diluent can exert toxicity both at the molecular level, where the dissolved organic extractant and diluent can inhibit enzymes or modify cell membrane permeability, and at the phase level by direct contact of an organic phase with cells, where extractant or diluent coating of the cells may block nutrient diffusion and may also disrupt the cell wall due to increased surface tension.[11] Diluent toxicity was established by Laane et al.[12] as a function of log P, where log P is the logarithm of the K_D of the diluent in a standard octanol−water system. The onset of toxicity was reported to be in range of log P = 4−6, and diluents with log P < 4 are considered toxic, whereas those having values greater than 6 are considered to be nontoxic. Zhong et al.[13] presented log P values for 2-octanol, witcohol 85 (*z*-octadeo-9-en-1-ol), and 1-dodecanol to be 2.86, 7.69, and 5.00, respectively. Thus the best option is to use a nontoxic diluent or blend a toxic diluent with a nontoxic diluent to yield a biocompatible mixture. Various nontoxic solvents like sunflower oil, soybean oil, rice bran oil, corn oil, D-limonene, linseed oil, etc. are available for the extraction. However it has been found that the toxicity of a diluent depends on the microorganism used. Roffler et al.[14] reported that the effect of diluent toxicity depended on whether yeast or bacteria were used and also on the particular strain of bacteria.

Reactive extraction has received increasing attention over the past decade particularly for recovery of various carboxylic acids.[15−17] In this process, an extractant is used to remove the acid from the aqueous phase. Extractants are usually classified as (i) anion exchange extractants, (ii) cation exchange extractants, (iii) solvating extractants, and (iv) chelate forming extractants.

Diluents provide the solution of the extractants and also the solvation of the extractant−acid complexes formed. Strongly solvating extractants like organophosphorous compounds have primarily been used in inorganic analysis for the extraction and separation of inorganic acids or metal species. Since phosphoryl can form hydrogen bonds to proton donors, strongly solvating extractants can also be used for the extraction of acidic organic compounds. Weak organic acids are extracted by organophosphorous compounds with a significantly higher distribution ratio. The high polarity of the phosphoryl group in tributyl phosphate (TBP) enables it to act as a strong Lewis base, and as a result it can form an acid−base complex when contacted with acid.[18]

Literature is widely available on the reactive extraction of different carboxylic acids from aqueous streams, but very little work on picolinic acid is available. Also no work is available on the reactive extraction of picolinic acid using natural nontoxic diluents like sunflower oil and castor oil.[19] Sunflower oil is a nonvolatile oil extracted from sunflower (*Helianthus annuus*) seeds and predominantly contains linoleic acid in the triglyceride form. Castor oil is a colorless to very pale yellow liquid with mild or no odor or taste extracted from castor (Euphorbiaceae) seeds and majorly contains ricinoleic acid. Senol[1] studied the reactive extraction of picolinic acid from aqueous solution using Alamine 336 as an extractant and 1,2-dichloroethane, MIBK, benzyl alcohol, and toluene as diluents. The results were interpreted in terms of distribution ratio (K_D), degree of extraction (E%), overall (total) loading factor (Z_t), stoichiometric loading factor (Z_s), and modified separation factor (s_f). Tuyun and Uslu[20] studied the extraction of picolinic acid by tridodecylamine (TDA) dissolved in two different acetates (ethyl acetate and propyl acetate), two different alcohols (1-octanol and 1-decanol), and two different ketones (2-heptanone and 2-octanone), as well as single solvents. Tuyun et al.[21,22] reported the values of distribution coefficients, loading factors, Z, and extraction efficiency, E, for the recovery of picolinic acid using TOA with various diluents (isoamyl alcohol, 1-hexanol, ethyl acetate, propyl acetate, *n*-heptane, toluene)[21] and (*n*-octane, *n*-decane, octan-1-ol, decan-1-ol, diisobutyl ketone, octan-2-one).[22]

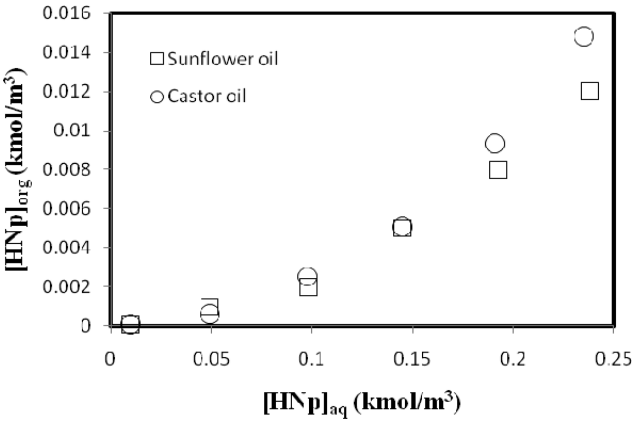

Figure 1. Physical equilibria for extraction of picolinic acid using various diluents at 301 K.

The present study focuses on the influence of nontoxic diluents polarity and hydrogen bonding ability on the extraction equilibrium. The influence of diluents on the formation of complexes was also investigated. Physical and chemical extraction experiments were conducted. Values of distribution coefficient, degree of extraction using physical and chemical extraction were compared. Three models: relative basicity, mass action law, and Langmuir models were used to represent the reactive extraction equilibrium for picolinic acid−TBP−diluent.

2. MATERIALS AND METHODS

2.1. Chemicals. Picolinic acid is obtained from SD. Fine-Chem Ltd., India. TBP (mass fraction of 99%) (CDH Laboratory Reagent, India), a phosphorus-bonded oxygen donor, is a light colorless liquid with the molar mass of 266.32 g·mol^{-1} and density of 0.975 g·cm^{-3} and is used as an extractant. Sunflower oil and castor oil (Agro Tech Foods Ltd., India) are used as diluents. Distilled water obtained from a distilled water unit (Remi India Ltd.) was used to prepare the solutions of various concentrations of picolinic acid. NaOH (SD. Fine-Chem Ltd., India) used for titration is of laboratory grade. For the standardization of the NaOH, oxalic acid (mass fraction of 99.8%) was used. Phenolphthalein solution (pH range 8.2−10.0) was used as an indicator. The initial TBP concentrations of 0.732, 1.464, 2.197, and 2.928 mol·L^{-1} and the initial aqueous acid concentration range of 0.01−0.25 mol·L^{-1} were used. Low concentration was used because picolinic acid concentration in the fermentation broth is not greater than 0.25 mol·L^{-1}.[1]

2.2. Extraction Experiments. The extraction experiments were performed using a temperature-controlled reciprocal shaker (Remi Equipment Pvt. Ltd., India) at constant temperature (301 ± 1 K) and atmospheric pressure. Equal volumes (15 cm^3) of aqueous and organic phases were taken in a 100 mL conical flask and were shaken for 12 h. This could be considered as an appropriate time for attaining equilibrium.[13] For the clear phase separation after each extraction, the mixed phase was then allowed to settle for at least 2 h. Aqueous phase pH was measured by a digital

Table 1. Partition and Dimerization Coefficients, Distribution Coefficient, and Degree of Extraction for Picolinic Acid Extracted from Water into Both Solvents at 301 K

$([HN_P]_{aq\,initial} = 0.01 \text{ to } 0.25 \quad \text{mol L}^{-1})$

$[\text{HNp}]_{org} = P[\text{HNp}]_{aq} + D[\text{HNp}]_{aq}^{2}$

diluent	partition coefficient (P)	dimerization coefficient (D)	range of K_D	average K_D	range of %E	average %E
sunflower oil	0.004	0.184	0.007−0.051	0.027	0.65−4.77	2.65
castor oil	0.004	0.295	0.009−0.064	0.032	0.90−5.92	3.1

pH meter (model R/594, Superfit, India). It was assumed that there was no change in phase volumes after extraction. The aqueous phase acid concentration was determined by titration with NaOH which was freshly prepared. A weighing balance of Shimadzu make (model AW220 with accuracy up to 0.1 mg) was used to weigh the solid NaOH for preparation of NaOH solution. The concentration of acid in organic phase was determined by material balance. To check the consistency of results, a few experiments were repeated and the results were found within limit of ±2%.

3. RESULTS AND DISCUSSION

3.1. Physical Extraction. The physical extraction of picolinic acid using sunflower oil and castor oil was performed and shown in Figure 1. Extraction of picolinic acid by diluent alone was accounted due to three steps: (i) ionization of acid in the aqueous phase (K_{HNp}); (ii) partition of the undissociated acid in organic phase (P); and (iii) dimerization of acid in the organic phase (D).[7] These have been described as what follows:

1. Ionization of the acid in the aqueous solution:

$$\text{HNp} \leftrightarrow \text{H}^+ + \text{Np}^- \tag{1}$$

$$K_{HNp} = [\text{H}^+][\text{Np}^-]/[\text{HNp}] = 3.98 \times 10^{-6} \quad \text{mol L}^{-1} \tag{2}$$

2. Partition of the undissociated molecular acid between the two phases, aqueous (aq) and organic (org):

$$[\text{HNp}]_{aq} \leftrightarrow [\text{HNp}]_{org} \tag{3}$$

$$P = [\text{HNp}]_{org}/[\text{HNp}]\text{aq} \tag{4}$$

3. Dimerization of the acid in the organic phase:

$$2[\text{HNp}]_{org} \leftrightarrow [\text{HNp}]_{2org} \tag{5}$$

$$D = [\text{HNp}]_{2,org}/[\text{HNp}]^2_{org} \tag{6}$$

Overall distribution coefficient for physical extraction ($K_D^{diluent}$) can be written in terms of these parameters as

$$K_D^{diluent} = \frac{[\text{HNp}]_{org\ Total}}{[\text{HNp}]_{aq\ Total}} = \frac{[\text{HNp}]_{org} + 2[\text{HNp}]_2}{[\text{HNp}]_{aq} + [\text{Np}-]} = \frac{P + 2P^2D[\text{HNp}]_{aq}}{1 + K_{HNp}/[\text{H}^+]_{aq}} \tag{7}$$

For the dilute concentration of acid (used in the study), it can fairly be assumed that the second term in the denominator of above equation can be neglected, thus

$$K_D^{diluent} = P + 2P^2D[\text{HNp}]_{aq} \tag{8}$$

or it can written in other form as

$$[\text{HNp}]_{org} = P[\text{HNp}]_{aq} + 2P^2D[\text{HNp}]_{aq}^{2} \tag{9}$$

The degree of extraction (E %) of picolinic acid in respective diluents is expressed as

$$E\% = K_D^{diluent} \times 100/(1 + K_D^{diluent}) \tag{10}$$

Equation 9 was fitted to the experimental value (Figure 1) to yield the values of P and D. The values of partition coefficient, dimerization constant, distribution coefficient, and degree of extraction are given in Table 1. It is observed that the K_D values for picolinic acid in sunflower oil and castor oil are not sufficiently high. Also the degree of extraction is very low.

The extent of hydration of the acid and energy of the bond to water molecules are the two factors that affect extractability. These low values of distribution coefficients (<1) and degree of extraction may be due to the higher affinity of picolinic acid for water which makes it difficult to separate. However, it is observed that the K_D values are higher in castor oil than sunflower oil. Thus the conventional extraction techniques are unprofitable. Better possibilities are offered by the reactive extraction technique by employing organophosphorous compounds which have proven to be effective in the recovery of carboxylic acids.[7]

3.2. Chemical Extraction. Tributyl phosphate (TBP), an organophosphorous compound, was used in the concentration range of 20−80% (0.7322−2.928 kmol/m^3) for extraction of picolinic acid. The chemical stability of organophosphorous compounds plays an important role in the possibility of its use as an efficient extractant with good separation effect with solutions containing chemically similar elements. TBP contains a phosphoryl group which is a stronger Lewis base than the carbonyl group. This leads to higher distribution coefficient.[16] Since TBP is highly viscous; diluents are used in association with it to improve its physical properties, thus allowing its easier handling. The diluent lowers the viscosity of TBP and decreases the surface tension at the interface. TBP is selected because of low water coextraction (mass fraction is 4.67%) and very low solubility in the aqueous phase (mass fraction is 0.039%). TBP contains $=PO_4-$ group, which has a marked tendency toward an intermolecular hydrogen bonding. Because of the presence of both electron donor and electron acceptor groups in the $=PO_4-$ grouping, it undergoes specific interactions like self-association and molecular complex formation with diluents or other solutes.[23] For the extraction of picolinic acid by TBP with chemical interaction,

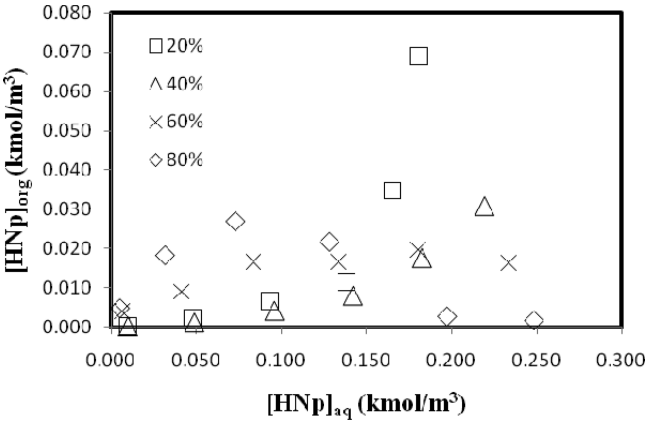

Figure 2. Chemical equilibria for extraction of picolinic acid using various percentages of TBP in sunflower oil.

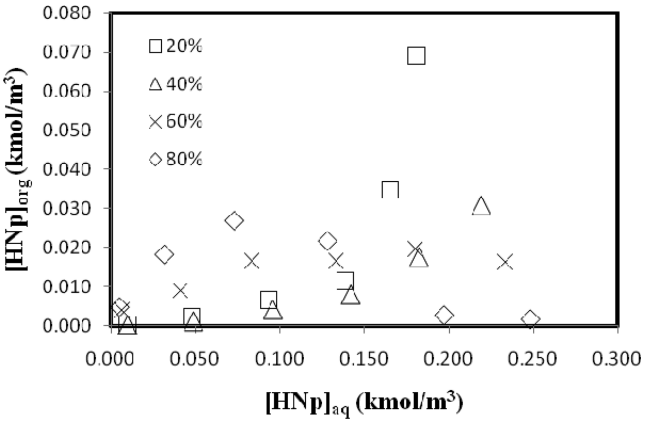

Figure 3. Chemical equilibria for extraction of picolinic acid using various percentages of TBP in castor oil.

the distribution coefficient and degree of extraction ($E\%$) was defined as

$$K_D^{\text{overall}} = \frac{[\text{HNp}]_{\text{org}}}{[\text{HNp}]_{aq} + {}^{aq}[\text{Np}^-]_{\text{aq}}} \tag{11}$$

and

$$E\% = \frac{100 \times K_D^{overall}}{1 + K_D^{overall}} \tag{12}$$

The extraction involves a chemical reaction between TBP and acid. Figures 2 and 3 show the chemical equilibria of extraction of picolinic acid using TBP in sunflower oil and castor oil, respectively. Tables 2 and 3 show the values of various parameters for reactive extraction of picolinic acid using TBP [0.7322−2.928 kmol/m^3 (20−80%)] in sunflower oil and castor oil, respectively. Extraction involving TBP with sunflower oil and castor oil shows little enhanced extraction as compared to physical extraction. It can be found that with the addition of tri-*n*-butyl phosphate, the degree of extraction ($E\%$) increases by about 10 times. This increase in $E\%$ clearly suggests that chemical extraction is better than physical extraction.

3.2.1. Effect of Acid Concentration on Distribution Coefficient. Estimated values of distribution coefficients for the chemical extraction by TBP in diluents for various acid concentrations (0.01−0.25 kmol/m^3) are shown in Tables 2 and 3. It is observed that the distribution coefficients are found to be higher at lower concentration of acid (0.01 kmol/m^3) for both the diluents. This may be due to the limiting factor of amount of TBP at higher initial picolinic acid concentration or due to the inability of the extractant at a fixed concentration in sunflower and castor oil to load more acid. Also it is found that the values of distribution coefficients are higher than for pure diluents, which signifies the advantage of chemical extraction over physical extraction.

3.2.2. Effect of Diluent and Extractant Concentration on Distribution Coefficient. The effect of a diluent mainly depends on its ability to solvate polar ion-pair organic species through dipole−dipole interaction or hydrogen bonding, favoring the formation of one or simultaneously at least two acid−amine complexes. Diluent is added to improve the physical properties of extractant and the solvation efficiency of the acid−extractant complex. The distribution coefficient also depends on the type of diluent and the resulting concentration of extractant in the solvent phase.[7]

Because it is a highly viscous extractant, TBP is used along with the diluents which act to reduce its viscosity and to improve its physical properties. The amount of acid removed strongly depended on the concentration of TBP and diluting solvents. In Figure 4 the effect of TBP in the organic phase on the distribution coefficient at a fixed concentration of picolinic acid is demonstrated. It can be observed that, at a fixed concentration of picolinic acid, the distribution coefficient increases with an increase in the extractant concentration (20−80%), whereas from Tables 2 and 3 it can be observed that, upon varying the acid concentration for a fixed extractant concentration, K_D values increase for 20% extractant and decrease for the remaining percentages (40, 60 and 80%). At the 20−80% extractant−diluent system, diluents are able to solvate the complex even at higher concentrations of acid. But at higher concentrations of extractant (more than 20%), the viscosity of the system increases so high that the nonpolar diluents may not be able to solvate the complex at higher acid concentrations. It can be observed from Tables 2 and 3 that a considerable amount of picolinic acid was removed from the aqueous solution by TBP. The maximum removal of picolinic acid was 74.60% with castor oil for the concentration of TBP of 2.928 mol/L. The distribution coefficient increased from 0.072 to 0.37 with an increase in the amount of TBP from 0.732 to 2.928 mol/L for castor oil. For sunflower oil, the maximum removal of picolinic acid was 42.90% for the concentration of TBP of 2.928 mol/L. Also it can be seen from Tables 2 and 3 that by increasing the TBP volume fraction from 0 to 80% in the diluents, the average K_D values of acid increased from 0.032 to 0.35 for castor oil and from 0.027 to 0.313 for sunflower oil, respectively. It was found that the extraction power of TBP is more effective in the presence of castor oil than sunflower oil.

3.2.3. Extraction Mechanism and Equilibrium Complexation Constant. It is well-known from the literature that carboxylic acid dissociates in aqueous solution. The effect of acid dissociation was found negligibly small under the experimental condition where the pH of the aqueous solution was smaller than pK_a of the acid (5.4).[1] Thus the aqueous phase is found to contain only the undissociated form of the acid. The mass law equilibria describing the extraction of picolinic acid by TBP in different diluents

Table 2. Extraction Equilibrium Results for Picolinic Acid + TBP + Sunflower Oil at 301 K for Various Concentrations of TBP and Picolinic Acid

($S_{org}^{initial}$) (mol·L^{-1})	([HNp]^{o}) (mol·L^{-1})	([HNp]$_{aq}$) (mol·L^{-1})	([HNp]$_{org}$) (mol·L^{-1})	K_D	%E	Z	pH$_{eq}$	pK_B	K_{11} (expt)	K_{11} basicity model	K_{11} Langmuir model	K_{11} mass action model	K_{11} (expt) (av)	K_{11} basicity model (av)	K_{11} Langmuir model (av)	K_{11} Mass action model (av)
0	0.01	0.0099	0.0001	0.006	0.65											
	0.05	0.049	0.001	0.010	1.00											
	0.1	0.098	0.002	0.021	2.05											
	0.15	0.145	0.005	0.035	3.38											
	0.2	0.192	0.008	0.042	4.03											
	0.25	0.238	0.012	0.050	4.77											
0.732	0.01	0.009	0.0001	0.019	1.92	0.001	3.77	7.54	0.026	0.0226	0.027	0.026				
	0.05	0.048	0.002	0.042	4.03	0.003	3.69	7.34	0.057	0.052	0.058	0.057				
	0.1	0.096	0.004	0.043	4.19	0.005	3.57	7.14	0.060	0.1207	0.060	0.061				
	0.15	0.128	0.022	0.171	14.6	0.03	3.50	7.00	0.244	0.216	0.244	0.244	0.205	0.188	0.2057	0.205
	0.2	0.166	0.034	0.205	17.0	0.046	3.45	6.90	0.301	0.3298	0.301	0.301				
	0.25	0.188	0.062	0.331	24.8	0.085	3.43	6.86	0.544	0.390	0.545	0.544				
1.464	0.01	0.007	0.003	0.450	31.0	0.002	3.70	7.40	0.309	0.404	0.309	0.189				
	0.05	0.038	0.012	0.305	23.3	0.008	3.54	7.08	0.211	0.133	0.211	0.131				
	0.1	0.087	0.013	0.145	12.6	0.009	3.46	6.92	0.100	0.0765	0.1003	0.061				
	0.15	0.136	0.014	0.10	9.80	0.010	3.91	6.90	0.075	0.0714	0.0755	0.046	0.132	0.133	0.1323	0.0815
	0.2	0.183	0.017	0.09	8.87	0.012	3.43	6.86	0.061	0.0622	0.675	0.041				
	0.25	0.240	0.010	0.042	4.10	0.007	3.41	6.82	0.029	0.0541	0.0295	0.018				
2.196	0.01	0.006	0.004	0.664	39.9	0.002	3.65	7.30	0.306	0.300	0.300	0.300				
	0.05	0.039	0.011	0.279	21.8	0.005	3.50	7.00	0.120	0.140	0.120	0.128				
	0.1	0.079	0.021	0.259	20.5	0.010	3.36	6.72	0.110	0.070	0.110	0.119				
	0.15	0.127	0.023	0.185	15.1	0.010	3.35	6.70	0.080	0.060	0.080	0.080	0.120	0.304	0.120	0.120
	0.2	0.167	0.033	0.199	10.6	0.015	3.33	6.66	0.050	0.060	0.050	0.054				
	0.25	0.231	0.019	0.084	7.76	0.009	3.32	6.64	0.030	0.050	0.038	0.038				
2.928	0.01	0.006	0.004	0.75	42.9	0.001	3.60	7.20	0.259	0.220	0.2596	0.034				
	0.05	0.039	0.011	0.29	23.0	0.004	3.48	6.96	0.103	0.137	0.1036	0.128				
	0.1	0.081	0.019	0.23	20.4	0.006	3.34	6.88	0.089	0.720	0.089	0.119				
	0.15	0.120	0.030	0.25	20.3	0.010	3.33	6.66	0.089	0.074	0.089	0.080	0.112	0.109	0.112	0.028
	0.2	0.167	0.033	0.20	17.3	0.011	3.32	6.64	0.072	0.071	0.072	0.050				
	0.25	0.216	0.034	0.16	14.2	0.012	3.31	6.62	0.057	0.068	0.057	0.030				

dx.doi.org/10.1021/ie201228u |Ind. Eng. Chem. Res. 2011, 50, 13526–13537

Table 3. Extraction Equilibrium Results for Picolinic Acid + TBP + Castor Oil at 301 K for Various Concentrations of TBP and Picolinic Acid

($S_{org}^{initial}$) (mol·L^{-1})	([HNp]°) (mol·L^{-1})	([HNp]$_{aq}$) (mol·L^{-1})	([HNp]$_{org}$) (mol·L^{-1})	K_D	%E	Z	pH$_{eq}$	pK_B	K_{11} (expt)	K_{11} basicity model	K_{11} Langmuir model	K_{11} mass action model	K_{11} (expt) (av)	K_{11} basicity model (av)	K_{11} Langmuir model (av)	K_{11} Mass action model (av)
0	0.01	0.0099	0.0001	0.009	0.90											
	0.05	0.049	0.001	0.012	1.18											
	0.1	0.097	0.003	0.026	2.53											
	0.15	0.145	0.005	0.035	3.38											
	0.2	0.191	0.009	0.049	4.67											
	0.25	0.235	0.015	0.063	5.92											
0.732	0.01	0.0009	0.0001	0.019	1.92	0.0009	3.40	7.80	0.026	0.023	0.026	0.026				
	0.05	0.048	0.002	0.050	4.79	0.003	3.81	7.60	0.057	0.066	0.057	0.069				
	0.1	0.093	0.007	0.072	6.79	0.010	3.77	7.54	0.105	0.104	0.100	0.100				
	0.15	0.139	0.011	0.083	7.73	0.015	3.75	7.50	0.116	0.132	0.116	0.116	0.172	0.170	0.172	0.196
	0.2	0.165	0.035	0.210	17.3	0.048	3.69	7.38	0.299	0.28	0.299	0.299				
	0.25	0.181	0.069	0.381	22.5	0.094	3.65	7.30	0.432	0.418	0.432	0.568				
1.464	0.01	0.010	0.0009	0.010	1.05	0.0009	3.83	7.60	0.007	0.007	0.007	0.073				
	0.05	0.049	0.001	0.023	2.24	0.001	3.74	7.50	0.016	0.014	0.016	0.015				
	0.1	0.096	0.004	0.043	4.02	0.003	3.65	7.10	0.030	0.027	0.030	0.03				
	0.15	0.142	0.008	0.056	5.25	0.005	3.57	6.46	0.038	0.047	0.038	0.038	0.043	0.042	0.043	0.042
	0.2	0.182	0.018	0.096	8.80	0.012	3.52	6.84	0.066	0.066	0.066	0.066				
	0.25	0.219	0.031	0.140	12.2	0.021	3.47	6.80	0.098	0.090	0.098	0.048				
2.196	0.01	0.006	0.004	0.66	39.9	0.002	3.8	7.60	0.306	0.148	0.306	0.305				
	0.05	0.041	0.009	0.221	18.1	0.004	3.75	7.50	0.102	0.106	0.102	0.102				
	0.1	0.083	0.017	0.20	16.6	0.008	3.56	7.10	0.092	0.090	0.090	0.090				
	0.15	0.133	0.017	0.125	11.7	0.008	3.48	6.96	0.058	0.080	0.050	0.050	0.106	0.090	0.1066	0.01075
	0.2	0.180	0.020	0.11	9.99	0.009	3.42	6.84	0.045	0.082	0.040	0.050				
	0.25	0.234	0.016	0.07	7.25	0.007	3.40	6.80	0.035	0.0256	0.035	0.030				
2.928	0.01	0.005	0.005	0.94	74.6	0.002	3.75	7.50	1.04	1.204	1.048	1.04				
	0.05	0.032	0.018	0.58	37.0	0.006	3.65	7.30	0.207	0.323	0.207	0.207				
	0.1	0.073	0.027	0.37	27.4	0.009	3.55	7.10	0.131	0.087	0.131	0.131	0.242	0.242	0.242	0.2749
	0.15	0.128	0.022	0.17	15.0	0.008	3.45	6.90	0.06	0.023	0.060	0.060				
	0.2	0.197	0.003	0.014	1.44	0.001	3.36	6.72	0.005	0.007	0.005	0.005				
	0.25	0.248	0.002	0.007	0.78	0.001	3.32	6.64	0.002	0.004	0.002	0.002				

dx.doi.org/10.1021/ie201228u |Ind. Eng. Chem. Res. 2011, 50, 13526–13537

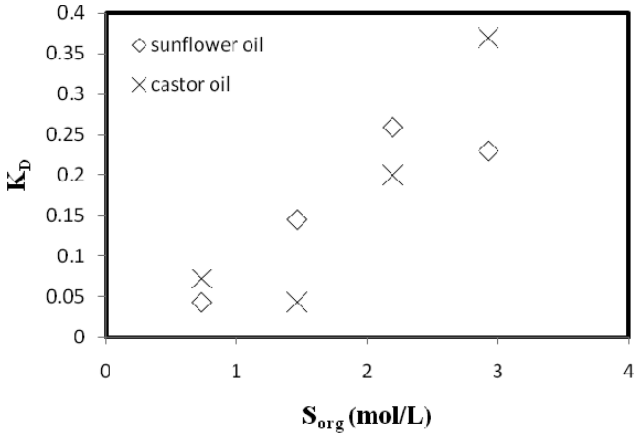

Figure 4. Plot of distribution coefficient vs TBP concentration in different diluting solvents. ($[HNp]_{aq}$ = 0.1 kmol/m^3).

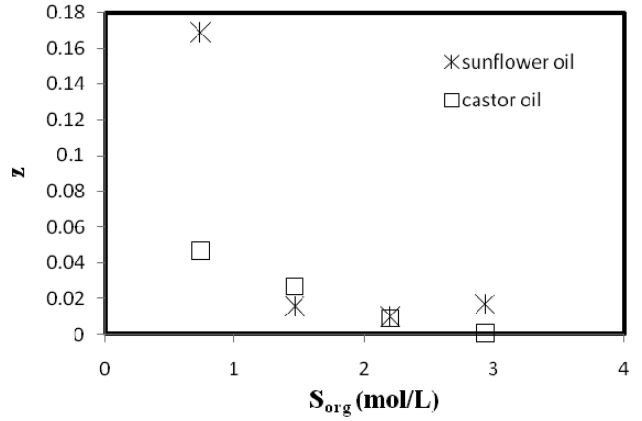

Figure 5. Plot of loading factor vs TBP concentration in different diluting solvents.

can be represented as

$$[HNp]_{aq} + pS_{org} \leftrightarrow (HNp \cdot S_p)_{org} \quad (13)$$

where subscript "aq" and "org" stands for aqueous and organic phases and p is the solvation number of TBP. The extraction of the picolinic acid−TBP complex in the organic phase is considered to be rapid. The extraction equilibrium constant (K_{11}) and the number of reacting molecules of extractant are computed by applying the law of mass action, that is, the ratio between concentration of reactant molecules and the concentration of the product species, according to the general equation of interaction between the extractant and the extracted species.[24]

$$K_{11} = [(HNp) \cdot (S)_p]_{org}/[HNp]_{aq}[S]^p_{org} \quad (14)$$

where $[HNp]_{aq}$, $[S]_{org}$, $[(HNp \cdot S)]_{org}$ represent acid, extractant, and complex concentration in the respective phases. K_{11} is expected to depend on the properties of the acid and the solvation efficiency of the diluents. The dissociation of the acid in the aqueous phase is given as

$$HNp \leftrightarrow H^+ + Np^- \qquad K_{HNp} = \frac{[H^+][Np^-]}{[HNp]} \quad (15)$$

$[H^+]$ and $[Np^-]$ are concentrations of proton and anion of acid and K_{HNp} is dissociation constant.

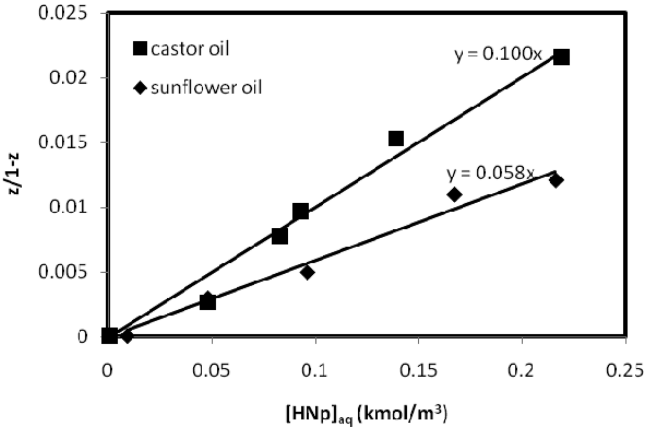

Figure 6. Plot of $z/(1 - z)$ vs $[HNp]_{aq}$ for the estimation of (1:1) picolinic acid−TBP equilibrium complexation constant in sunflower oil and castor oil.

Table 4. Equilibrium Complexation Constant for Extraction of Picolinic Acid Using TBP (0.732−2.928 kmol/m^3) in Various Diluents

diluent	K_{11} (m^3/kmol)
sunflower oil	0.058
castor oil	0.100

The value of p in eq 13 for picolinic acid can be taken as 1 since the solvation number of the aliphatic carboxylic acids were the same as the number of carboxyl groups on each acid.[25]

Niitsu and Sekine[25] indicated a stoichiometric association between an individual phosphoryl group and an individual acid group that displays the strong effect of acid concentration on the experimentally determined distribution ratio. The value of equilibrium complexation constants (K_{11}) are given in Tables 2 and 3 for sunflower oil and castor oil in TBP.

The extent to which the organic phase (TBP + diluent) can be loaded with carboxylic acid is expressed as the loading ratio (z). Figure 5 shows the effect of TBP on loading of the extractant (z). It is observed that, loading increases with increasing TBP concentration for all concentrations of acid in both the diluents. Since the nonpolar diluents by themselves are relatively poor solvating medium for the polar complexes, although loading increases with increasing extractant concentration in the sunflower oil and castor oil, the values of loading are relatively low (<0.5). As TBP itself is highly viscous, at higher concentrations, it needs diluents of low viscosity for solvation. Sunflower oil and castor oil are more viscous than the conventional diluents, which limits the use of TBP at higher concentrations.

The value of z depends on the extractability of the acid (strength of the acid−base interaction) and its aqueous concentration. The stoichiometry of the overall extraction reaction is based on the loading ratio in the organic phase, z. Since in the extraction of picolinic acid using TBP in various diluents, the organic phase is not highly concentrated, that is, the loading ratio is less than 0.5, the (1:1) complex is formed and the following eq 16 holds:

$$\frac{z}{1-z} = K_{11}[HNp]_{aq} \quad (16)$$

Figure 6 shows the plot of $z/(1 - z)$ vs $[HNp]_{aq}$ for the extraction of picolinic acid using TBP in sunflower oil and castor

Table 5. Water Coextraction Results for Picolinic Acid + TBP + Diluents System at 301 K for Various Concentrations of TBP and Picolinic Acid

		after extraction			
		sunflower oil		castor oil	
% diluent	acid concentration (kmol/m^3)	organic phase volume (mL)	aqueous phase volume (mL)	organic phase volume (mL)	aqueous phase volume (mL)
20	0.01	15.15	14.85	15.22	14.78
	0.05	15.18	14.82	15.23	14.77
	0.10	15.20	14.80	15.23	14.77
	0.15	15.21	14.79	15.24	14.76
	0.20	15.22	14.78	15.25	14.75
	0.25	15.23	14.77	15.25	14.75
40	0.01	15.11	14.89	15.17	14.83
	0.05	15.12	14.88	15.18	14.82
	0.10	15.13	14.87	15.19	14.81
	0.15	15.12	14.88	15.17	14.83
	0.20	15.11	14.89	15.16	14.84
	0.25	15.11	14.89	15.15	14.85
60	0.01	15.12	14.88	15.13	14.87
	0.05	15.12	14.88	15.13	14.87
	0.10	15.11	14.89	15.13	14.87
	0.15	15.11	14.89	15.12	14.88
	0.20	15.00	15.00	15.11	14.89
	0.25	15.00	15.00	15.11	14.89
80	0.01	15.11	14.89	15.12	14.88
	0.05	15.00	15.00	15.00	15.00
	0.10	15.00	15.00	15.00	15.00
	0.15	15.00	15.00	15.00	15.00
	0.20	15.00	15.00	15.00	15.00
	0.25	15.00	15.00	15.00	15.00

oil, respectively. A linear relation was obtained and the values of K_{11} are summarized in Table 4. Differences among K_{11} values for the same acid in different diluents indicate that solvation by the diluent is a critical factor in the extraction of acid. As discussed earlier, poor solvation of the polar complexes results in the lower values of equilibrium constants and 1:1 complex formation. Results showed that castor oil has a little better solvation ability than sunflower oil.

3.2.4. Water Coextraction. Water coextraction means the carry over of water in the extract with the solute. This phenomena occurs when there is a mutual solubility between the diluent and the water. The mutual solubility between an aqueous solution and a given solvent at a fixed temperature is affected by the nature of the acid and its concentration. With weak acids like picolinic acid, mutual solubilities cause substantial volume changes, which can be related to the coextraction of water along with the acid. Volume changes depend on the type of diluent and the type and concentration of the extractant as well as the temperature. Since in most of the cases it may be necessary to recover pure acid from an aqueous solution, water coextraction may lead to an extra expenditure on power and cost and hence affect the process economics.[26]

In the present paper, study on water coextraction for picolinic acid + TBP + diluents system at 301 K for various concentrations of TBP and picolinic acid has been done and the results are reported in Table 5. Initial volume of aqueous phase and organic phase was 15 mL, respectively, for both the diluents. From Table 5 it was found that, for extraction involving 20% TBP in both diluents, the ratio of the organic phase volume to the aqueous-phase volume increases with an increase in the acid concentration. For 40% TBP concentration, with an increase in the acid concentration, the value of the phases first increases and then decreases. For 60% TBP concentration, the water coextraction decreases. For 80% concentration, no substantial volume change was observed. This may be due to the following reason: since the diluent is mainly responsible for water coextraction, at higher diluent concentration, more water will be extracted if more acid is present, which forms more acid−TBP complexes and produces a better solvation by the diluents; thus the higher water coextraction is provided, whereas at low diluent concentrations, solvation of the complexes is limited by the availability of diluent. Wasewar et al.[24] studied the extraction of itaconic acid by quaternary amine (Aliquat 336) and observed similar results.

3.2.5. Backextraction/Regeneration. The economic feasibility of the reactive extraction process mainly depends on the amount of extractant requirement. Recovery of extractant and acid from the organic phase is the important step in this process. There are various methods available in the literature for the backextraction process like temperature swing regeneration, wherein the extract is contacted with a fresh aqueous stream at

Table 6. Values of Model Parameter Constants

		relative basicity model		
diluent	%TBP	C_1	C_2	Langmuir model c
sunflower oil	20	−1.819	0.6989	−0.426
	40	1.506	−1.1461	−1.170
	60	1.098	1.3802	−3.710
	80	0.885	1.5051	−5.590
castor oil	20	−2.503	1.9395	25.00
	40	−1.495	1.9867	4.540
	60	0.361	2.029	1.810
	80	2.853	2.0718	−2.770

a higher temperature to produce an acid-laden aqueous product stream and an acid-free organic phase.[26] But because of the lower free enthalpy change, the extraction of picolinic acid by TBP in sunflower oil and castor oil does not show a large temperatute effect. Hence this method proves to be unsuitable for back-extraction. Other methods include backextraction with caustic, distillation, diluent swing regeneration, and using a volatile amine.[26]

3.2.6. Toxicity. The presence of an organic solvent can give rise to a series of physical microbial and biochemical effects on the catalytic activity of the microorganisms. Toxicity of the organic solvent and extractant to microbes is the critical problem in fermentation. The degree of toxicity depends on the combination of microbe and extractant solution used. Brink and Tramper[27] reported that the least toxicity is expected from the solvents of low polarity in combination with high solvent molecular weight. Avoidance of direct contact of the microorganism with the organic phase can substantially reduce toxic effects. With regard to solvent toxicity, Bar and Gainer[28] have discussed the toxicity of the solvent due to the soluble portion of the solvent and the presence of two phases.

Various investigators have used membranes to prevent direct contact of the solvent with the cell containing broth.[29−31] Tik et al.[32] obtained a maximum total lactic acid concentration (2.5 times that without extraction) when 15% Alamine 336 in oleyl alcohol together with immobilized cells with 15% sunflower oil was used. The sunflower oil can also extract Alamine 336 that diffused into the gels and prevent the toxic effect of the solvent. These are the reasons why sunflower oil was used in the extractive fermentation experiments. Harington and Hossain[33] studied the reactive extraction of lactic acid with a combination of carriers like TOA and Aliquat 336 dissolved in either sunflower oil or its mixture with TBP. They reported that a cheap and nontoxic solvent such as sunflower oil with less environmental impact can be used alone or in combination with tributyl phosphate (TBP) for extraction of lactic acid. Wasewar et al.[34] also reported that a natural nontoxic diluent like sunflower oil can be successfully employed in a reactive extraction of itaconic acid using TBP.

As noted above avoidance of direct contact of the organism with the organic phase or use of nontoxic diluents can substantially reduce toxic effects. In the present case, although TBP is toxic to microbes, the diluents (sunflower oil and castor oil) are totally nontoxic in nature. So these diluents can be successfully employed in combination with TBP for the extraction of picolinic acid.

3.3. Model Parameter Estimation and Reliability Analysis. The results, presented in Tables 2 and 3, were interpreted in terms of the relative basicity model, mass action model, Langmuir model, and an extraction equilibrium constant for the reactive extraction of picolinic acid using TBP in sunflower oil and castor oil. The model reliability was also studied through a plot of the modeled values against the observed performance.

3.3.1. Relative Basicity Model. The relative basicity model proposed by Shan[35] relates the 1:1 equilibirum complexation constant with relative basicity. Three major factors have been identified which influence the extraction equilibrium behavior of carboxylic acids, namely, the acid hydrophobicity, log$P$, the dissociation equilibrium constant of the acid, pK_a, and the apparent basicity of extractant to HCl, pK_B. A model equation is of the following form:

$$\log K_{11} = [C_1(\mathrm{p}K_B - \mathrm{p}K_a) + \log(C_2P)] \quad (17)$$

Equation 17 can be used to predict the extraction equilibrium behavior of carboxylic acids with the extractant/diluents system. K_{11} in eq 17 represents the extraction capacity of the acid by forming the complex of ion-pair, H-bond association, and solvating power of the complex. The solvating power is a complicated H-bonding association between the complex and the diluent, which depends on the nature of the solute, extractant, and diluent. Furthermore, pK_B in eq 17 is the relative basicity of the extractant mixture to HCl, excluding the nature of solute. If the basicity of the extractant mixture is relative to the solute, this relative basicity of the extractant can represent all of the nature of the solute, diluent, and extractant, as well as special associations, for example, solvating power.[36] The model eq 17 was fitted for experimental data and the values of C_1 and C_2 are reported in Table 6.

The % of TBP and diluents are given by volume at 301K and atmospheric pressure. The model values for K_{11} for reactive extraction of Picolinic acid using TBP in Sunflower oil and Castor oil have been studied for various concentrations of acid and extractant. It is evident that a good fit was obtained and all the data is within ±10% except few data points. Hence this model validates the experimental values of K_{11} and can be used to describe the reactive extraction of picolinic acid using TBP in various diluents.

3.3.2. Mass Action Law Model. The mass law equilibria describing the extraction of picolinic acid by TBP in different diluents can be represented by eq 13. The overall distribution coefficient is evaluated as the function of extraction constant and the number of reacting species as

$$K_D = \frac{[\mathrm{HNp}\cdot \mathrm{S_p}]_{org}}{[\mathrm{HNp}]_{aq} + [\mathrm{Np^-}]_{aq}} = \frac{K_{11}[\mathrm{HNp}]_{aq}[\mathrm{S}]^p_{org}}{[\mathrm{HNp}]_{aq} + K_a[\mathrm{HNp}]_{aq}/[\mathrm{H^+}]_{aq}} = \frac{K_{11}[\mathrm{S}]^p_{org}}{1 + K_a/[\mathrm{H^+}]_{aq}} \quad (18)$$

Since the effect of the acid dissociation was negligibly small, eq 14 can be modified and then solved to get

$$\log(K_D) = \log(K_{11}) + p\log[\mathrm{S}]_{org} \quad (19)$$

where $[\mathrm{S}]_{org}$ can be expressed as

$$[S]_{org} = [S]^{initial}_{org} - \mathrm{p}[HNp]_{org} \quad (20)$$

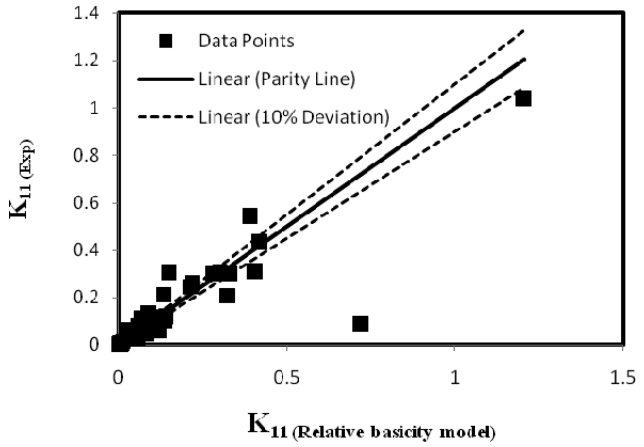

Figure 7. Parity plot for relative basicity model predicted K_{11} for extraction of picolinic acid using TBP in various diluents.

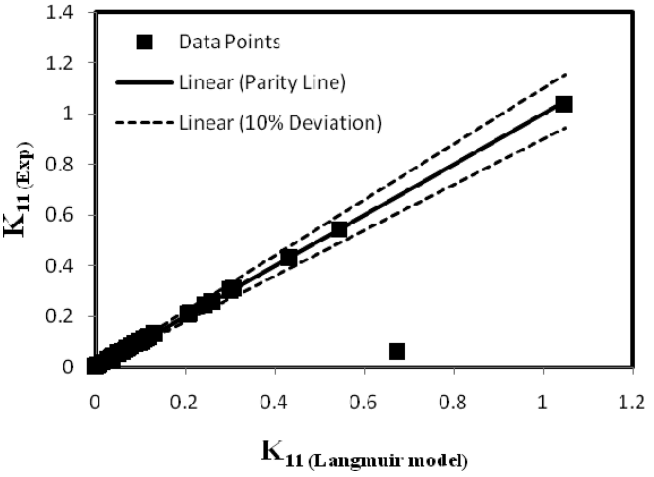

Figure 8. Parity plot for Langmuir model predicted K_{11} for extraction of picolinic acid using TBP in various diluents.

thus the plot of $\log(K_D)$ versus $\log[S]_{org}$ would yield a straight line with the slope of p (solvation number) and the intercept of $\log(K_{11})$, from where K_{11} can be obtained.

The solvation number of the aliphatic carboxylic acids were the same as the number of carboxyl groups on each acid, thus the value of p for picolinic acid can be taken as 1. This indicated a stoichiometric association between an individual phosphoryl group and an individual acid group and displays the strong effect of acid concentration on the experimentally determined distribution ratio. The value of equilibrium complexation constants (K_{11}) for mass action law model are presented in Tables 2 and 3 for sunflower oil and castor oil in TBP, respectively. It can be seen that model values are in good agreement with the experimental values. The data of Table 2 and 3 show that castor oil has a higher K_{11} value than sunflower oil; hence, castor oil is preferred over sunflower oil for the extraction of picolinic acid using TBP.

3.3.3. Langmuir Model. The equilibrium behavior of the acid and extractant was modeled by postulating the formation of various stoichiometric complexes of acid and extractant, as the chemical interaction between the components of the acid−extractant complex are strong compared to the physical interactions in the system. In the Langmuir isotherm,[37,38] the individual complexes

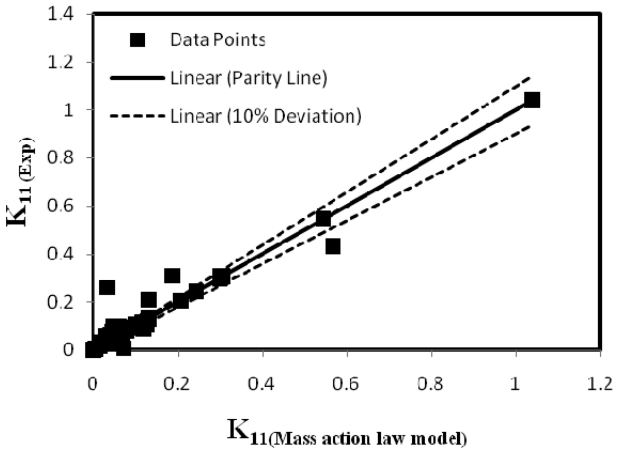

Figure 9. Parity plot for mass action law model predicted K_{11} for extraction of picolinic acid using TBP in various diluents.

present in the organic phase were identified, and their contribution to the overall extraction were determined as a function of relevant process parameters. The model is useful to interpret the equilibrium data and is represented as

$$\frac{[\mathrm{HNp}]_{org}}{[\mathrm{HNp}]_{org}^{max}} = \frac{K_{11}([\mathrm{HNp}]_{aq})^{c}}{1 + K_{11}([\mathrm{HNp}]_{aq})^{c}} \quad (21)$$

where $c = ([\mathrm{HNp}]_{org}^{max})/([S]_{o;org})$ is assumed to be constant in the concentration range considered.

The modified Langmuir isotherm was fitted to the equilibrium data, and the best fitted model parameter constants obtained were reported in Table 6.

3.3.4. Model Comparison. Three different models (relative basicity model, mass action law model, and Langmuir model) were used to represent the equilibrium behavior for the reactive extraction of picolinic acid using TBP in sunflower oil and castor oil. The comparison of model predicted values of K_{11} are shown in Table 2 and 3. It can be observed that the trend of accuracy of model based on the averaged values is ordered as follows: (1) Langmuir model, (2) relative basicity model, and (3) mass action law model. Thus the Langmuir model is the best suited model to explain the reactive extraction of picolinic acid using TBP in sunflower oil and castor oil. From parity plots (Figures 7−9) it can be observed that for the Langmuir model the best fit was obtained and almost all values are lying within ±10% of the range, whereas for the mass action and relative basicity models most values are lying within the ±10% range except for a few points.

4. CONCLUSION

The isothermal equilibrium distribution of picolinic acid onto an aqueous/organic two-phase system containing TBP as a reactive extractant has been elucidated by simultaneous effects of chemical and physical interactions closely related to the nature of the diluent used. Inexpensive and nontoxic solvents with less environmental impact such as sunflower oil and castor oil were used alone and in combination with tributyl phosphate (TBP) for extraction of picolinic acid. Different parameters like distribution coefficient, degree of extraction, loading ratio, and equilibrium complexation constants were determined. Since the loading ratio

was less than 0.5 in most of the cases, no overloading was obtained and only a (1:1) acid−TBP complex was observed.

Physical extraction yields the values of partition coefficient (P) and dimerization constants (D) for both diluents. The experimental values of picolinic acid−TBP equilibrium complexation constant (K_{11}) are calculated and compared with the modeled values. Castor oil is found to be more preferable over sunflower oil for the extraction of picolinic acid using TBP.

Different models (relative basicity model, mass action law model, and Langmuir model) were used to represent the equilibrium behavior for the reactive extraction of picolinic acid using TBP in sunflower oil and castor oil. The trend of accuracy of model is (1) Langmuir model, (2) relative basicity model, and (3) mass action law model. Hence the Langmuir model is the best suited model to explain the reactive extraction of picolinic acid using TBP in sunflower oil and castor oil.

AUTHOR INFORMATION

Corresponding Author

*E-mail: k_wasewar@rediffmail.com. Tel.: +91-712-2801561. Fax: +91-712-2801563.

NOMENCLATURE

[HNp] = picolinic acid concentration (kmol/m^3)
[H^+] = H^+ ion concentration in aqueous phase (kmol/m^3)
[Np^-] = concentration of dissociated picolinic acid in aqueous phase (kmol/m^3)
K_{HNp} = ionization constant of picolinic acid (kmol/m^3)
P = partition coefficient
D = dimerization constant (m^3/kmol)
K_D = distribution coefficient of acid in organic phase
E% = degree of extraction
[S] = concentration of extractant in organic phase (kmol/m^3)
K_{11} = extraction equilibrium constant for (1:1) acid−extractant complex (m^3/kmol)
z = loading ratio

Subscripts

aq = aqueous phase
org = organic phase
o = initial

Superscript

diluent = for diluent only
overall = for extractant + diluents
max = maximum

REFERENCES

(1) Aynur, S. Influence of Conventional Diluents on Amine Extraction of Picolinic Acid. *Sep. Purif. Technol.* **2005**, *43*, 49.

(2) Tuyun, A. F.; Uslu, H. Extraction Equilibria of Picolinic Acid from Aqueous Solution by Tridodecylamine (TDA). *Desalination.* **2011**, *268*, 134.

(3) Smith, A. J.; Stone, T. W.; Smith, R. A. Neurotoxicity of Tryptophan Metabolites. *Biochem. Soc. Trans.* **2007**, *35*, 1287.

(4) Kencaly, W. R.; Cao, Y.; Weimcr, P. J. Production of Caproic Acid by Cocultures of Ruminal Cellulolytic Bacteria and *Clostridium Kluyveri* Grown on Cellulose and Ethanol. *Appl. Microbiol. Biotechnol.* **1995**, *44*, 507.

(5) King, C. J.; Tamada, J. A. Extraction of Carboxylic Acids with Amine Extractants, (3) Effect of Temperature, Water Coextraction, and Process Considerations. *Ind. Eng. Chem. Res.* **1990**, *29*, 1327.

(6) Wasewar, K. L.; Heesink, A. B.; Versteeg, G. F.; Pangarkar, V. G. Equilibria and Kinetics for Reactive Extraction of Lactic Acid Using Alamine 336 in Decanol. *J. Chem. Technol. Biotechnol.* **2002**, *77*, 1068.

(7) Kertes, A. S.; King, C. J. Extraction Chemistry of Fermentation Product Carboxylic Acids. *Biotechnol. Bioeng.* **1986**, *28*, 269.

(8) Ricker, N. L.; Pittman, E. F.; King, C. J. Solvent Extraction with Amines for Recovery of Acetic Acid from Dilute Aqueous Industrial Streams. *J. Sep. Process Technol.* **1980**, *1*, 23.

(9) Jung, M.; Schierbaum, B.; Vogel, H. Extraction of Carboxylic Acids from Aqueous Solutions with the Extractant System- Alcohol /Tri-*n*-alkyl Amines. *Chem. Eng. Technol.* **2000**, *23*, 70.

(10) Uslu, H. Liquid + Liquid Equilibria of the (Water + Tartaric Acid + Alamine 336 + Organic Solvents) at 298.15 K. *Fluid Phase Equilib.* **2007**, *12*, 253.

(11) Solichien, M. S.; Brien, O.; Hammond, D.; Glaz, C. E. Membrane Based Extractive Fermentation To Produce Propionic Acid and Acetic Acid: Toxicity and Mass Transfer Considerations. *Enzyme Microb. Technol.* **1995**, *17*, 23.

(12) Laane, C.; Boeren, S.; Vos, K. On Optimizing Organic Solvents in Multi-liquid-phase Biocatalysis. *Trends Biotechnol.* **1985**, *3*, 251.

(13) Zhong, G.; Bonita, A. G.; Charles, E. G. Propionic Acid Production by Extractive Fermentation. I. Solvent Considerations. *Biotechnol. Bioeng.* **1998**, *57*, 454.

(14) Roffler, S. R.; Randolph, T. W.; Miller, D. A.; Blanch, H. W.; Prausnitz, J. M. Extractive Bioconversions with Non-aqueous Solvents. *Extractive Bioconversions*; Mattiasson, B.; Holst, O., Eds.; Marcel Dekker Inc.: New York, 1991; p 135.

(15) Wasewar, K. L.; Heesink, A. B. M.; Versteeg, G. F.; Pangarkar, V. G. Intensification of Enzymatic Convertion of Glucose to Lactic Acid by Reactive Extraction. *Chem. Eng. Sci.* **2003**, *58*, 3385.

(16) Wasewar, K. L.; Pangarkar, V. G. Intensification of Propionic Acid Production by Reactive Extraction: Effect of Diluents on Equilibrium. *Chem. Biochem. Eng* **2006**, *20*, 1.

(17) Senol, A. Extraction Equilibria of Nicotinc Acid Using Alamine 300/Diluent and Conventional Solvent Systems. *Turk. J. Chem.* **2002**, *26*, 77.

(18) Ingale, M. N.; Mahajani, V. V. Recovery of Carboxylic Acids, C_2−C_6, from an Stream Using Tributylphosphate (TBP): Effect of Aqueous Waste Presence of Inorganic Acids and Their Sodium Salts. *Sep. Technol.* **1996**, *6*, 1.

(19) Matsumoto, M.; Taiyo, O.; Kazuo, K. Synergistic Extraction of Organic Acids with Tri-*n*-Octylamine and Tri-*n*-Butylphosphate. *Sep. Purif. Technol.* **2001**, *24*, 337.

(20) Tuyun, A. F.; Uslu, H. Extraction Equilibria of Picolinic Acid from Aqueous Solution by Tridodecylamine (TDA). *Desalination* **2011**, *268*, 134.

(21) Tuyun, A. F.; Uslu, H.; Selahattin, G. kmen, Yorulmaz, Y. Recovery of Picolinic Acid from Aqueous Streams Using a Tertiary Amine Extractant. *J. Chem. Eng. Data* **2011**, *56*, 2310.

(22) Tuyun, A. F.; Uslu, H. Investigation of Picolinic Acid Extraction by Trioctylamine. *Int. J. Chem. Reactor Eng.* **2011**, *9*, A29.

(23) Keshav, A.; Wasewar, K. L.; Chand, S. Equilibrium Studies for Extraction of Propionic Acid using Tri-*n*-butyl Phosphate in Different Solvents. *J. Chem. Eng. Data* **2008**, *53*, 1424.

(24) Wasewar, K. L.; Shende, D.; Keshav, A. Reactive Extraction of Itaconic Acid Using Quaternary Amine Aliquat 336 in Ethyl Acetate, Toluene, Hexane, and Kerosene. *Ind. Eng. Chem. Res.* **2011**, *50*, 1003.

(25) Niitsu, M.; Sekine, T. Solvent Extraction of Ionic Solutes in Aqueous Solutions. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 705.

(26) Wasewar, K. L.; Yawalkar, A. A.; Moulijn, A.; Pangarkar, V. G. Fermentation of Glucose to Lactic Acid Coupled with Reactive Extraction: A Review. *Ind. Eng. Chem. Res.* **2004**, *43*, 5969.

(27) Brink, L. E. S.; Tramper, J. Optimization of Organic Solvent in Multiphase Biocatalysis. *Biotechnol. Bioeng.* **1985**, *27*, 1258.

(28) Bar, R.; Gainer, J. L. Acid Fermentation in Water−Organic Solvent Two−Liquid−Phase Systems. *Biotechnol. Prog.* **1987**, *3*, 109.

(29) Matsumura, M.; Markl, H. Elimination of Ethanol Inhibition. *Biotechnol. Bioeng.* **1986**, *28*, 534.

(30) Frank, G. T.; Sirkar, K. K. Alcohol Production by Yeast Fermentation and Membrane Extraction. *Biotechnol. Bioeng. Symp.* **1985**, *15*, 621.

(31) Cho, T.; Shuler, M. L. Multimembrane Bioreactor for Extractive Fermentation. *Biotechnol. Prog.* **1986**, *2*, 53.

(32) Tik, N.; Bayraktar, E.; Mehmetoglue, U. *In-situ* Reactive Extraction of Lactic Acid from Fermentation Media. *J. Chem. Technol. Biotechnol.* **2001**, *76*, 764.

(33) Harington, T.; Hossain, M. Extraction of Lactic Acid into Sunflower Oil and Its Recovery into an Aqueous Solution. *Desalination* **2008**, *218*, 287.

(34) Wasewar, K. L.; Shende, D. Z.; Keshav, A. Reactive Extraction of Itaconic Acid Using Aliquat 336 and TBP in Sunflower Oil as a Nontoxic Solvent. *J. Chem. Technol. Biotechnol.* **2010**, *86*, 319.

(35) Shan, X. C. Study on Extraction Equilibria Behavior of Carboxylic Acids with Relative Basicity. Bachelor Thesis, Tsinghua University. 2003.

(36) Shan, X.; Qin, W.; Dai, Y. Dependence of Extraction Equilibrium of Monocarboxylic Acid from Aqueous Solutions on the Relative Basicity of Extractant. *Chem. Eng. Sci.* **2006**, *61*, 2574.

(37) Bauer, U.; Marr, R.; Ruckl, W.; Siebenhofer, M. Reactive Extraction of Citric Acid from an Aqueous Fermentation Broth. *Ber. Bunsen. Phys. Chem.* **1989**, *93*, 980.

(38) Poposka, F. A.; Nikolovski, K.; Tomovska, R. Equilibria and Mathematical Models of Extraction of Citric Acid with Isodecanol/*n*-Paraffins Solutions of Tri-octylamine. *J. Chem Eng. Jpn.* **1997**, *30*, 777.