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Extraction of *D*-(−)-Quinic Acid Using an Amine Extractant in Different Diluents

Amaç Fatih Tuyun* and Hasan Uslu

Chemical Engineering Department, Engineering & Architecture Faculty, Beykent University, Ayazağa, İstanbul, Turkey

ABSTRACT: The extraction of quinic acid was studied by using an amine extractant with respect to the functional groups of the diluents. All experiments were reported on the extraction of quinic acid by tridodecylamine (TDA) dissolved in two different acetates (ethyl acetate and hexyl acetate), two different alcohols (octan-1-ol and decan-1-ol), and two different ketones (heptan-2-one and octan-2-one), as well as single solvents. The experimental results of extraction experiments are reported as distribution coefficients ($K_D = (C^*_{PA}/C_{PA})$), loading factors, Z, and the extraction efficiency, E. The recovery problem has been reduced by using an amine as an extractant in different diluents. The addition of the extractant was found to improve the extraction.

INTRODUCTION

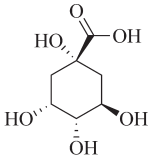
Quinic acid is a cyclitol, a cyclic polyol shown in Figure 1. It is a crystalline acid obtained from cinchona bark, coffee beans, and other plant products and made synthetically by the hydrolysis of chlorogenic acid. Quinic acid is implicated in the perceived acidity of coffee. It is a constituent of tara tannins. Apples (*Malus domestica Borkh.*) have been shown to have significant cancer-preventive effects in several studies, and apple constituents have shown corresponding activities in vitro.[1,2] Possible apple constituents responsible for the positive effects may include vitamins, minerals, and secondary metabolites like *D*-(−)-quinic acid. *D*-(−)-Quinic acid is known to exhibit antioxidative and anti-inflammatory effects, as well as the ability to chelate transition metals in vitro.[3−5] Therefore, *D*-(−)-quinic acid is likely to play an important role in the cancer-preventive potential of apples.[6]

Quinic acid as a sugar compound from nature is found in many different plants, such as tobacco leaves, carrot leaves, apples, peaches, pears, plums, vegetables, and so forth. Quinic acid and shikimic acid (another types of this compound) are key intermediates in the biosynthesis of aromatic compounds in living systems.[7,8]

Many studies have demonstrated protective effects of apple constituents or apple juice extracts in vitro,[1] but it is difficult to transfer the results of these studies to in vivo situations, since factors like bioavailability and metabolism have to be taken into account. Cyclic polyhydroxy compounds can be absorbed, degraded, or metabolized in the small intestine as well as in the colon.[9] To determine the amount of cyclic polyhydroxy compounds reaching the colon, studies with ileostomy probands are valuable because it can be assumed that all substances detected in the ileostomy bags would reach the colon in healthy human subjects.[10]

Marks et al.[11] have examined cyclic polyhydroxy compound contents of bags from five subjects, after they had consumed 500 mL of apple cider, and found that bags collected over 24 h contained 38.6 % of the ingested dihydrochalcones.

Because of the importance of quinic acid and in continuation of our research, the present study aims to study the reactive extraction of quinic acid in different media. The study of reactive extraction of quinic acid in different media was achieved from the determination of the distribution coefficients, loading factor, and extraction efficiency of quinic acid.



D-(-)-Quinic Acid

Figure 1

Physical extraction with pure organic solvents not containing amine- and phosphorus-structured extractants have been verified to be unsuitable for the recovery of organic acids. Because organic acids have high affinity to water it gives low distribution coefficients. The pure diluents do not extract the solute, while the modifier influences the extracting power of the amine. When the amine salts with carboxylic acids are slightly soluble in the aqueous phase, a vital role of the modifier is to improve the solubility of the salts in the extracted phase.[12] Reactive liquid−liquid extraction of the acid by a suitable extractant found to be a promising alternative to conventional processes. Some scientists[13−15] have studied the recovery of carboxylic acids by liquid−liquid extraction with aliphatic tertiary amines dissolved in organic diluents. The behavior and base strength of various amine types and classes in the reactive extraction of hydrochloric acid in toluene diluents has been investigated.[16] It is noteworthy in this study that the base strength increased in the order: tertiary > secondary > primary. Extraction of carboxyl acids by using extractants and gel used successfully and some of reports can be found in the literature.[17−33]

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THEORETICAL SECTION

The extraction of quinic acid (HA) with tridodecylamine (R_3N) can be described by the following reaction.

$$HA(1) + *R_3N(2) \leftrightarrow *(HA)\cdot(R_3N)(3) \quad (1)$$

where HA represents the nondissociated part of the acid present in the aqueous phase and organic phase species are marked with an asterisk (*). Reaction 1 can be characterized by the overall thermodynamic extraction constant K.

The loading of the extractant, Z, is defined as the total concentration of acid in the organic phase divided by the total concentration of amine in the organic phase.[14] The expression for Z can be written in the form

$$Z = C^*_{QA}/C^*_{TOA} \quad (2)$$

In eq 2, C^*_{QA} is the total concentration of acid in the organic phase, mol·kg^{-1} and C^*_{TDA} is the total concentration of amine in the organic phase. The partitioning coefficients, K_D, for quinic acid extracted from water into the organic phase were determined by

$$K_D = C^*_{QA}/C_{QA} \quad (3)$$

The efficiency of extraction, E, is expressed as

$$E = [1 - (C_{QA}/C_{QA0})]\cdot 100 \quad (4)$$

where C_{QA} is the concentration of acid in the aqueous phase after extraction and C_{QA0} is the initial concentration of acid in the aqueous phase.

EXPERIMENTAL SECTION

TDA (M = 522.01 g·mol^{-1}) (purity > 99 % in mass), quinic acid (purity > 98 % in mass), and the solvents were purchased from Merck Co., (Darmstadt, Germany). All chemicals were used without further purification. Alcohols (octan-1-ol and decan-1-ol), ketones (heptan-2-one and octan-2-one), and esters (ethyl acetate and hexyl acetate) (purities > 99 % in mass) were supplied from Merck and Fluka.

Quinic acid was dissolved in distilled water to prepare the solutions with initial concentrations of acid of 6.86 % in mass (0.357 mol·kg^{-1}). The initial organic phases were prepared by the dissolution of TDA in the diluents to produce solutions with approximately constant concentrations. Liquid−liquid equilibrium experiments were conducted on an Erlenmeyer flask. The extraction was done in a closed 50 mL Erlenmeyer flask in which both aqueous solutions of a quinic acid and organic phase (pure solvent or solvent enriched with TDA) were introduced. The concentration of TDA in diluents as an organic solvent was varied between 0 (pure solvent) mol·kg^{-1} and 1.148 mol·kg^{-1}.

After the introduction of both phases the Erlenmeyer flasks were agitated in a GFL shaker (an orbital shaking incubator at 100 rpm) for 2.5 h at (25.0 ± 0.1) °C to ensure equilibrium. After agitation, the Erlenmeyer flasks were transferred into trays, and a settling time of at least 6 h was allowed and shown to be sufficient. After settling, samples of the aqueous phase were taken. The accuracy of the analytical method was determined to hold within 3 %. The concentration of quinic acid in the aqueous phase was determined by titration with aqueous 0.1 mol.·kg^{-1} sodium hydroxide (relative uncertainty 1 %) in the presence of phenolphthalein as the indicator. In most cases, the relative uncertainty of aqueous phase determination did not exceed 3 %.

Table 1. Results of Physical Extraction of Quinic Acid with Pure Solvents[a]

	solvents	pH_{aq}	C^*_{QA} / mol·kg^{-1}	K_D	E
esters	ethyl acetate	2.40	0.001	0.003	0.333
	hexyl acetate	2.34	0.001	0.002	0.167
ketones	heptan-2-one	2.35	0.001	0.003	0.333
	octan-2-one	2.34	0.000	0.000	0.000
alcohols	octan-1-ol	2.32	0.008	0.022	2.161
	decan-1-ol	2.32	0.004	0.012	1.149

[a] pH_{aq} is the pH of the aqueous phase after extraction; C^*_{QA} is the total concentration of acid in the organic phase; K_D is the distribution coefficient; E is the extraction efficiency.

Table 2. Results of Extraction of Quinic Acid with TDA + Ester Systems[a]

solvents (esters)	C^*_{TDA} / mol·kg^{-1}	pH_{aq}	C^*_{QA} / mol·kg^{-1}	K_D	Z	E
ethyl acetate	0.157	2.43	0.004	0.012	0.026	1.165
	0.314	2.54	0.028	0.084	0.089	7.784
	0.471	2.55	0.036	0.112	0.076	10.088
	0.628	2.57	0.039	0.122	0.062	10.909
	0.785	2.58	0.051	0.165	0.065	14.185
hexyl acetate	0.157	2.36	0.004	0.010	0.023	0.998
	0.314	2.39	0.018	0.054	0.058	5.143
	0.471	2.40	0.023	0.069	0.049	6.465
	0.628	2.42	0.030	0.090	0.047	8.279
	0.785	2.44	0.045	0.146	0.058	12.712

[a] C^*_{TDA} is the total concentration of amine in the organic phase; pH_{aq} is the pH of the aqueous phase after extraction; C^*_{QA} is the total concentration of acid in the organic phase; K_D is the distribution coefficient; Z is the loading factor; E is the extraction efficiency.

The pH value of the aqueous phase was determined with a pH meter (Mettler Toledo pH meter) with the uncertainty of 1 %.

RESULTS AND DISCUSSION

Since most of extractants used for reactive extraction are toxic for bacteria in the bioreactor, it was preferable to use low concentrations of these in the present study. The result of the reactive extraction of quinic acid using TDA in different diluents is presented in Tables 1 and 2. It can be seen that increasing extractant concentration increases the distribution coefficient.

The physical extraction of quinic acid was studied for a better understanding of the amine effect on quinic acid (reactive extraction). Table 1 presents and Figure 2 shows the extraction of quinic acid by pure solvents without TDA. With the help of pure octan-1-ol the highest extraction degree was raised to 2.161 % of quinic acid from the aqueous phase to organic phase. In the diluent categories, alcohols dominated more than others did since they have a high polarity. The extraction of quinic acid by TDA dissolved in alcohols (octan-1-ol and decan-1-ol), ketones (heptan-2-one and octan-2-one), and esters (ethyl acetate and hexyl acetate) were studied. Results of the equilibrium data on

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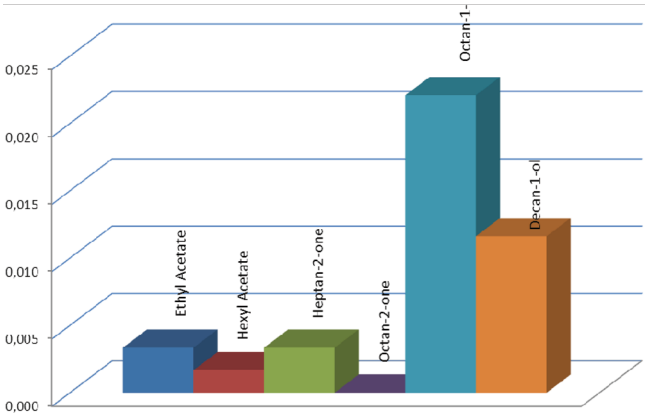

Figure 2. Distribution coefficients of quinic acid between water and solvents used in this study.

Table 3. Results of Extraction of Quinic Acid with TDA + Ketone Systems[a]

solvents (ketones)	C^*_{TDA} mol·kg^{-1}	pH_{aq}	C^*_{QA} mol·kg^{-1}	K_D	Z	E
heptan-2-one	0.157	2.37	0.003	0.008	0.019	0.832
	0.314	2.40	0.004	0.012	0.013	1.165
	0.471	2.42	0.008	0.022	0.016	2.161
	0.628	2.43	0.009	0.027	0.015	2.659
	0.785	2.45	0.010	0.029	0.013	2.825
octan-2-one	0.157	2.37	0.002	0.007	0.015	0.666
	0.314	2.40	0.004	0.010	0.011	0.998
	0.471	2.47	0.007	0.020	0.015	1.995
	0.628	2.48	0.038	0.118	0.060	10.581
	0.785	2.49	0.050	0.163	0.064	14.021

[a] C^*_{TDA} is the total concentration of amine in the organic phase; pH_{aq} is the pH of aqueous phase after extraction; C^*_{QA} is the total concentration of acid in the organic phase; K_D is the distribution coefficient; Z is the loading factor; E is the extraction efficiency.

Table 4. Results of Extraction of Quinic Acid with TDA + Alcohol Systems[a]

solvents (alcohols)	C^*_{TDA} mol·kg^{-1}	pH_{aq}	C^*_{QA} mol·kg^{-1}	K_D	Z	E
octan-1-ol	0.157	2.44	0.033	0.102	0.211	9.266
	0.314	2.57	0.177	0.979	0.563	49.477
	0.471	2.67	0.223	1.665	0.474	62.472
	0.628	2.68	0.234	1.914	0.373	65.685
	0.785	2.70	0.239	2.022	0.304	66.906
decan-1-ol	0.157	2.41	0.017	0.049	0.106	4.647
	0.314	2.62	0.196	1.218	0.624	54.919
	0.471	2.67	0.197	1.234	0.419	55.229
	0.628	2.68	0.199	1.257	0.317	55.693
	0.785	2.69	0.200	1.281	0.255	56.157

[a] C^*_{TDA} is the total concentration of amine in the organic phase; pH_{aq} is the pH of the aqueous phase after extraction; C^*_{QA} is the total concentration of acid in the organic phase; K_D is the distribution coefficient; Z is the loading factor; E is the extraction efficiency.

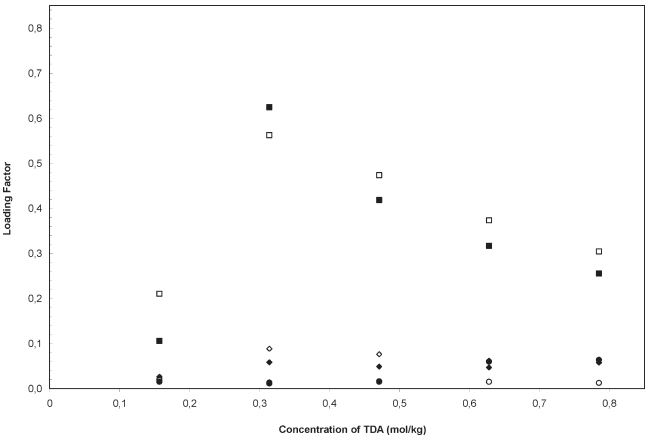

Figure 3. Variation of the loading factor with concentrations of TDA in different individual diluting solvents: ◇, ethyl acetate; ◆, hexyl acetate; ○, heptan-2-one; ●, octan-2-one; □, octan-1-ol; ■, decan-1-ol.

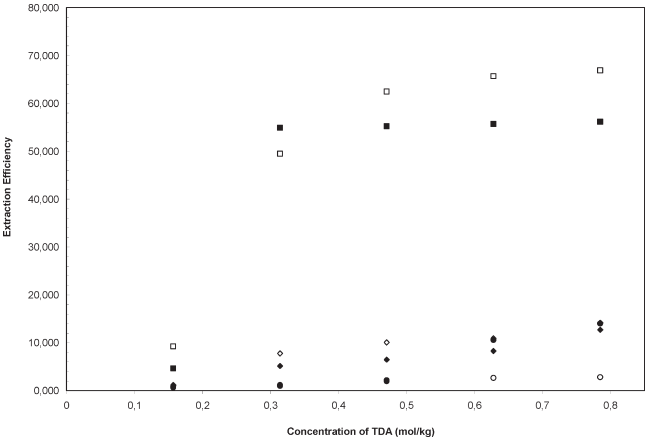

Figure 4. Variation of the extraction efficiency with the concentration of TDA in different individual diluting solvents: ◇, ethyl acetate; ◆, hexyl acetate; ○, heptan-2-one; ●, octan-2-one; □, octan-1-ol; ■, decan-1-ol.

the reactive extraction of quinic acid from aqueous phase to organic phase are presented from Tables 2 to 4. The prepared constant concentrations of TDA in various solvents were between 0.157 mol·kg^{-1} and 0.785 mol·kg^{-1}. The quinic acid concentration in the initial aqueous phase was 0.357 mol·kg^{-1}.

It has been obviously seen from Figure 3, in contrast to the action of K_D values, that the loading factors shown gradually decrease when increasing the amine concentration in the organic phase. At low concentrations, overloading ($Z > 1$) was observed.[19]

Figure 4 demonstrates that the extraction efficiency of TDA—diluent mixtures changes when increasing the initial concentration of TDA in the organic phase. The highest extraction efficiency of quinic acid has been found to be 66.906 % using octan-1-ol at a 0.785 mol·kg^{-1} initial concentration of TDA. The acid concentration in the organic phase at equilibrium C^*_{QA} increases from 0.033 mol·kg^{-1} to 0.239 mol·kg^{-1} with increasing concentrations of TDA from 0.157 mol·kg^{-1} to 0.785 mol·kg^{-1}. The distribution coefficient has increased from 0.102 to 2.022 with increasing initial TDA concentration among all diluents used in this study, as seen in Figure 5. Obviously, it can be seen from Tables 2 to 4 that the increase of amine concentration brings

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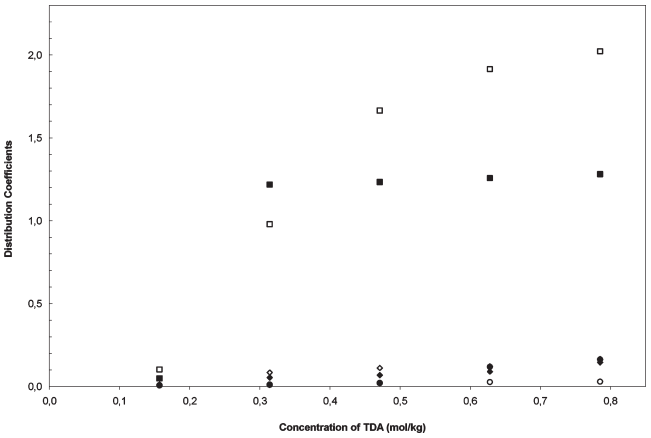

Figure 5. Variation of distribution coefficients with the concentration of TDA in different individual diluting solvents: ◇, ethyl acetate; ◆, hexyl acetate; ○, heptan-2-one; ●, octan-2-one; □, octan-1-ol; ■, decan-1-ol.

about a gradual increase of extraction efficiency. At 0.785 mol·kg^{-1}, the maximum values of 66.906 % and 56.157 % of the quinic acid (for two diluents) are extracted with octan-1-ol and decan-1-ol, respectively. The equilibrium data about distribution of quinic acid between water and TDA dissolved in heptan-2-one and octan-2-one were presented in Table 3. It was found that the extraction power of TDA is more effective in the presence of octan-2-one than heptan-2-one.

CONCLUSIONS

The extraction of quinic acid using TDA was studied in the presence of ethyl acetate, hexyl acetate, octan-2-one, heptan-2-one, octan-1-ol, and decan-1-ol as diluents. TDA is viscous and is thus used in different diluents. The work was to determine the effectiveness of the respective diluents in extraction of quinic acid using TDA. Chemical extractions were studied, and the better performances of extractant−diluent combination over the diluent alone were observed. Different parameters like the distribution coefficient, degree of extraction, and loading ratio were determined. The highest synergistic extraction efficiency was found for the TDA + octan-1-ol extractant system with a K_D value of 2.022. According to Tables 2, 3, and 4 and Figure 5, the distribution coefficients for quinic acid extraction by TDA were obtained in the following order: in esters: ethyl acetate > hexyl acetate; in ketones: octan-2-one > heptan-2-one; in alcohols: octan-1-ol > decan-1-ol.

AUTHOR INFORMATION

Corresponding Author

*Tel.: +90 212 4441997. Fax: +90 212 8675066. E-mail: aftuyun@gmail.com.

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