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Reactive Separation of Nicotinic Acid Using Tri-n-Butyl Phosphate in Ethyl Acetate

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Highlights

- Ethyl acetate, an eco-friendly and non-reactive diluent, showed better performance than traditional toxic solvents.
- Reactive extraction of nicotinic acid using TBP and ethyl acetate was performed at 298K.
- The maximum extraction efficiency (87.25%) was obtained at a nicotinic acid concentration of 0.0102 mol.L^{-1} using 40 % TBP

Abstract

Nicotinic acid has high commercial value and is widely used in food, pharmaceutical, and biochemical industries. Due to strict environmental regulations, its recovery from the aqueous stream is essential. Nicotinic acid can be recovered from aqueous solution through various methods, including ion exchange chromatography, membrane filtration, extraction, electrodialysis, precipitation, adsorption, desorption, and crystallisation. The present paper investigated the separation of aqueous nicotinic acid using tri-n-butyl phosphate (TBP) in ethyl acetate, a greener and less toxic ester as a diluent which improved phase separation compared to conventional solvents. Key equilibrium parameters, distribution coefficient (K_D), loading ratio (Z), extraction efficiency ($E\%$), and extraction equilibrium constant (K_E), were determined. The distribution coefficients ranged from 1.22 to 4.22, with extraction efficiencies of 40.01% to 87.25% at 10-50 vol% of TBP in ethyl acetate. The highest nicotinic acid separation was observed at a concentration of 0.102 mol. L^{-1} of nicotinic acid and 40% TBP. The system also showed clear phase disengagement and good recyclability, highlighting its potential for industrial applications. The findings indicate that a TBP-ethyl acetate solvent system effectively separates nicotinic acid, contributing to the advancement of a sustainable separation process. The present data is relevant to the sustainable separation process.

Paper type: Research Paper

Keywords: Nicotinic acid, Separation, Tri-n-butyl phosphate, Extraction efficiency, Distribution Coefficient, Sustainability.

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1. Introduction

From a sustainability perspective, extracting nicotinic acid from an aqueous stream has significant economic value. Practical, economical, and ecological friendly techniques are becoming increasingly necessary as the global demand for sustainable energy

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solutions rises (Ramesh et al., 2024) . The market value of nicotinic acid might change depending on several factors, including supply and demand, production costs, and industry dynamics, as of the last update in January 2024. The market for vitamin B3, also known as nicotinic acid, was projected to reach $837.1 million by 2024. Between 2024 and 2030, this is predicted to increase at a compound annual growth rate of 4.7%, reaching $1,162 billion (*Market Value of Nicotinic Acid*, 2024). Nicotinic acid (NA), also called Niacin (3-pyridine carboxylic acid), $C_6H_5NO_2$, is a kind of heterocyclic carboxylic acid due to the nitrogen-containing ring structure. It is a white, translucent, crystalline solid chain at position 3 and can attract water. (Kumar, et al., Kumari et al., 2022)

Nicotinic acid has a water solubility of 1.67 g/ml solution. *pH* of (3.0-4.0) and density of 1.47 g/ml at 20°C (*Physical Properties of Nicotinic Acid*, 2024). Nicotinic acid has two dissociation stages and a *pKa* value of 4.75; it can be produced through the fermentation method. Nicotinic acid is found in avocados, peas, lentils, nuts and seeds, as well as in meals and meats, and is an essential human nutrient that plants and animals produce.(Kumar, et al., 2008). Nicotinic acid has the potential to exhibit anti-inflammatory and analgesic effects. (Freitas et al., 2015; Lisicki et al., 2022) Nicotinic acid is widely applied in biological and industrial systems, serving as a metal ion stabiliser in agriculture and as a key component in pharmaceuticals for chelation therapy and drug formulations (Li et al., 2012). It also finds applications in skincare, cosmetics, and micronutrient fertilisers. It is essential in the production of pharmaceuticals, dyes, animal feed, and other fine chemicals. Nicotinic acid is widely distributed in foods such as cereals, legumes, fish, and meat, and functions as a precursor of the coenzymes NAD^+ and $NADP^+$ (Singh et al., 2025). Recent studies have highlighted its broader physiological roles in lipid metabolism, cardiovascular protection, and the control of inflammation, as well as its therapeutic potential in metabolic and neurodegenerative disorders. The growing relevance has increased the demand for high-purity nicotinic acid in pharmaceutical and nutraceutical applications. (Zapata-Pérez et al., 2021) Nicotinic acid can be readily extracted from the aqueous stream through reactive liquid-liquid extraction.(Li et al., 2012). Nicotinic acid is produced from various sources, including vitamin and nutraceutical manufacturing, fermentation processes, pharmaceutical effluents, and chemical synthesis methods. Several techniques, including liquid-liquid extraction, chromatography, adsorption, distillation, evaporation, and reactive extraction be used to separate nicotinic acid. Reactive extraction, in particular, has been proposed as a viable method for recovering carboxylic acids, especially when the extractant used has a higher distribution coefficient. Reactive extraction is an exciting technique for recovering solute from its diluent aqueous solution with high efficiency and selectivity.(De et al., 2018) It is based on the distinct reaction between the solute and extractant functional groups.(Antony & Wasewar, 2018). Separating nicotinic acid from the downstream is crucial and challenging because of the high processing costs.

Reactive extraction is driven by the interactions between the solute and the extractants.(Wasewar & Shende, 2010, 2011b) The organic phase consists of extractants, primarily aliphatic amines, phosphorus, and hydrocarbons, which react with the aqueous phase material to form soluble reaction complexes.(Senol, 2002; Waghmare et al., 2013) Various extractants, such as tri-n-octylamine, trialkyl amine, Aliquat 336, and tributyl phosphate(Demir et al., 2021; Kar et al., 2017; Kumar, et al, 2008; Rewatkar et al., 2016; Senol, 2002). The efficiency of valuable chemical separation was enhanced by using tri-n-octylphosphine oxide.(Datta & Kumar, 2013; Kumar et al., n.d.; Kumar, Wasewar, & Babu, 2008; Li et al., 2012a; Waghmare et al., 2013) High distribution coefficients and low toxicity.(De et al., 2018a; Keshav, et al., 2008a; Wasewar & Shende, 2011b). In other words, the extractant should be as insoluble in water as possible to avoid significantly raising the chemical oxygen demand of the aqueous raffinate. (Ingale & Mahajani, 1994; Wasewar & Shende, 2011b) Environmentalists can utilize the solvent tri-n-butyl phosphate (TBP) in their research.2009; Amit Keshav, Senol et al., 2015; Wasewar & Shende, 2010, 2011a). Most extractants are viscous, so diluents are dissolved in them to improve their physical characteristic. Efficiency is achieved by facilitating the solvation of the formed extractant-acid complexes. Strong solvating extractants, such as phosphorus-bonded weak acid extraction, can be achieved with oxygen-donor extractants. Considering a phosphoryl group, which is a more effective Lewis base than extractants in carbon-bonded oxygen donors(Ki Hong et al., 2001; Senol et al., 2015). Due to its strong Lewis base properties and its high polarity, the phosphoryl group in tri-n-butyl phosphate can react with an acid to form an acid-base complex.

While selecting a diluent for the reactive extraction of nicotinic acid with tributyl phosphate (TBP), ethyl acetate is preferred over other ketones (e.g., acetone, methyl ethyl ketone, or methyl isobutyl ketone) (Demir et al., 2021; Raghuwanshi et al., 2024) due to its more favourable physicochemical properties, as described in Table 1.(*Physico-Chemical Properties of Diluent (Ethyl Acetate)*, 2024.) Ethyl acetate exhibits relatively low water solubility (~1.9 g/100 mL), which minimises diluent loss to the aqueous phase and enhances phase separation. Its higher boiling point (~116 °C) further reduces evaporative losses and simplifies solvent recovery during processing. In contrast, ketones such as acetone and methyl ethyl ketone are more volatile and substantially more water-soluble, increasing the risk of solvent loss and third-phase formation. Ethyl acetate, due to its moderate polarity, provides an optimal balance between solvation of TBP and stabilisation of the extracted TBP–acid complex, ensuring efficient transfer of nicotinic acid into the organic phase without excessive water co-extraction (Wasewar et al., 2011). Finally, ethyl acetate offers a safer handling profile and lower toxicity, making it a practical and environmentally acceptable diluent for large-scale reactive extraction operations. Compared to inert diluents (e.g., kerosene, hexane, toluene), ethyl acetate offers a better polarity match with typical extractants, thereby enhancing the solubility of the extractant and facilitating phase disengagement. Unlike completely nonpolar diluents, it also reduces third-phase formation and improves selectivity without the need for modifiers. Furthermore, the carbonyl oxygen in ethyl acetate can form hydrogen bonds, thereby establishing specific interactions with TBP molecules. This enhances its solubility in the organic phase and promotes its transfer across the interface. Additionally, ethyl acetate's relatively low toxicity and commercial availability make it a more practical choice for scale-up. To establish a viable liquid-liquid extraction process for nicotinic acid, both

the extraction and stripping steps must be optimised, ensuring high recovery of the acid and efficient regeneration of the organic phase. During reactive extraction, the carbonyl oxygen of the solute forms specific interactions with TBP molecules, facilitating its transfer into the organic phase.

Despite numerous studies on the reactive extraction of nicotinic acid with various extractants and diluents, the application of tributyl phosphate (TBP) in ethyl acetate (EA) has been largely overlooked. Most reported systems employ hydrocarbons or ketones, while systematic evaluation of ester diluents such as ethyl acetate is scarce, leaving the influence of its polarity, hydrogen-bonding ability, and phase-separation behaviour on extraction performance insufficiently understood. Furthermore, the advantages of EA in terms of lower toxicity, better environmental compatibility, and higher recycling potential compared to conventional diluents have not been systematically investigated. This investigation is the first comprehensive evaluation of nicotinic acid extraction using TBP in ethyl acetate, a greener ester diluent offering improved phase-separation behaviour and reduced toxicity relative to MIBK, n-octanol, and hydrocarbon systems.

To address this gap, the present study investigates a TBP + ethyl acetate mixed solvent system for the reactive extraction of NA. The approach offers several benefits: high extraction efficiency with low energy consumption, excellent solvent recyclability leading to cost savings, and adaptability for producing high-purity NA from various feedstocks. Additionally, the method shows potential for applications in the pharmaceutical, nutraceutical, and food sectors, as well as integration into sustainable biorefinery processes. Therefore, this work evaluates the equilibrium performance of the TBP–EA system by examining key parameters such as the distribution coefficient (K_D), extraction efficiency (E%), loading ratio (Z), and the extraction equilibrium constant (K_E).

2. Materials and Methods

2.2 Materials

Nicotinic acid (NA) with (99.5 % purity, density of 1473 kg/m^3) was procured from SD Fine Chem Ltd., India. The extractant used was tri-n-butyl phosphate (TBP, 99% purity), purchased from Spectrochem Pvt. Ltd., India. Ethyl acetate, 99 % purity, was used as a diluent and supplied by Merck Specialities Pvt Ltd., India. NaOH flakes were used to titrate the aqueous solution supplied by Merck Specialities Pvt Ltd., India. Phenolphthalein indicator (*pH* 8–10) was provided by Fischer Scientific (India) for the titrations. Oxalic acid was used and purchased from SD Fine Chem Ltd., India, for standardising the NaOH solution. In the experimental investigation, all chemicals were used directly, without any pretreatment.

2.3 Sample preparation

A stock solution of nicotinic acid (0.102 mol L^{-1}) was prepared, and the initial concentration of nicotinic acid in the aqueous phase solution varied from 0.01 mol L^{-1} to 0.102 mol L^{-1} by diluting it with distilled water. The organic phase was prepared by diluting ethyl acetate with tri-n-butyl phosphate (TBP) in ethyl acetate by 10-15 vol% % to achieve a volume concentration ranging from 0.366–0.548 mol·L^{-1}.

2.4 Experimental procedure

For the extraction experiments, equal volumes (10 mL each) of the aqueous and organic phases were mixed in 100 mL conical flasks and shaken at 230 RPM for 5 h in a temperature-controlled orbital incubator (Model S-24BL, REMI, India) at 298 K to reach equilibrium. The mixtures were allowed to settle for 5 h and then centrifuged (REMI CENTRIFUGE R-4C, India) at 3930 RPM for 5 min for complete phase separation. The aqueous phase was filtered (0.22 µm), and its pH and nicotinic acid concentration were measured using a digital pH meter (Superfit, India) and titration with freshly prepared 0.01 N NaOH, respectively. The organic phase acid content was calculated by material balance. Selected experiments were repeated, with results consistent within ±2%. The overall procedure is summarised in Figure 1. All experiments were repeated three times, and standard deviations for K_D, E%, Z, and K_E have been calculated.

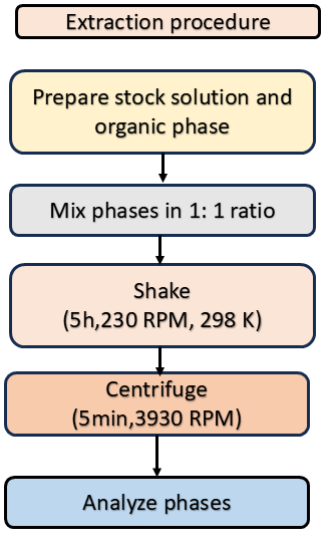

Fig. 1. Experimental procedure for reactive extraction at 298 K

2.5 Standard uncertainty analysis

For accurate results and to check consistency, a set of three experiments was repeated. Instrumental error or any random fluctuation may cause the outcome to be uncertain. The calculations were performed using the mean or average values of the experimental parameters. Consideration was given to the 1% error that was repeated due to an experimental error of less than 2%. The average experimental uncertainty was observed close to x ± 0.002 using Eq. (1):

$$A(x) = \sqrt{\frac{\sum_{i=n}^{n}(x_i - \bar{x})^2}{n-1}} \quad (1)$$

where n represents the number of experimental observations, x_i represents an experimental observation, and $\bar{x}$ represents the mean of experimental values.

3. Results and Discussion

The extraction efficiency for the separation of nicotinic acid with ethyl acetate was determined to be 26.47% (Kolhatkar et al., 2025). To improve the separation performance, TBP (10-50 Vol% was used as a reactive extractant in ethyl acetate to extract nicotinic acid (0.01-0.102 mol.L^{-1}) from the aqueous phase and ethyl acetate. Figure 2 depicts the chemical equilibrium between the aqueous and organic phases at different TBP and acid concentrations. In all cases, $[NA]_{org}$ increases with $[NA]_{aq}$, confirming a favourable distribution of solute toward the organic phase. The equilibrium curves shift upward with increasing TBP content, indicating enhanced extraction capacity due to stronger NA–TBP complex formation and higher availability of active extractant sites. At 40% TBP shows the highest loading is shown, whereas 10% TBP exhibits the lowest, demonstrating that extraction efficiency is strongly governed by extractant concentration. The smooth trend of the plots reflects consistent equilibrium behaviour and supports the reliability of the experimental data.

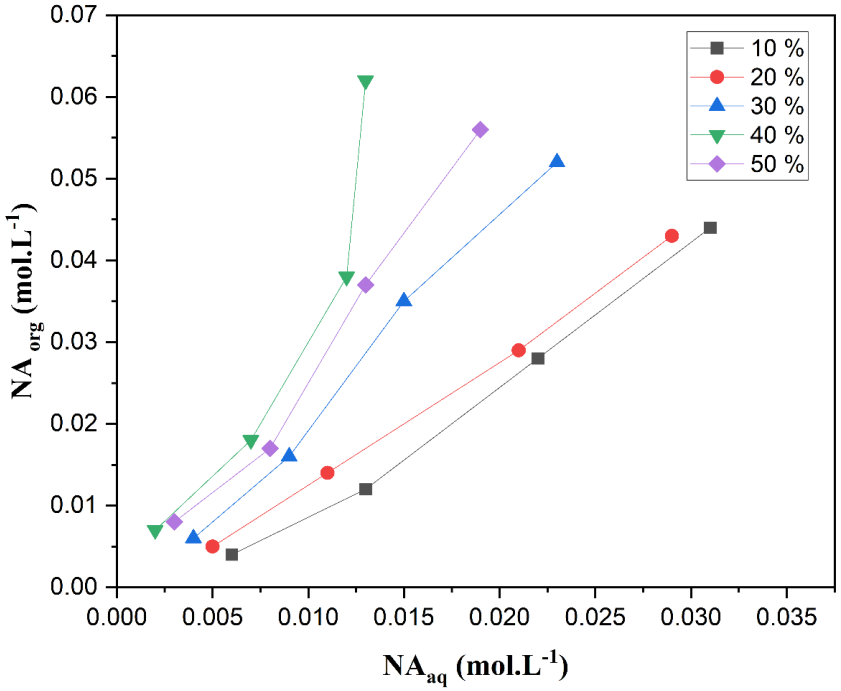

Fig. 2. Equilibrium data for the extraction of Nicotinic acid with TBP and ethyl acetate at 298 K

Under equilibrium conditions, the extraction data show that as the concentration of nicotinic acid in the aqueous phase rises, nicotinic acid molecules are always relatively soluble in the organic phase. The experimental data and estimated parameters K_D, *E%*, *Z*, and K_E are presented in the Table.1

Table 1. Separation of Nicotinic acid using ethyl acetate with TBP at 298 K

TBP (%)	$[NA]_{in}$ mol.L^{-1}	$[NA]_{aq}$ mol.L^{-1}	$[NA]_{org}$ mol.L^{-1}	K_D	E%	Z	K_E
10	0.01	0.006	0.004	0.666	40.01	0.166	1.20
	0.025	0.013	0.012	0.923	48.02	0.192	
	0.05	0.022	0.028	1.272	56.01	0.227	
	0.075	0.031	0.044	1.419	58.67	0.241	
	0.102	0.036	0.066	1.833	64.71	0.283	
20	0.01	0.005	0.005	1.002	50.01	0.133	0.20
	0.025	0.011	0.014	1.272	55.98	0.138	
	0.05	0.021	0.029	1.381	58.02	0.140	
	0.075	0.032	0.043	1.343	57.31	0.140	
	0.102	0.028	0.074	2.642	72.56	0.156	
30	0.01	0.004	0.006	1.52	60.01	0.125	0.09
	0.025	0.009	0.016	1.777	63.98	0.127	
	0.05	0.015	0.035	2.333	70.02	0.130	
	0.075	0.023	0.052	2.261	69.35	0.130	
	0.102	0.023	0.079	3.434	77.46	0.134	
40	0.01	0.003	0.007	2.333	70.04	0.121	0.08

	0.025	0.007	0.018	2.571	72.02	0.121	
	0.05	0.012	0.038	3.166	76.01	0.123	
	0.075	0.013	0.062	4.769	82.66	0.126	
	0.102	0.011	0.091	8.272	89.22	0.128	
50	0.01	0.002	0.008	0.251	50.03	0.119	0.02
	0.025	0.008	0.017	2.125	68.04	0.115	
	0.05	0.013	0.037	2.846	74.05	0.117	
	0.075	0.019	0.056	2.947	74.67	0.117	
	0.102	0.013	0.089	6.846	87.25	0.121	

where, *TBP:* Conc of Tri-n-butyl Phosphate, $[NA]_{in}$: Initial concentration of nicotinic acid, $[NA]_{aq}$: concentration of nicotinic acid in the aqueous phase, $[NA]_{org}$: concentration of nicotinic acid in the organic phase, K_D: Distribution coefficient, *E%:* Extraction efficiency, *Z*: Loading Ratio, K_E: Equilibrium Constant.

3.1 Reactive extraction mechanism

The distribution coefficient of nicotinic acid in ethyl acetate is influenced by the organic phase concentration of tri-n-butyl phosphate. The diluent chosen for the study belonged to the category of oxygenated diluent, ethyl acetate. The transfer of carboxylic acid into the organic phase occurs through three pathways: the ionisation of the acid in the aqueous phase, the distribution of the carboxylic acid between the organic and aqueous phases, and the formation of the dimers within the organic phase (Antony & Wasewar, 2018; Eshwar et al., 2024). Concentrations of acid were chosen to be 0.01, 0.025, 0.05, 0.075, and 0.102 mol/L in the diluent (ethyl acetate).

In the organic phase, acid forms a complex combination with TBP, which can be shown by the following:

$$[NA]_{aq} + [TBP]_{org} \overset{K_{E(1:1)}}{\longleftrightarrow} [TBP: NA]_{org} \quad (2)$$

where $K_{E\,(1:1)} = \frac{[(NA).(TBP)_P]_{org}}{[NA]_{aq}[TBP]_{p\,org}}$

Where E represents the extractant, K_E refers to the equilibrium complexation constant. The uptake of nicotinic acid by the extractant determines the type of complex formed, i.e., a 1:1 complex of nicotinic acid and extractant.(De et al., 2018; Pal & Keshav, 2014; Wasewar & Shende, 2010) It has been observed that K_E is dependent on both acid characteristics and the efficiency of diluent solvation. It may be represented as

$$[NA]_{(aq)} + [E]_{(org)} \leftrightarrow [NA\,.\,E]_{(org)} \quad (3)$$

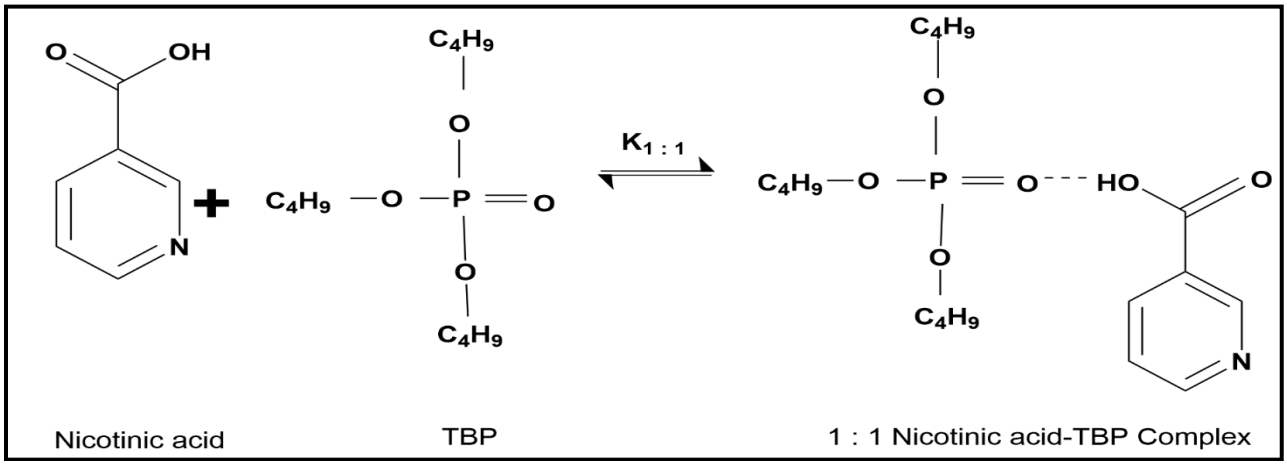

Fig. 3. Nicotinic acid–TBP complex (1:1) in diluent (ETHYL ACETATE) (De et al. (2018); Pal & Keshav (2014))

TBP facilitates the recovery of nicotinic acid by forming a complex through an interfacial reaction. As the nicotinic acid-TBP complex forms, nicotinic acid is rapidly transferred into the organic phase. Figure 3 illustrates the extraction process for the reactive separation of nicotinic acid using TBP in ethyl acetate. Based on the law of mass action, the equilibrium constant for complexation and the number of extractant molecules involved are governed by the general interaction equation between the extractant and the species being extracted(Senol et al., 2015). The typical comparison of various diluents and extractants is represented in Table 2.

The TBP–ethyl acetate system shows superior performance compared to conventional solvents, as shown in Table 2. With 40 vol% TBP, an extraction efficiency of 89.2% and K_D of 8.27 were achieved, exceeding typical values reported for TBP–MIBK (K_D 13.5 - 48) and TBP–n-octanol (Kumar et al., 2008, Wasewar & Shende, 2011; Kumari et al., 2022). This comparison indicates that ethyl acetate serves not only as a greener diluent but also facilitates efficient complexation and phase separation, highlighting its potential for industrial-scale nicotinic acid extraction.

Table 2. Comparison of nicotinic acid extraction with different extractants/diluents

Extractant	**Diluent**	**Distribution Coefficient**	**Max. Extraction Efficiency**	**Reference**
Tri-n-butyl phosphate (TBP)	Ethyl Acetate	8.27	89.25	Present work
TBP and Tri-n-Octylphosphine Oxide (TOPO)	MIBK 1-octanol Di ethyl ether	3.10	75.6*	Wasewar & Shende (2011b)
TBP	Soyabean oil	0.075	6.99*	Lisicki et al. (2022)
TBP	-	0.87	46.52*	Silveira et al. (2023)
Di (2-ethylhexyl) phosphoric acid (D2EHPA)	Dichlormethane	0.042	4.030*	Silveira et al. (2023)
	n-butylacetate	0.36	26.47*	
	n-heptane	0.714	41.65*	
Amberlite LA-2	Dichlormethane	0.098	8.92*	Silveira et al. (2023)
	n-butylacetate	1.13	53.05*	
	n-heptane	3.10	75.60*	
TOPO	Binary diluent (MIBK, Kersoene)	4.17	80.65*	Eshwar et al. (2024)
TOA	*n*-dodecane + lauryl alcohol	7	87.5*	Beg et al. (2022)
TBP	Butyl-3-methylimidazolium hexafluorophosphate	9.05 and 15.45	90.05 and 93.92	Kumari et al. (2022)

* In the absence of reported extraction efficiency values for nicotinic acid, the efficiency was estimated using distribution coefficient (K_D) data.

3.2 Influence of pH on Extraction Efficiency

The *pH* depends on the molar fraction of nicotinic acid (NA), and it significantly influences the *pH*-dependent variation of the distribution coefficient (K_D). As shown in Figure 4, K_D initially increases with rising *pH* and then decreases at a constant nicotinic acid concentration. The maximum K_D values are observed when the pH lies between 2.87 and 3.37. It suggests that TBP can interact not only with neutral nicotinic acid molecules but also with anionic nicotinic acid species after protonation, resulting in the formation of an ion-pair association complex. At a lower equilibrium (*pH* < 2.87), both TBP and the carboxyl group of nicotinic acid are fully protonated, which hinders the formation of the TBP-nicotinic acid complex. In contrast, at higher *pH* (> 3.37), neutral TBP and anionic nicotinic acid predominate, which is also unfavourable for complex formation due to reduced affinity. However, within the intermediate *pH* range of approximately 2.87–3.37, TBP exists predominantly as a neutral or partially protonated species, while nicotinic acid is present as a mixture of neutral and anionic forms. These conditions favorable the interaction between the TBP nicotinic acid complex and lead to higher distribution coefficients (K_D). Thus, optimised control of *pH* is critical to maximise the extraction efficiency of nicotinic acid by TBP, especially when the solute is a weak acid. Variations in *pH* can alter the ionisation of components, thereby affecting the distribution between the aqueous and ethyl acetate phases. Together, TBP and ethyl acetate can slightly shift the *pH* of the system, thereby impacting the ionisation state of nicotinic acid. Once ionised, the *pH* becomes more basic, causing nicotinic acid to deprotonate into its conjugate base, which may have a reduced affinity for the ethyl acetate phase, leading to a decrease in the K_D. Nicotinic acid contains both a carboxylic acid group and a pyridine ring, which are capable of forming hydrogen

bonds. TBP, with its phosphoryl groups, affects the availability of nicotinic acid for transfer into the ethyl acetate phase by forming stronger interactions, potentially retaining more of the acid in the aqueous phase(Kumar, 2008).

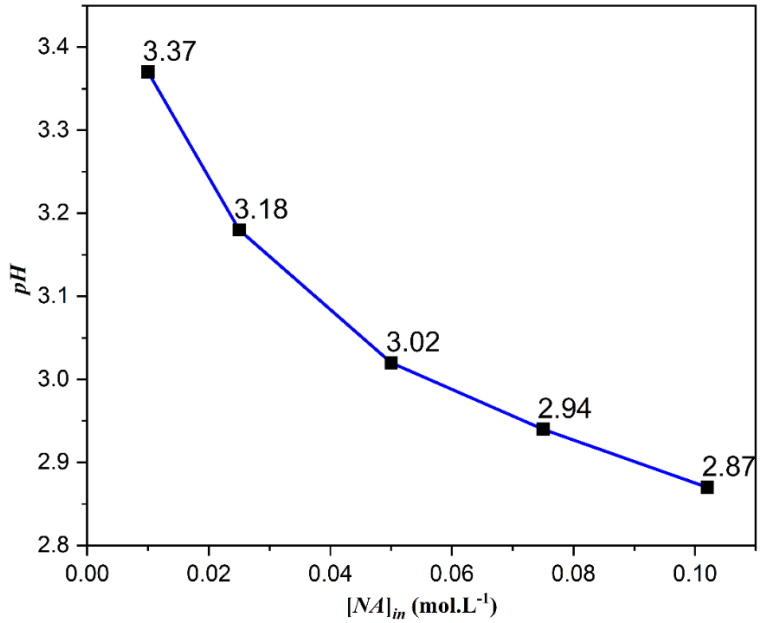

Fig. 4. Variation of pH with initial nicotinic acid concentration

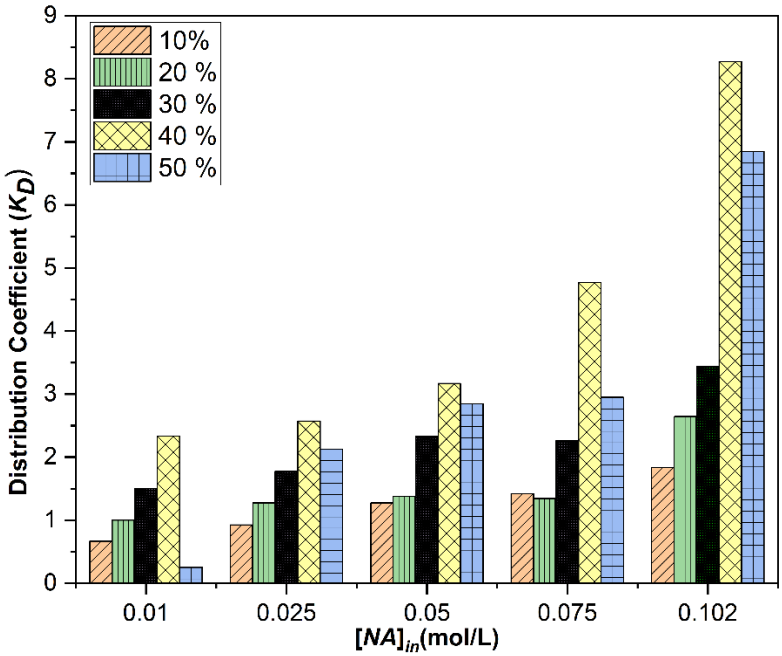

Fig.5. Effect of initial acid concentration on the distribution coefficient

3.3 Distribution coefficient

The distribution coefficient is defined as the ratio of the concentration of nicotinic acid in the organic phase to its concentration in the aqueous phase at equilibrium is reached:

$$K_D = \frac{[NA]_{org}}{[NA]_{aq}} = \frac{[NA.TBP]_{org}}{[NA]_{aq}+[\overline{NA}]_{aq}} \quad (4)$$

Where $[NA]_{org}$ is the concentration of nicotinic acid in the organic phase, $[NA]_{in}$ is the concentration of nicotinic acid in the aqueous phase. The highest K_D of nicotinic acid was observed as 8.272 with 40% of TBP. Table 1 shows that the distribution coefficients and the amount of TBP in the organic phase are significantly correlated. Figure 5 shows that the K_D value increased in association with the first concentration range of 0.01-0.102 mol.L^{-1} of NA. The concentration of TBP was increased by 10-40% (v/v), resulting in a higher distribution coefficient; however, at 50%, the distribution coefficient decreased. With 0.102 mol·L^{-1} TBP/ethyl acetate as the extractant, the effect of initial nicotinic acid concentration on K_D was studied.

3.4 Extraction efficiency (E%)

The extraction efficiency *(E%)* was estimated as :

$$E\% = \frac{K_D}{1+K_D} \times 100 \quad (5)$$

As the concentration of TBP as an extractant in ethyl acetate solvent increased from 10% to 40% (v/v), the efficiency improved from 40.01% to 89.22%, as shown in Figure 6. Due to its P-(O)-OH molecular structure, which allows phosphorus to interact with both oxygen donors and electron acceptors, TBP achieved a maximum separation efficiency of 89.22% for NA. Ethyl acetate has a strong polarity, and its ability to donate hydrogen atoms from the -O-(O-H) group enhances the distribution coefficient, thereby improving extraction efficiency. However, when using 50% TBP as an extractant in ethyl acetate solvent, this can be attributed to an increase in organic phase viscosity, which reduces mass transfer and diffusivity. Additionally, excessive TBP content alters the polarity of the solvent mixture, leading to lower solvation capacity and decreased availability of free TBP molecules for complex formation, thereby reducing extraction efficiency compared to 40%, likely due to *pH* changes in the aqueous phase, which can affect the ionisation state of nicotinic acid. The ionised form of nicotinic acid (its conjugate base) may be less soluble in the organic phase, resulting in a decrease in extraction efficiency. As illustrated in Figure 6, extraction efficiency (*E%*) shows an increasing trend with the initial concentration of nicotinic acid. This implies that, up to a certain point, a higher acid concentration could drive the (*E%*) closer to 90%. However, it must be recognised that equilibrium constraints, extractant capacity, and complex formation limit the achievable extraction efficiency (*E%*) in the reactive extraction process.

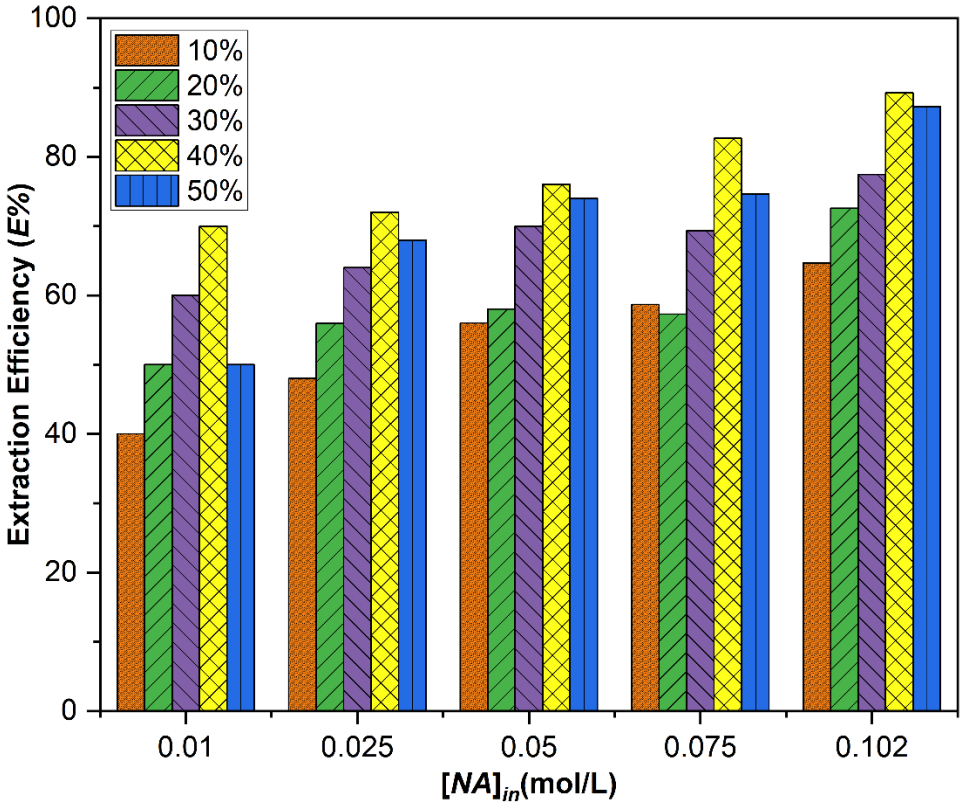

Fig. 6. Variation of initial nicotinic acid concentration against extraction efficiency with TBP.

3.5 Loading ratio (Z)

Loading ratio *Z* represents the extent to which the extracted phase, i.e., the organic phase, gets loaded with nicotinic acid molecules.

$$Z = \frac{[NA]_{org}}{[TBP]_{in,org}} \quad (6)$$

where $[TBP]_{in,org}$ represents the initial extractant concentration of TBP in the organic phase, and $[NA]_{org}$ represents the concentration in the organic phase. The value of Z is primarily influenced by the acid extractability and its concentration in the aqueous phase. As the extractant concentration in ethyl acetate rises, the loading also increases because the solvent becomes a more effective solvating agent, able to dissolve polar complexes independently despite its nonpolar nature. This indicates that higher extractant concentrations can lead to improved separation of nicotinic acid. Figure 7 illustrates the effect of TBP on the loading ratio when ethyl acetate is used as the diluent. The loading ratio decreases as the TBP concentration increases for all concentrations of nicotinic acid in ethyl acetate. At low TBP concentrations and higher nicotinic acid concentrations, higher loading was reached. In the organic phase, the loading ratio defines the stoichiometry of the extraction reaction. The observed values of Z_{NA} < 0.02 for all TBP and nicotinic acid concentrations indicate that the organic phase remains diluent during the extraction of nicotinic acid. Suggesting the absence of overloading, this confirms that complexation between TBP and nicotinic follows 1:1 stoichiometry, as shown in Figure 4. The extraction equilibrium (K_E) for the 1:1 complex was calculated as 1.20172, 0.20899, 0.09581, 0.08243, and 0.02981, respectively, using 10-50% TBP as shown in Table 1. Ethyl acetate, an aliphatic solvent with moderate polarity, enhances extraction due to its branched chemical structure and its ability to form hydrogen bonds with TBP in the organic phase. The extraction of nicotinic acid demonstrated a higher extraction efficiency and a higher distribution coefficient. When combined with ethyl acetate, TBP can be regarded as an effective extractant for the separation of nicotinic acid. A higher extraction efficiency was achieved by determining the extraction equilibrium constant, which was found to be 0.082 with 40% TBP, thereby providing a clearer understanding of the reaction. The extraction equilibrium constant provided less efficiency, which was determined to be 0.029 in the case of 50% TBP. The findings demonstrate that TBP can be used to separate NA from ethyl acetate.

TBP can form complexes with nicotinic acid, which alters its solubility. This complex formation decreases the concentration of free nicotinic acid available for extraction, leading to a reduced effective loading ratio. Together, TBP and ethyl acetate create a unique solvent environment. As the proportion of TBP or nicotinic acid increases, the polarity of the organic phase may shift, potentially making it less favourable for the extraction of additional nicotinic acid and thus reducing the loading ratio.

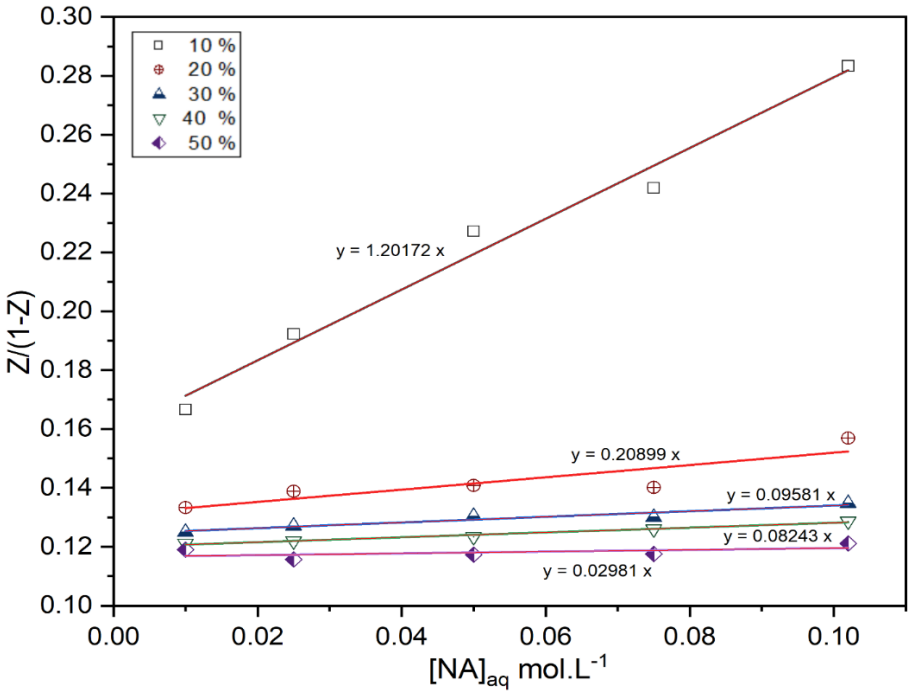

Fig. 7. Graph plotting between Z/(1-Z) and $[NA]_{aq}$ to calculate the extraction equilibrium constant.

3.6 Extraction equilibrium constant (K_E)

The extraction equilibrium constant determines how the nicotinic acid and TBP complexes develop. 1:1 complex forms in the organic phase. The equilibrium constant for the tri-n-butyl phosphate-nicotinic acid system, K_E (NA), is defined by the number of extractant molecules involved and the concentration of the equilibrium product species (Kumar, 2014b) K_E (NA) is influenced by the characteristics of nicotinic acid and the diluent's solvation capacity. The extraction equilibrium constant can be calculated using the following equation.

$$K_E[\mathrm{NA}]_{\mathrm{aq}} = \frac{Z}{1-Z} \quad (7)$$

A plot of Z/(1−Z) versus the equilibrium aqueous concentration of nicotinic acid $[NA]_{aq}$ showed a strong linear relationship (R^2 = 0.98), mechanistic validation using a linearised equilibrium model, consistent with the formation of a 1:1 nicotinic acid–TBP complex in the organic phase. The slope of the regression line corresponded to an equilibrium constant K_E = 0.08, confirming favourable complexation and supporting the proposed extraction mechanism. This linear fit demonstrates that the experimental data are well-described by the equilibrium model.

The solubility of nicotinic acid in the organic phase or a decrease in the interaction strength between nicotinic acid and TBP can reduce the equilibrium constant. According to Le Chatelier's Principle, $K_{E,}$ as shown in Table 1, is a thermodynamic constant that depends only on temperature (and pressure, for gas-phase reactions), not on the initial concentrations of nicotinic acid. Changing the concentration of reactants or products will shift the equilibrium position. Still, it will not alter the value of K_E. In certain instances, changes in concentration gradients can cause nicotinic acid to migrate back to the aqueous phase, thereby decreasing the equilibrium constant as the distribution shifts away from the organic phase. As the initial concentration of nicotinic acid increases, the loading ratio also increases but eventually stabilises, forming a plateau. This is due to the limited capacity of the organic phase (TBP + ethyl acetate) to hold nicotinic acid. Once all available sites in the organic phase are filled, adding more nicotinic acid to the aqueous phase will not increase the loading ratio, as it reaches a point of saturation. When diluent is used with TBP to reduce its viscosity, lower interfacial tension, and enhance its physical properties. The effect of the diluent primarily depends on its ability to solvate polar ion-pair organic species through hydrogen bonding or dipole-dipole interactions, thereby promoting the formation of acid-extractant complexes. TBP is selected as an extractant because it exhibits minimal water co-extraction (mass fraction: 4.67%) and has very low solubility in the aqueous phase (mass fraction: 0.039%) (Keshav a,b,c,d 2009, et al., 2008).

3.7 Comparative assessment of separation methods for nicotinic acid

A comparative assessment of nicotinic acid separation methods was conducted to benchmark the present reactive extraction system. Table 3 summarises the extraction efficiency and solvent recovery across conventional solvent extraction, ion-exchange/adsorption, crystallisation, membrane processes, and the current method. The results indicate that reactive extraction achieves higher efficiency, greater selectivity, and improved solvent recovery compared to conventional approaches, which are often limited by poor selectivity, high energy demand, or scale-up challenges. Thus, reactive extraction offers a favourable balance of efficiency, scalability, and product quality for the recovery of pharmaceutical-grade nicotinic acid. Back-extraction of the loaded organic phase was performed using temperature swing and NaOH stripping. Heating the organic phase weakened the TBP–acid association, enabling the release of nicotinic acid in free form. In contrast, alkaline contact rapidly transferred the solute as sodium nicotinate due to neutralisation. Thus, temperature swing yields pure acid, while NaOH treatment recovers the salt form.

The primary limitations of this study include the moderate solubility of nicotinic acid in organic solvents, the potential for side effects at higher concentrations, and the difficulty of achieving high selectivity in extraction processes. In addition, the present work is restricted to laboratory scale, with potential solvent toxicity posing concerns for food and pharmaceutical applications. A comprehensive techno-economic analysis will also be required to establish the feasibility of large-scale industrial implementation.

The findings demonstrate that the TBP–ethyl acetate system offers several significant advantages: high extraction efficiency (K_D = 1.22–4.22; % E = 40–87%), use of a greener, biodegradable diluent, clear phase separation, and tunable performance across a broad range of TBP concentrations. Compared to physical solvents and natural oils (Beg et al., 2022; Raghuwanshi et al., 2024), TBP–EA achieves markedly higher performance while remaining industrially relevant due to the low cost, availability, and safety profile of ethyl acetate. When compared to other reactive extraction systems (e.g., TOA, TOPO, or ionic liquids), TBP–EA strikes a balance between efficiency and sustainability. Although ionic liquids offer stronger interactions, higher selectivity, and the potential for integrated extraction–recovery, they are often limited by higher costs and synthesis complexity. In contrast, the TBP–EA system provides a more practical and industrial pathway, aligning with green chemistry principles while delivering superior efficiency compared to conventional diluents.

Table 3. Comparative Evaluation of Nicotinic Acid Recovery Methods and Their Limitations

Method	Extraction efficiency/ Yield (%)	selectivity	Solvent reagent recovery	Advantage	Limitation	Ref
Reactive extraction	High (70-87)	High	High	High extraction efficiency, reduced energy input, scalability, adaptable with green solvents	Dependent on solvent choice, it requires optimisation for toxicity and cost	Present work
Conventional solvent extraction	Moderate (40–60)	Low-moderate	Moderate	Simple process, established technology	Poor selectivity, higher solvent consumption, and energy-intensive solvent recovery	Djas & Henczka (2018)
Ion exchange/adsorption	High (50-70)	Resin regeneration is possible but costly	High	High selectivity, no volatile solvents	Resin fouling, regeneration costs, and limited capacity	Inyang & Lokhat (2020)
Crystallization	40-70	moderate	High	Produces crystalline product	Energy-intensive, requires supersaturation control, limited efficiency for dilute feeds	Eshwar et al. (2024)
Membrane separation	50-70	Moderate (carrier regeneration possible)	Moderate high	Mild operating conditions, continuous operation possible	Membrane stability issues, carrier loss, scale-up challenges	Keshav et al. (2008)

4. Conclusions

Nicotinic acid (pyridine), a monocarboxylic acid, has applications across various industries. Its separation using TBP in ethyl acetate was investigated via reactive extraction. At 40 vol% TBP, an extraction efficiency of 89.22% with a distribution coefficient of 8.27 was achieved, confirming strong complexation and effective phase separation. TBP effectively forms a 1:1 complex with nicotinic acid in the organic phase and the equilibrium constants (K_E) were 1.20, 0.20, 0.09, 0.08, and 0.02. Extraction equilibrium constant at 40% TBP with loading ratio (Z) 0.08. Carbonyl oxygen of ethyl acetate enhances extraction through dipole-dipole interactions and hydrogen bonding, further increasing efficiency. These results support the design of continuous separation systems, such as mixer-settler reactors and columns, and highlight the potential for industrial nicotinic acid recovery with TBP–ethyl acetate. Pilot-scale validation of the TBP–ethyl acetate extraction system, including solvent regeneration and reuse studies, will be undertaken to evaluate long-term economic and environmental feasibility.

CRediT Author Contribution Statement

Vaishnavi Kolhatkar: Conceptualisation, Methodology, Formal analysis, Investigations, Resources, Data curation, Writing-original draft, Review and Editing, Visualization, Supervision
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Declaration Statements

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Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this work.

Nomenclature

Abbreviation	Full term
$[CTBP]_{org}$	Concentration of tri-n-butyl phosphate in the organic phase
$[NA]_{aq}$	Concentration of nicotinic acid in aqueous phase
$[NA]_{in}$	Initial concentration of nicotinic acid
$[NA]_{org}$	Concentration of nicotinic acid in the organic phase
$E\%$	Extraction efficiency
K_D	Distribution coefficient
K_E	Extraction Equilibrium Constant
S_{Water}	Solubility in water
Z	Loading Factor
μ	Viscosity
ρ	Density

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