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## Intensified Sustainable Approaches for Separation of Glutaric Acid

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**Key words:** Intensification, Sustainable, Glutaric Acid, Reactive extraction, Ionic liquids, Deep Eutectic Solvents, Ultrasound Assisted, Microwave Assisted

Glutaric acid is a five-carbon dicarboxylic acid with the chemical formula  $C_5H_8O_4$ , obtained from fermentation is known for its diverse applications in various industries, including pharmaceuticals, plastics, and food additives. The separation of glutaric acid from the fermentation broth using green solvents is crucial for both process efficiency and product purity. The sustainable separation of glutaric acid from aqueous solutions is a vital process in the production of bio-based chemicals, playing a crucial role in promoting green chemistry and minimizing environmental impact. Conventional approaches are limited with many drawbacks including toxicity and negative environment impact, high energy requirement and capital cost. Further, process intensification can contribute significantly in development of sustainable process for the separation of glutaric acid. The various intensified sustainable approaches comprises: reactive extraction, natural solvents, ionic liquids, deep eutectic solvents, microwave assisted, ultrasound assisted, hybrid and combination of solvents, microfluidic separation, inverted coiled separation etc. Theoretical aspects of these processes have been discussed based on key features. Also few experimental results on separation of glutaric acid using natural non-toxic solvents, physical extraction, reactive extraction, ionic liquids, deep eutectic solvents, microwave assisted, ultrasound assisted, hybrid and combination of solvents, etc. have been presented. Key factors impacting separation efficiency, including solvent composition, molar ratios, hydrogen bonding interactions, and operational conditions, are thoroughly examined. The study underscores the effectiveness of various solvent and approaches in extracting biochemicals like carboxylic acids, amino acids, and natural phenolic compounds, achieving enhanced selectivity and yield compared to traditional methods. The presented innovative technique has demonstrated significant potential to separation practices. Additionally, the reusability and stability of solvents under diverse operational conditions reinforce their economic and ecological advantages. These advancements align with global efforts toward greener and more efficient bioprocessing technologies. The obtained results are useful for the selection of suitable intensified sustainable approach and its design for a specific application. This work establishes a scalable, green approach for glutaric acid recovery, advancing the sustainable production of valuable bio-based acids from fermentation and supporting broader applications in green separation technologies.

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### Abstract

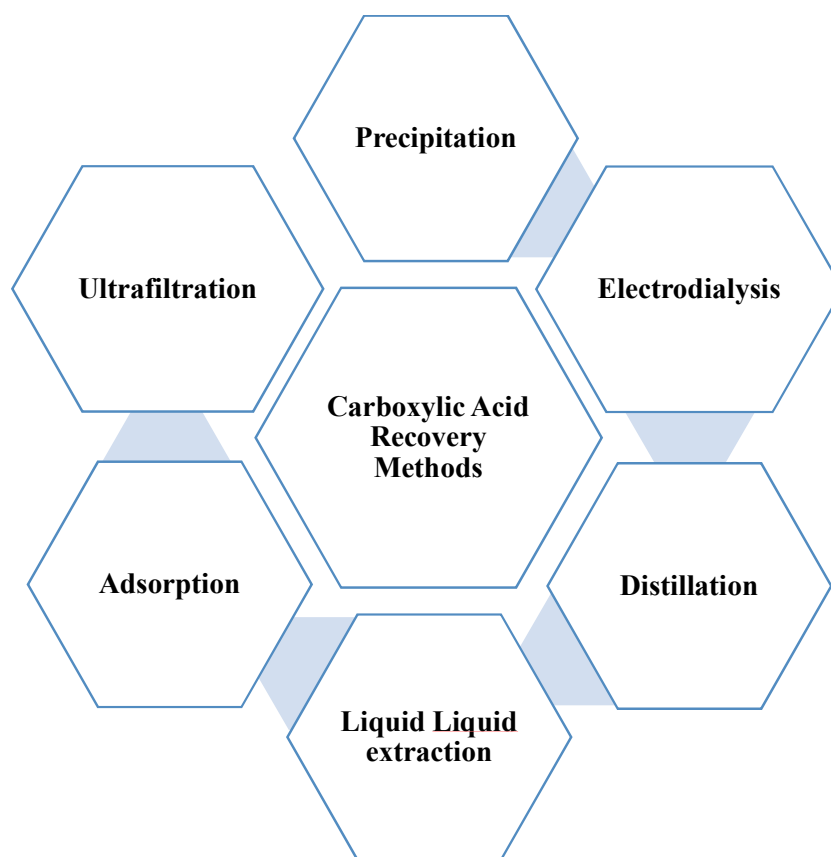
Glutaric acid a five-carbon dicarboxylic acid with the chemical formula  $C_5H_8O_4$ , obtained from fermentation is known for its diverse applications in various industries, including pharmaceuticals, plastics, and food additives. The separation of glutaric acid from the fermentation broth using green solvents is crucial for both process efficiency and product purity. The sustainable separation of glutaric acid from aqueous solutions is a vital process in producing bio-based chemicals, playing a crucial role in promoting green chemistry and minimizing environmental impact. Conventional approaches are limited with many drawbacks, including toxicity and negative environment impact, high energy requirement, and capital cost. Further, process intensification can contribute significantly to the development of a sustainable process for the separation of glutaric acid. The various intensified sustainable approaches comprise reactive extraction, natural solvents, ionic liquids, deep eutectic solvents, microwave-assisted, ultrasound-assisted, hybrid and combination of solvents, microfluidic separation, inverted colied separation, etc. The theoretical aspects of these processes have been discussed based on key features. Also few experimental results on the separation of glutaric acid using natural non-toxic solvents, physical extraction, reactive extraction, ionic liquids, deep eutectic solvents, microwave-assisted, ultrasound-assisted, hybrid and combination of solvents, etc. have been presented. Key factors impacting separation efficiency, including solvent composition, molar ratios, hydrogen bonding interactions, and operational conditions, are thoroughly examined. The study underscores the effectiveness of various solvents and approaches in extracting biochemicals like carboxylic acids, amino acids, and natural phenolic compounds, achieving enhanced selectivity and yield compared to traditional methods. The presented innovative technique has demonstrated significant potential to separation practices. Additionally, the reusability and stability of solvents under diverse operational conditions reinforce their economic and ecological advantages. These advancements align with global efforts toward greener and more efficient bioprocessing technologies. The obtained results are useful for the selection of a suitable intensified sustainable approach and its design for a specific application. This work establishes a scalable, green approach for glutaric acid recovery, advancing the sustainable production of valuable bio-based acids from fermentation and supporting broader applications in green separation technologies.

**Keywords:** Intensification, Sustainable, Glutaric Acid, Reactive extraction, Ionic liquids, Deep Eutectic Solvents, Ultrasound Assisted, Microwave Assisted

## Introduction

The increasing demand for bio-based chemicals and the global drive toward environmental sustainability have intensified the need for greener and more efficient separation technologies, particularly in the context of platform chemicals like carboxylic acids. Carboxylic acids including acetic, lactic, succinic, citric, and glutaric acids are widely used in the food, pharmaceutical, and polymer industries. These compounds are often produced via microbial fermentation, resulting in aqueous systems that pose significant challenges for downstream processing. Traditional separation techniques, such as distillation, crystallization, or solvent extraction, tend to be energy-intensive and environmentally taxing. Therefore, developing intensified sustainable approaches for separating carboxylic acids has become a focal point of modern chemical engineering and green technology research. Sustainability in separation processes implies the use of low-toxicity materials, reduced energy input, minimal waste generation, and high selectivity. In recent years, the integration of green solvents, novel extraction techniques, and process intensification strategies has emerged as a promising solution to address the shortcomings of conventional methods. These strategies are designed not only to improve the overall efficiency of carboxylic acid recovery but also to minimize environmental and economic burdens associated with large-scale production. Traditional separation techniques, such as distillation and solvent-based purification, are often energy-intensive and generate considerable waste, leading to substantial environmental concerns (Binnemans et al. 2015; Zhang et al. 2021). To address these challenges, sustainable separation technologies are being explored to minimize environmental impact and energy consumption. Techniques such as membrane separation, solvent extraction, and crystallization have shown considerable promise in enhancing the efficiency, purity, and sustainability of separation processes (Gryta 2018; Kerton and Marriott 2013; Sharma and Mandal 2020). Membrane-based technologies, for instance, are recognized for their lower energy requirements and reduced environmental footprint compared to thermal separation processes (Van der Bruggen and Vandecasteele 2003). Similarly, solvent extraction using green solvents or ionic liquids has demonstrated improved selectivity and recyclability, making it a sustainable option for separating bio-based chemicals like glutaric acid (Xu et al. 2017; Cui et al. 2019). Crystallization techniques, particularly those aided by process intensification or supersaturation control, offer advantages in scalability and product recovery while maintaining minimal energy input (Myerson et al. 2019). Fig 1 depicts few recovery methods of carboxylic acid from fermentation broth. Adopting such sustainable technologies not only reduces ecological impact but also helps conserve natural resources by decreasing the reliance on hazardous chemicals, water consumption, and waste generation (Zimmerman et al. 2020; Anastas & Warner 1998). The growing emphasis on sustainability in chemical industries fueled by stricter environmental policies and increased public awareness has accelerated the transition to green chemistry and cleaner production strategies (Clark and Macquarrie 2012). Moreover, sustainable separation methods support circular economy objectives by promoting resource efficiency,

recycling, and material reuse, reducing operational costs and enhancing long-term economic viability (Ragaert et al. 2017; Sheldon 2016). This study provides a detailed investigation into both the theoretical foundations and experimental validation of intensified sustainable methods for separating glutaric acid from fermentation broths.

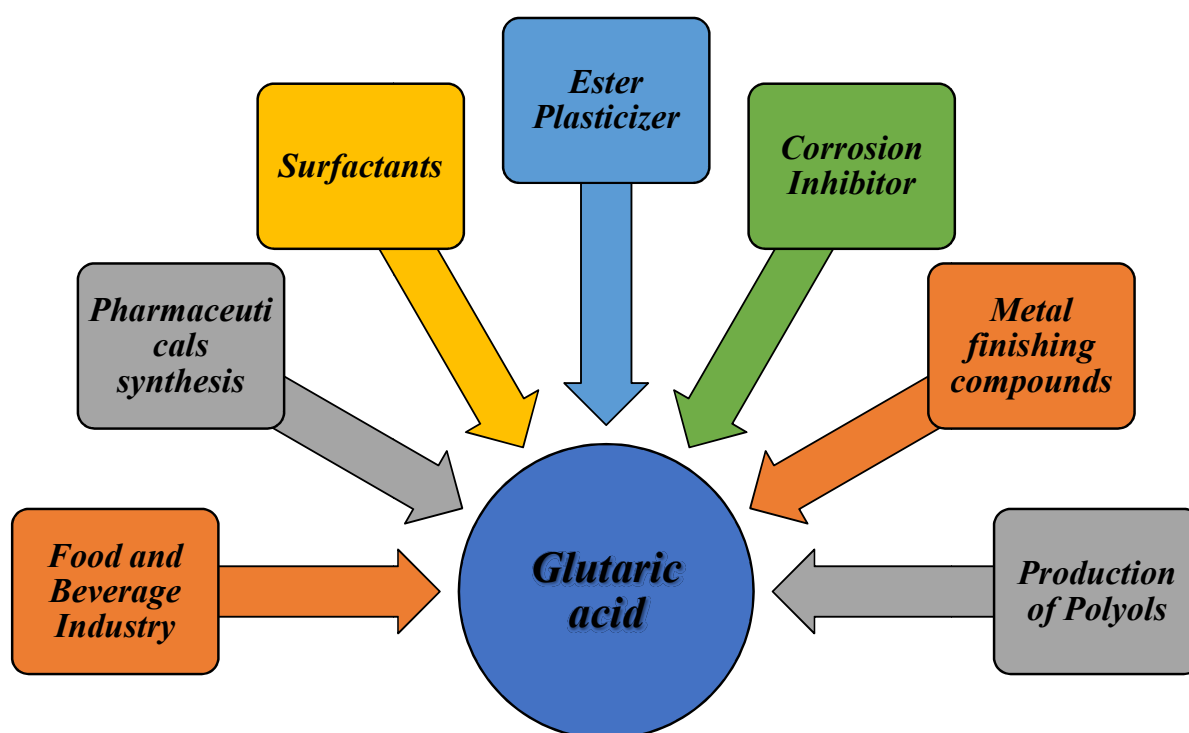


**Fig. 1** Various recovery methods of Carboxylic acid from fermentation broth

### **Glutaric Acid**

Glutaric acid, chemically known as pentanedioic acid,  $C_5H_8O_4$  is an organic compound characterized by two terminal carboxylic acid functional groups separated by three methylene units. It appears as a white crystalline solid, known for its water-soluble and biodegradable properties (Han et al. 2020). Traditionally, it is synthesized through petrochemical routes involving the oxidation of cyclopentane, adipic acid, or 1,5-pentanediol using harsh chemicals and energy-intensive conditions. However, with the growing demand for sustainable and eco-friendly production methods, bio-based synthesis of glutaric acid has gained significant attention. In particular, microbial fermentation using engineered strains of *Escherichia coli*, *Corynebacterium glutamicum*, and *Pseudomonas putida* (Han et al. 2020) has shown promise in converting renewable carbon sources such as glucose, glycerol, or lignocellulosic hydrolysates into glutaric acid under mild conditions. This biotechnological approach not only reduces environmental impact but also

aligns with circular economy principles by utilizing waste-derived substrates for value-added chemical production. This dicarboxylic acid is widely utilized due to its versatility and reactivity in numerous chemical processes and industries. Naturally occurring in various plants and produced synthetically via biochemical or chemical methods, glutaric acid serves as an important intermediate for numerous chemical syntheses. In pharmaceuticals, glutaric acid plays a pivotal role as an intermediate in drug synthesis, aiding in the development of medications such as antiseptics and anaesthetics (Uslu and Inci 2009). Its chemical structure provides unique reactivity, making it suitable for constructing complex pharmaceutical compounds. It also finds significant applications in the food industry as a food additive and acidity regulator. It is commonly used to maintain the pH balance, enhance flavor, and prolong the shelf life of various food products due to its safe and biodegradable nature. Additionally, it is employed in the formulation of plasticizers, corrosion inhibitors, and solvents, demonstrating its broad-based functional utility. The compound also finds use in agrochemicals, aiding in developing herbicides and pesticides, thus enhancing agricultural productivity (Athankar et al. 2017) and efficiency as shown in Fig 2.

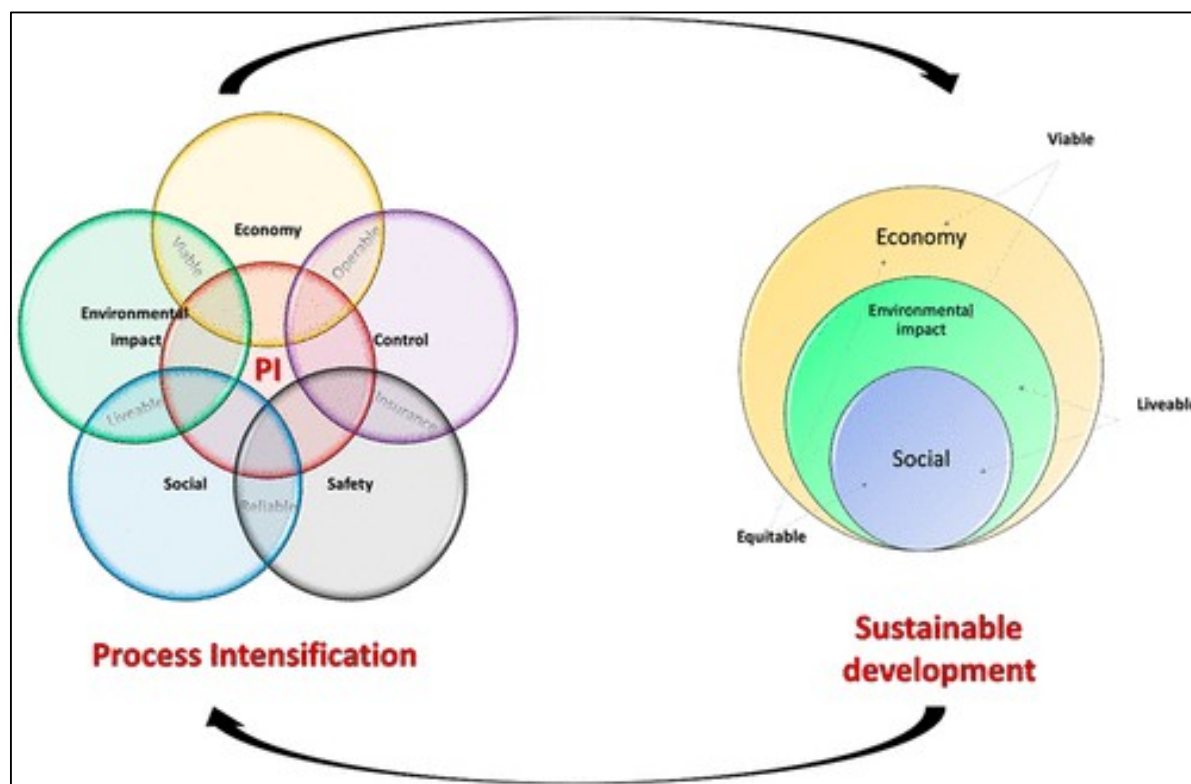


**Fig 2.** Few Applications of Glutaric acid

### Process Intensification

Process Intensification (PI) is an innovative approach in processing technology that focuses on enhancing the efficiency, effectiveness, and quality of product manufacturing by minimizing energy and resource usage (Srivastava et al. 2024). This advanced strategy is gaining traction as a

lower the costs of various processing activities. By enabling the development of efficient, time-saving, and resource-conserving operations with reduced byproduct formation, PI supports greener processing methods and contributes to lowering carbon emissions(Dutta et al. 2023). One of the key advantages of PI is increased efficiency. Techniques such as microreactors and high-gravity rotating packed beds dramatically improve heat and mass transfer, enabling faster reaction rates and shorter processing times (Stankiewicz & Moulijn 2000). This efficiency leads to smaller equipment sizes, which not only reduces capital costs but also supports modular and decentralized production systems, crucial for on-site and on-demand manufacturing (Hessel et al.2005). Finally, PI enhances product selectivity and yield due to better control over process conditions, and its flexibility allows for easier scaling and process modification, making it suitable for industries focusing on specialty chemicals and pharmaceuticals. In summary, process intensification represents a paradigm shift in chemical process design by merging efficiency, safety, environmental performance, and cost-effectiveness as shown in Fig 3.



**Fig. 3** Processes Intensification for Sustainability: Prospects and Opportunities  
(Márquez et al.2023)

Its implementation can significantly enhance competitiveness and sustainability in the chemical industry. The study explores green and intensified methods, including reactive extraction, natural solvents, ionic liquids, deep eutectic solvents, microwave- and ultrasound-assisted separations, and hybrid or microfluidic systems for the efficient recovery of glutaric acid from

fermentation broths. Emphasis is placed on understanding the theoretical principles and operational parameters influencing separation efficiency, such as solvent composition, molar ratios, hydrogen bonding, and reusability under various conditions.

### **Overview of Intensified Sustainable Approaches**

Intensified sustainable approaches offer transformative advancements in chemical separations by boosting efficiency, decreasing energy demand, and reducing ecological footprints. For glutaric acid recovery from fermentation broths, these methods provide alternatives to conventional energy-intensive processes such as distillation or solvent-based extraction. Technologies like reactive extraction using green solvents have shown high selectivity for carboxylic acids while reducing solvent toxicity and improving biodegradability (Sharma & Mandal 2020; Binnemans et al. 2015). Deep eutectic solvents (DES) and Ionic liquids (ILs), due to their customizable physicochemical properties and low vapor pressure, have emerged as promising sustainable solvents capable of efficiently separating organic acids from aqueous media (Cui et al. 2019; Zhang et al. 2021). Microwave and ultrasound-assisted separations further enhance mass transfer rates, reduce extraction times, and lower energy requirements compared to traditional thermal methods (Kujawski et al. 2020; Nanda et al. 2021). Additionally, hybrid systems, which combine multiple intensification principles such as solvent extraction coupled with physical activation, offer synergistic effects, improving both separation performance and operational sustainability (Sheldon 2016). Emerging platforms like microfluidic devices and inverted coiled separation systems allow for enhanced phase contact, rapid mixing, and precise control over process conditions at micro scales, providing opportunities for scale-up and continuous processing (Kerton and Marriott 2013; Van der Bruggen and Vandecasteele 2003). These intensified sustainable approaches align with green chemistry principles, promote solvent reuse, and support circular economy goals, making them highly relevant for industrial-scale recovery of glutaric acid and other bio-based chemicals (Anastas and Warner 1998; Zimmerman et al. 2020).

### **Physical Extraction**

Liquid–liquid extraction (LLE) is a widely used separation technique that involves partitioning components of a liquid mixture (referred to as the feed) into a second, immiscible liquid phase known as the solvent. This process yields two distinct streams: an extract phase enriched with the desired solute and a raffinate phase depleted of that solute. LLE is commonly applied in diverse industries such as bioproduct recovery from fermentation broths, pharmaceutical production, food processing, and the treatment of industrial wastewater (Seader et al. 2010; Smith et al. 2005). The separation efficiency depends on the differences in the feed components' physicochemical properties like polarity and hydrophilic/hydrophobic behavior. The driving force for solute transfer between phases is the deviation from thermodynamic equilibrium, and this transfer is also governed



by the interactions between the solvent and the feed constituents, which ultimately influence the equilibrium state (Treybal 1980; Hati and Mukhopadhyay 2012). The efficient separation and recovery of organic acids are crucial for both economic and environmental sustainability. Among the various techniques available such as dialysis, adsorption, precipitation, crystallization, and distillation, liquid-liquid extraction stands out due to its operational simplicity, potential for selectivity, and scalability. This approach has shown promising results for recovering a wide range of valuable acids, including lactic (Djukić-Vuković et al. 2019; Han and Hong 1996; Marták and Schlosser 2006; Mungma et al. 2019; Othman et al. 2017; Wasewar et al. 2004), acrylic (Kar et al. 2017; Keshav et al. 2009), nicotinic (Gautam and Datta 2022; Kumar et al. 2008), levulinic (Gutiérrez et al. 2022; Kumar et al. 2019), caproic (Wasewar and Shende 2011; Wasewar and Shende 2010), gallic (Athankar et al. 2016; Pandey and Kumar 2020), protocatechuic (Antony and Wasewar 2022; De et al. 2018), propionic (Bilgin et al. 2009; Wasewar and Keshav 2010), and vanillic acids (Dandekar and Wasewar 2021) using a variety of extractants. For physical extraction, different kinds of conventional solvents can be used as diluents such as polar-nonpolar, protic-aprotic, inorganic-organic, natural solvents, etc (Wasewar 2012). The selection of extractants is based on their polarity and hydrophobicity, which are critical factors influencing the extraction efficiency. Polar solvents typically exhibit strong interactions with acidic solutes through hydrogen bonding or dipole-dipole interactions, enhancing the transfer of polar acids into the organic phase (Politzer and Murray, 2007). On the other hand, solvents with moderate hydrophobic character improve phase separation and reduce solute back-extraction. Natural extractants, in particular, present a more sustainable alternative to synthetic solvents, aligning with green chemistry principles while maintaining effective separation performance (Almohasin et al. 2023). Physical extraction involves the extraction of solute into inert non-reacting hydrocarbons and substituted hydrocarbons and is relatively free of complexities.

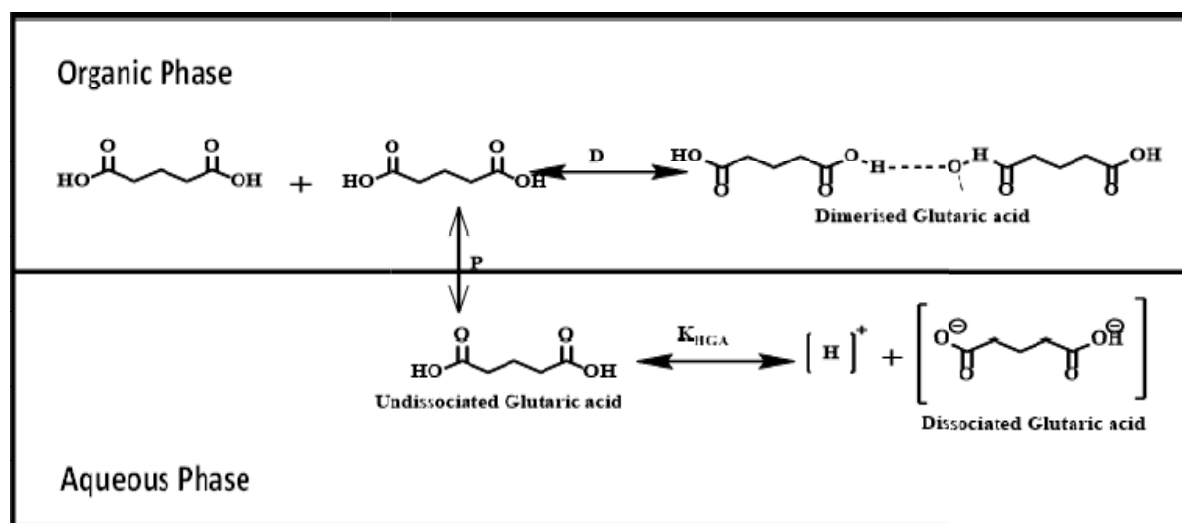


Fig. 4 The extraction of Glutaric acid from an aqueous phase

Three factors to be considered for physical extraction ( Wasewar et al. 2011; Wasewar and Keshav 2010): (a) ionization of the acid in the aqueous phase, (b) partial dissociation of the acids between two phases, and (c) dimerization of the acid in the organic phase. The concept of physical extraction is presented in Fig. 4.

#### ***Distribution Coefficient ( $K_D$ )***

The distribution coefficient ( $K_D$ ), also known as the partition coefficient, is defined as the ratio of the concentration of the solute (in this case, glutaric acid) in the organic phase to that in the aqueous phase at equilibrium. It reflects how well the solute partitions between the two immiscible phases and is mathematically expressed as:

$$K_D = \frac{C_{org}}{C_{aq}} \quad (1)$$

Where,  $C_{org}$  is the equilibrium concentration of glutaric acid in the organic phase,  $C_{aq}$  is the equilibrium concentration in the aqueous phase. A higher  $K_D$  value indicates better extraction performance and stronger solute affinity for the organic phase.

#### ***Extraction Efficiency ( $E\%$ )***

Extraction efficiency ( $E\%$ ) quantifies the percentage of solute that has been transferred from the aqueous phase into the organic phase during the extraction process. It is calculated using the initial and final solute concentrations in the aqueous phase or from the distribution coefficient as:

$$E\% = \frac{K_D \times 10}{1 + K_D} \quad (2)$$

**Table 1.** Distribution coefficients and extraction efficiency of various solvents used for the physical separation of Glutaric acid from the literature

<b>Solvent</b>	<b>Average Distribution Coefficient (<math>K_D</math>)</b>	<b>Average Extraction Efficiency (<math>E\%</math>)</b>	<b>References</b>
Ethyl Acetate	1.293	54.98	Athankar et al. (2017)
Hexanol	2.116	66.46	Athankar et al. (2017)
Cyclohexane	0.075	6.90	Mohadikar et al. (2022)
Rice Bran Oil	0.151	12.48	Mohadikar et al. (2022)
Sesame Oil	0.037	3.53	Mohadikar et al. (2022)

The Table compares the extraction performance of various solvents for glutaric acid based on their average distribution coefficients ( $K_D$ ) and Extraction efficiencies. Hexanol and ethyl acetate demonstrate significantly better extraction capabilities, while natural oils and cyclohexane show poor performance. Experiments were performed in our laboratory to investigate the separation of glutaric acid using natural and polar extractants. Polar solvents like oleyl alcohol and 1-octanol were used and sunflower oil and soybean oil were employed as natural solvents; these were chosen due to their functional groups' strong interaction with the formed complexes. The results showed that oleyl alcohol (avg.  $E\%$  is 57.28 % and avg  $K_D$  is 1.362) and octanol (avg.  $E\%$  is 53.88 % and avg.  $K_D$  is 1.177) exhibited greater values for both distribution coefficient as well as extraction

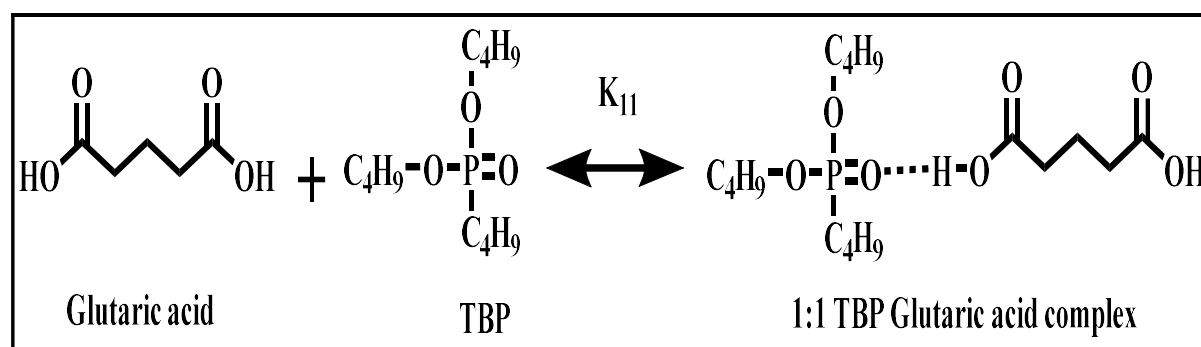
efficiency as shown respectively. Natural extractants like sunflower oil (avg  $E\%$  is 37.86% and avg  $K_D$  is 0.471) and soyabean oil (avg  $E\%$  is 22.64 % and avg  $K_D$  is 0.297) showed lower extraction efficiency than chemical extractants due to their fatty acid chain structure and non-polar nature (Thakre et al. 2025). Also, the natural extractants have high relative viscosity and density. With zero dipole moment, they lack free electrons for acid complexation in the organic phase and are less effective as hydrogen donors compared to oleyl alcohol and octanol. Consequently, their distribution coefficient and extraction efficiency were lower (Mohadikar et al. 2022).

### Reactive Extraction

Among the various recovery techniques described earlier, reactive (liquid) extraction has proven to be particularly effective for isolating organic acids from aqueous solutions. This method enhances separation efficiency by coupling chemical interaction between the solute and extractant with physical processes such as solute diffusion and dissolution (Kumar et al. 2021). Reactive extraction offers several advantages: (i) it is adaptable, suitable for a wide range of volumes and operable under varying temperature and pH conditions; (ii) it is cost-efficient, requiring relatively low infrastructure investment, with the added benefit of solvent recyclability; and (iii) it is rapid, as the extraction occurs over a shorter duration and can be implemented in continuous processing systems (Datta et al. 2015). In reactive extraction secondary phase containing an extractant is used to reversibly bind with a solute in a mixture. The ideal complexing agent forms a strong and easily reversible interaction with the solute (Wasewar and Shende 2011). Because many of these agents are either highly viscous, they are typically dissolved in low-viscosity, low-molecular-weight diluents (Wasewar et al. 2003). These diluents not only stabilize the equilibrium by solvating the complexes but also influence other factors, such as viscosity, density, and interfacial tension. The extraction process can be depicted as a chemical reaction where the solute reacts with multiple extractant molecules to form a complex, governed by an equilibrium constant (Wasewar et al. 2004). A variety of organic solvents can be employed for the extraction of different acids, and these are generally grouped into three main classes: (i) carbon-based, (ii) amine-based, and (iii) phosphorus-based solvents. Carbon-based solvents are further categorized into two types: (i) active (polar) and (ii) inert (non-polar) solvents (Wasewar et al. 2002). Active solvents, such as alcohols, ketones, chlorinated hydrocarbons, and halogen-substituted aromatic compounds, contain functional groups capable of forming O–H bonds with acid molecules during extraction (Wennersten 1983). These solvents provide a suitable medium for the formation of acid extractant complexes. In contrast, non-polar solvents like alkanes and alkyl-substituted aromatics (e.g., benzene derivatives) exhibit limited solvating capacity for polar complexes and show low acid distribution. Amine-based solvents (e.g., trioctylamine, Alamine 336, Aliquat 336) and phosphorus-containing extractants (e.g., tributyl phosphate, trioctyl phosphine oxide) are often more efficient than carbon-based ones, due to their ability to form strong ion pairs and hydrogen bonds with acids (Wasewar 2012).

Typically, these aminic and phosphoric solvents are used in combination with polar or non-polar diluents for effective acid extraction. Since the salts of amines and acids are slightly soluble in the aqueous medium, there is always the critical role of a modifier (polar solvent) to improve the solubility of the salts in the extracted phase (Kertes and King 1986). Physical properties such as density, viscosity, surface tension, etc., of the organic phase can be controlled by nonpolar/polar solvents (diluents) and provide the stability of the acid extractant complex (Keshav et al. 2008).

In chemical extraction, the solute and extractant interact through specific mechanisms such as ion-pair formation, hydrogen bonding, or a combination of both (Lund 1965). When strong interactions exist between the acid and the extractant molecules, the likelihood of acid dimer formation is significantly reduced. Typically, the initial acid molecule forms an ion pair with the extractant, while the second acid molecule is incorporated into the complex via hydrogen bonding. For di- and tricarboxylic acids, intramolecular hydrogen bonding influences the overall stoichiometry of the resulting complexes (Ronco et al. 2020). When partial dissociation of acid occurs in the aqueous phase, the resulting ions can interact with extractant molecules at the phase boundary, initiating ion-pair formation at the interface. When the acid molecules partially dissociate in the aqueous phase, the dissociated acid molecules interact with extractant molecules at the interface, and the ion-pair interaction enters the picture shown in Fig.5 (Athankar et al. 2015). Table 2 shows the various extractants used in the reactive extraction of glutaric acid in terms of distribution coefficient and extraction efficiency.



**Fig. 5** 1:1 Acid-TBP complex formation across various diluent systems

The initial concentration was set based on a reference range of  $0.19\text{--}1.10\text{ mol}\cdot\text{L}^{-1}$ , which is typical of glutaric acid concentrations found in fermentation broths and industrial downstream processes. Experiments were conducted in 100 ml Erlenmeyer flasks at a constant temperature of  $298.15 \pm 1\text{ K}$ . Aqueous solutions with the desired initial concentration were prepared by dissolving weighed amounts of glutaric acid in double-distilled water. The solutions were mixed in a 1:1 ratio with (an aqueous solution of 10ml mixed with a 10 ml pure solvent(extractant)). The flasks were placed in an orbital shaking incubator (Model: S-24BL, REMI India) set at  $298.15 \pm 1\text{ K}$  and 220 rpm for 5 hrs, which was sufficient time to reach equilibrium based on preliminary experimental

studies. Subsequently, the samples were centrifuged at 4000 rpm for 5 minutes (REMI CENTRIFUGE-4C, India) to separate the phases.

**Table 2.** Distribution coefficient and Extraction efficiency for Reactive extraction of glutaric acid using various extractants tabulated from literature

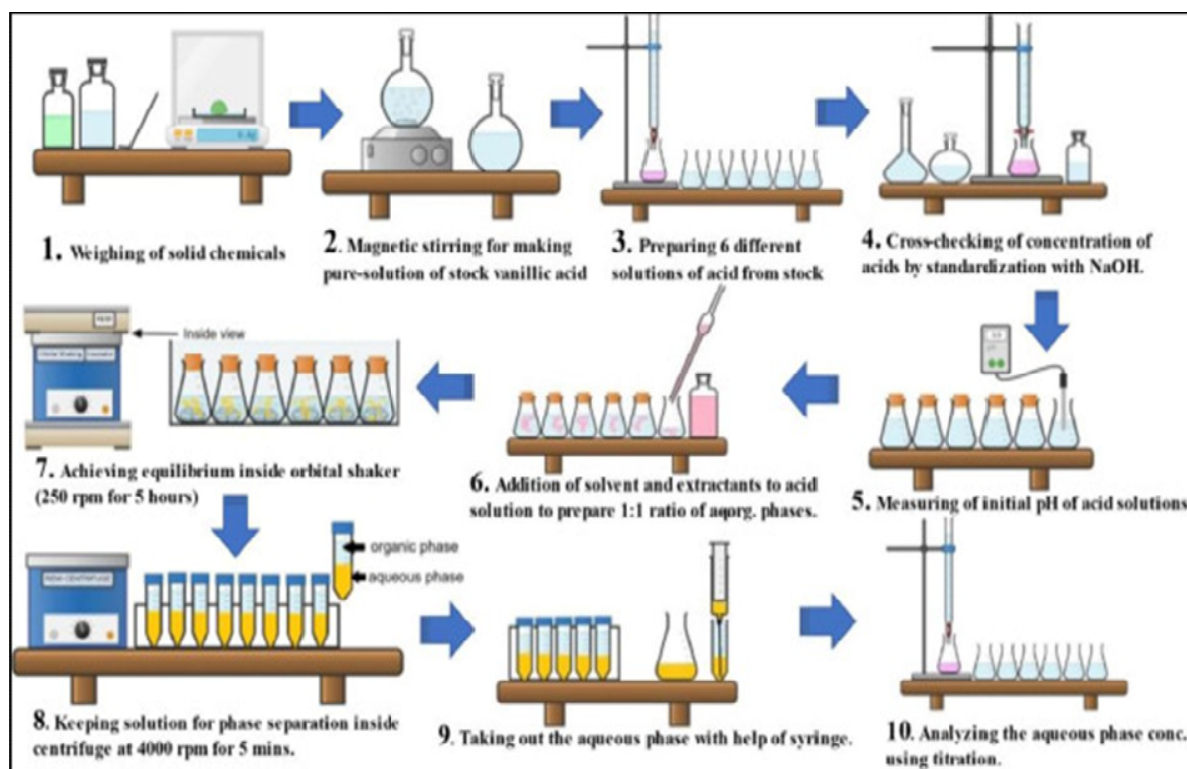
Extractant	Diluent	Avg $K_D$	Extraction efficiency (E%)	References
Aliquat 336	3-methyl-butan-1-ol	3.181	68.93	Pehlivanoğlu et al. (2010)
Aliquat 336	Octan-1-ol	1.89	68.22	Pehlivanoğlu et al. (2010)
Aliquat 336	2,6-dimethyl-4-heptanone	3.23	69.45	Pehlivanoğlu et al. (2010)
TBP	Ethyl acetate	2.497	70.96	Athankar et al. (2017)
TBP	Hexanol	2.06	52.22	Athankar et al. (2017)
TDA	MIBK	3.28	26.63	Uslu et al. (2009)
TDA	Toulene	2.72	21.69	Uslu et al. (2009)
TOA	Isomyl alcohol	2.161	60.13	Pehlivanoğlu et al. (2009)
TOA	Sunflower oil	11.12	91.68	Pehlivanoğlu et al. (2009)
TOA	Kerosene	3.95	60.67	Pehlivanoğlu et al. (2009)
TOA	MEK	2.44	52.76	Pehlivanoğlu et al. (2009)

# TOA is Trioctylamine, TBP is Tri-*n*-butylphosphate, TDA is Tridodecylamine, MIBK – Methyl ethyl Isobutylketone, MEK is Methyl Ethyl ketone

The equilibrium concentrations in the aqueous phase were measured through colorimetric titration, employing freshly prepared sodium hydroxide (NaOH) solutions that had been standardized with oxalic acid. The concentrations in the organic phase were then calculated using a mass balance approach. All experiments were repeated under identical conditions to ensure the reliability of the results. An experimental study for the glutaric acid separation through reactive extraction using various natural and conventional solvents, including oleyl alcohol, 1-octanol, with Tri-butyl phosphate (TBP) was carried out. The experimental procedure followed is summarized in Fig. 6.

Experiments for the reactive extraction of glutaric acid were performed in our laboratory to determine the extraction efficiency of the oleyl alcohol, octanol for TBP concentrations ranging from  $0.732 \text{ mol} \cdot \text{kg}^{-1}$  to  $3.6 \text{ mol} \cdot \text{kg}^{-1}$  in different diluents. The average extraction efficiencies observed were 59.66 % to 83.02 % for oleyl alcohol, and 56.96 % to 80.13% for octanol-TBP, with the highest recorded efficiency reaching 88.76% in oleyl alcohol. As TBP concentration increased from  $0.732 \text{ mol} \cdot \text{kg}^{-1}$  to  $3.6 \text{ mol} \cdot \text{kg}^{-1}$ ,  $K_D$  values also increased, ranging from 1.44 to 5.44 for oleyl alcohol and 1.29 to 4.24 for octanol. The polarity of the diluent is a key factor in reactive extraction, as it facilitates the solvation of polar and ion-paired organic compounds such as acid-extractant complexes via mechanisms like hydrogen bonding, dipole–dipole forces, and other intermolecular interactions. The highest glutaric acid efficiency was achieved using the oleyl alcohol-TBP, making

it the most effective choice for recovering glutaric acid from dilute aqueous solutions. A higher concentration of TBP led to increased values of both the distribution coefficient and extraction efficiency at a fixed glutaric acid concentration (Mukherjee et al. 2020). This behavior can be explained by the presence of a phosphoryl group in TBP, which acts as a strong Lewis base compared to carbonyl groups. Additionally, the presence of the  $\text{PO}_4^-$  group in TBP allows it to function as both an electron donor and an electron acceptor, supporting molecular interactions and complexation processes between solutes and solvent components (Joshi et al., 2019)



**Fig. 6** Experimental setup for the Reactive extraction of Carboxylic acid (Dandekar et al. 2022)

### *Effect of the Temperature*

Athankar et al. (2017) examined how temperature impacts the glutaric acid reactive extraction using tri-n-butyl phosphate (TBP) in two diluent hexanol and ethyl acetate and found that rising temperature adversely affects the extraction process. Increase in temperature from 308 K to 338 K, both the distribution coefficient ( $K_D$ ) and extraction efficiency ( $\eta\%$ ) showed a consistent decline. In ethyl acetate,  $K_D$  fell from 2.72 to 2.28, while in hexanol, it dropped from 2.28 to 1.84. Correspondingly, the extraction efficiency decreased from 73.1% to 69.5% in ethyl acetate and from 69.5% to 64.8% in hexanol. This negative correlation indicates that the extraction reaction is exothermic, a conclusion further supported by the negative values of enthalpy ( $\Delta H$ ) and entropy ( $\Delta S$ ) calculated during the study -935.06 J/mol and -1.35 J/mol·K for ethyl acetate, and -1110.38 J/mol and -2.19 J/mol·K for hexanol, respectively. The reduction in the equilibrium complexation

becomes less favorable at higher temperatures. Moreover, elevated temperatures enhance the ionization of glutaric acid in water, limiting the availability of the non-ionized form necessary for efficient extraction. These findings clearly suggest that operating at lower temperatures leads to better extraction performance.

### ***Effect of Aqueous Phase pH***

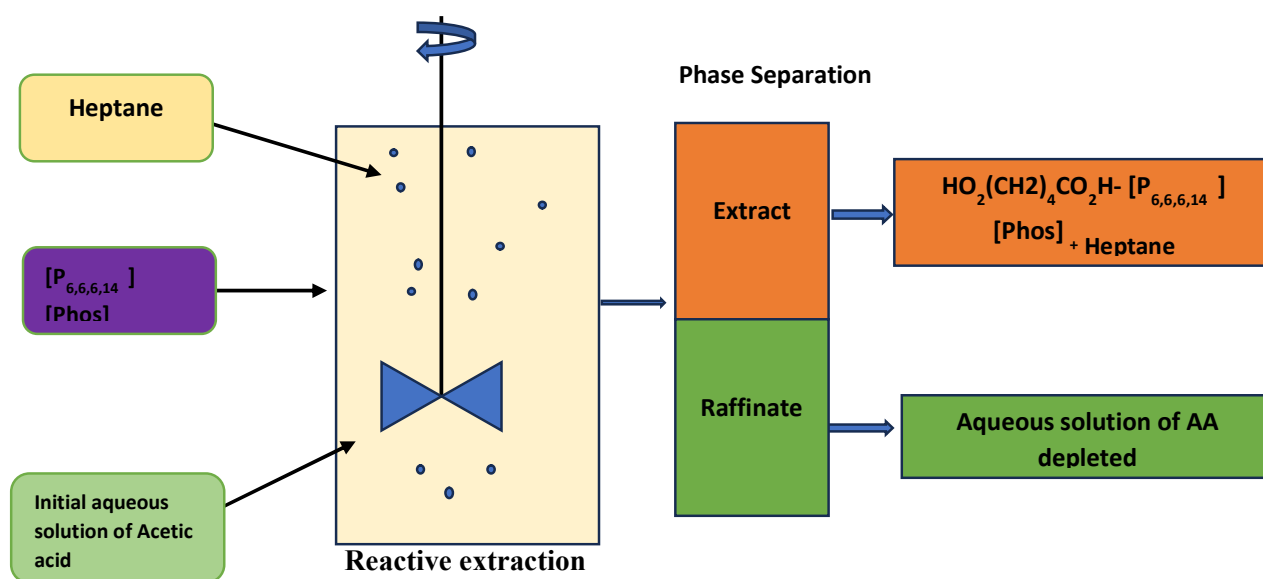
Aqueous phase pH is a key parameter governing the efficiency of reactive extraction. As a dicarboxylic acid with pKa values of approximately 4.31 and 5.41, glutaric acid remains mostly in its fully protonated form at pH values below 4. This protonated form interacts more readily with extractants, particularly aliphatic amines such as tri-n-octylamine (TOA) and Aliquat 336, which exhibit enhanced extraction efficiency under acidic conditions due to the formation of stable ionic complexes with the undissociated acid (Doeker et al. 2021). When the pH increases beyond 5.4, glutaric acid begins to lose protons, forming monoanionic or dianionic species that interact less effectively with amine-based extractants, thereby lowering the extraction efficiency. In contrast, organophosphorous extractants like tri-n-butyl phosphate (TBP) are more tolerant to pH variation and retain reasonable extraction performance across a broader pH range, typically from pH 3 to 6 (Wang et al. 2001). Adjusting the pH within this optimal range not only improves extraction efficiency but also aids in the selective separation of glutaric acid from other acids or impurities present in the mixture (Lee et al. 2018; Ramadoss and Vasudevan 2019). Therefore, controlling the pH between 3 and 5 is essential for maximizing the distribution coefficient and achieving effective recovery of glutaric acid. Therefore, maintaining an optimal pH level is essential for maximizing both distribution coefficients and separation effectiveness.

### ***Effect of Initial acid concentration***

The initial concentration of carboxylic acid in the aqueous phase is a key factor that affects the performance of reactive extraction. As this concentration increases, the mass transfer driving force improves, leading to a rise in extraction efficiency due to a steeper gradient between the two phases (Wasewar 2012). At lower acid concentrations, extractants such as tri-n-octylamine (TOA) or tributyl phosphate (TBP) efficiently form stable acid extractant complexes, enabling almost complete extraction of the acid into the organic phase (Abraham et al. 2017). However, when the acid concentration exceeds a certain limit, the extractant becomes saturated, which restricts the formation of additional complexes and decreases the extraction efficiency (Lalikoglu 2022). This limiting concentration is related to the complexation ratio, often observed as 1:1 or 2:1 (Wasewar & Keshav 2010). Additionally, acid dissociation plays a crucial role. Increased acid concentration usually lowers the pH of the aqueous phase, enhancing the proportion of undissociated acid molecules that are more readily extracted. Nonetheless, very high concentrations may lead to challenges such as third-phase formation and instability in the organic phase, which can hinder the separation process (Riveiro et al. 2020).

## Ionic Liquids (ILs)

The high volatility of traditional extractants in reactive extraction poses challenges for recovery and raises environmental concerns. These issues can be effectively addressed by using ionic liquids as alternative extractants. ILs are salts composed of anions and cations that remain in a liquid state at temperatures below 100°C. They exhibit several advantageous properties, including negligible vapor pressure, broad liquid range, excellent thermal and chemical stability, and nonflammability, making them ideal for safer and more eco-friendly applications (Antony et al. 2022). Their minimal vapor pressure helps prevent atmospheric solvent loss and lowers the health risks to workers, supporting their classification as green solvents. In the extraction of carboxylic acids from aqueous solutions, conventional solvents often offer only moderate selectivity or extraction efficiency and tend to suffer from considerable solvent loss. ILs can overcome these limitations due to their superior extraction abilities (Blaga et al. 2022). However, their relatively high viscosity can hinder mass transfer during extractive separation processes. This drawback can be mitigated by introducing a diluent, which reduces viscosity and enhances separation performance. As a result, ILs continue to attract significant attention for their potential use in extraction and separation technologies (Jacquemin et al. 2006).



**Fig 7.** Pictorial representation of Reactive extraction of acetic acid with heptane and Ionic liquids

Fig 7 shows the separation of carboxylic acid with Ionic liquids. Ionic liquids are organic salts in the liquid state, composed of carefully selected combinations of cations and anions. The hydrophobic nature of these liquids is primarily determined by the anionic component. These anions may be either organic or inorganic, including compounds such as bis(tri-fluoro-methane-sulfonyl)imide, hexa-fluoro-phosphate, tetra-fluoro-borate, acetate, nitrate, and halide ions (Kirchhecker et al. 2016). The cationic counterparts are typically organic in nature and include groups like phosphonium, ammonium, imidazolium, sulfonium, pyridinium, and pyrrolidinium.



Ionic liquids are salts in the liquid state with negligible vapor pressure and tunable physicochemical properties (Bodo 2021). They exhibit excellent solvation capabilities and can be tailored for selective extraction of carboxylic acids. Imidazolium- and phosphonium-based ILs have shown promising results for glutaric acid separation due to their affinity for hydrogen bonding with acidic groups. When an aqueous solution containing organic acids is brought into contact with an organic phase either a pure ionic liquid or a solvent system incorporating ionic liquids the acid may be transferred through physical means such as solubilization and diffusion (with the overbar denoting species present in the organic phase), or it may engage in complex formation involving one or more acid or ionic liquid molecules (denoted by  $n$ ,  $m$ ). as shown in equation 1:



where  $\text{RCOOH}$  is the undissociated acid and  $\text{IL}_m$  molecules of ionic liquids

Such interactions may lead to the formation of reverse micelles, where the ionic liquid behaves like a surfactant due to its asymmetric structure, characterized by distinct polar charged regions and extended cationic alkyl chains (Marták and Schlosser 2019; Shimizu et al. 2022a). These structures can encapsulate water, affecting its solubility, and tend to disassemble as the concentration of extracted acid increases. Alternatively, ionic liquid–acid interactions may result in the formation of IL–acid complexes, which can aggregate into clusters stabilized by electrostatic and intermolecular forces (Sprakel and Schuur 2019). To assess the efficiency of extraction, the distribution coefficient is employed, which represents the ratio of the organic acid concentration in the organic (ionic liquid-containing) phase to that in the aqueous (raffinate) phase. These associations can be obtained as reverse micelles (the ionic liquid act as surfactant due to asymmetrical structure with localized polar charged domains and prolonged cationic alkyl chain (Marták and Schlosser 2019; Shimizu et al. 2022), which influences water solubility by including it and are broken once the extracted acid concentration increases, or as IL-acid complexes that can exist as clusters due to electrostatic and intermolecular forces (Sprakel and Schuur 2019). For the extraction quantification, the distribution coefficient is used defined as the ratio between the organic acid concentrations in the organic phase (extract IL or solvent with IL) and the raffinate phase (exhausted initial aqueous solution).

Marták and Schlosser (2019) outlined three distinct mechanisms involved in the reactive extraction of carboxylic acids, such as lactic and butyric acid, when using ionic liquids (ILs): (a) competitive extraction, where both carboxylic acid and water vie for hydrogen bonding sites within the polar regions of the IL; (b) non-competitive extraction, in which water does not interact with the IL; and (c) co-extraction, where water is extracted alongside the acid. In the competitive model, extraction is driven by complexation between an IL ion pair and multiple acid molecules ( $\text{RCOOH}$ ), with stability constants ( $k_n$ ) describing the strength of the interaction. These constants typically decline as the number of acid molecules per complex increases ( $n > 2$ ). Phosphinate and carboxylate-based ILs have oxygen-containing anions that offer hydrogen bonding sites for water.

During extraction, acid molecules replace these water molecules within the IL's polar microenvironment. While hydrophobic ILs are generally favored due to their low water solubility (e.g., CYPHOS® IL 104 has a solubility of 9.1 g/m<sup>3</sup>), they can still absorb substantial moisture up to 15.3% at 25 °C because of their hygroscopic properties (Sheridan et al. 2016). The extent of water solubility is largely dependent on the IL's molecular structure, and reverse micelle formation may occur at low IL concentrations (Schlosser et al. 2018). In co-extraction, water molecules can act as bridges between acid chains and IL ion pairs, facilitating the process. In systems where the IL anion is water-soluble (e.g., chloride), ion exchange may occur, substituting the IL's original anion with that of the acid. However, when hydrophobic anions are present, the extraction proceeds primarily through hydrogen bonding with the undissociated acid, especially under conditions where pH is below the acid's pK<sub>a</sub> (Weiß et al. 2021). In the non-competitive mechanism, where  $k_n = 0$ , the acid-IL complexation occurs independently of water participation (Shimizu et al. 2022b). If the carboxylic acid involved is stronger than the hydrophobic acid derived from the IL anion as in the case of lactic acid interacting with phosphonium ILs it can displace the IL anion, leaving the weaker acid in the organic phase. The water solubility of the IL anion also plays a key role in influencing extraction efficiency, complex composition, and potential overloading effects. Notably, at elevated acid concentrations, the IL tends to retain less water (Bodo 2021). In the co-extraction mechanism, water present in the organic phase includes both that bound to the IL and that associated with hydrated acid molecules, with the amount of co-extracted water increasing proportionally to the extracted acid.

Nilay Baylon (2020) in his study investigated the reactive separation of glutaric acid from water by using four different types of imidazolium-based ionic liquids. An organophosphorus compound, TBP, dissolved in green ionic liquids, was used as the extractant. From the acquired data, extraction efficiencies (E), distribution coefficients (D), and loading factors (Z) were determined and shown in Table 3.

**Table 3.** Performance of 4 different Imidazolium-Based Ionic Liquids in Reactive Extraction of Glutaric Acid

<b>Ionic Liquid</b>	<b>Avg K<sub>D</sub></b>	<b>Extraction Efficiency (E%)</b>	<b>Loading Factor (Z)</b>
[BMIM][Tf2N]	3.54	77.98	0.041
[BMIM][PF6]	3.3	76.72	0.04
[HMIM][Tf2N]	3.33	76.9	0.04
[HMIM][PF6]	3.33	76.92	0.04

# [BMIM][Tf2N]-1-Butyl-3-methylimidazolium bis (trifluoromethyl sulfonyl) imide, [BMIM][PF6]-1-Butyl-3-methylimidazolium hexafluorophosphate, [HMIM][Tf2N]- 1-Hexyl-3-methylimidazolium bis (trifluoromethyl sulfonyl) imide, [HMIM][PF6]- 1-Hexyl-3-methylimidazolium hexafluorophosphate

This study investigated the potential of imidazolium-based ionic liquids as environmentally friendly solvents for the reactive extraction of glutaric acid from aqueous media. Four ionic liquids [BMIM][Tf<sub>2</sub>N], [BMIM][PF<sub>6</sub>], [HMIM][Tf<sub>2</sub>N], and [HMIM][PF<sub>6</sub>] were evaluated in combination with 3 mol·L<sup>-1</sup> TBP as the extractant. All tested ILs demonstrated high extraction performance, exhibiting favorable distribution coefficients. Notably, [BMIM][Tf<sub>2</sub>N] delivered the best results, achieving an extraction efficiency of 77.98% and a distribution coefficient of 3.54, highlighting its effectiveness in the separation process. These findings confirm the viability of these ILs particularly [BMIM][Tf<sub>2</sub>N] as sustainable alternatives to traditional organic solvents for efficient glutaric acid recovery. Experiments were conducted in our laboratory on the reactive extraction of glutaric acid using CYPHOS IL 167 Phosphonium salt in the concentration range of 0.0402 – 0.2011 mol. L<sup>-1</sup>, the highest extraction efficiency and K<sub>D</sub> was found to be of 89.02 % and 5.360, respectively.

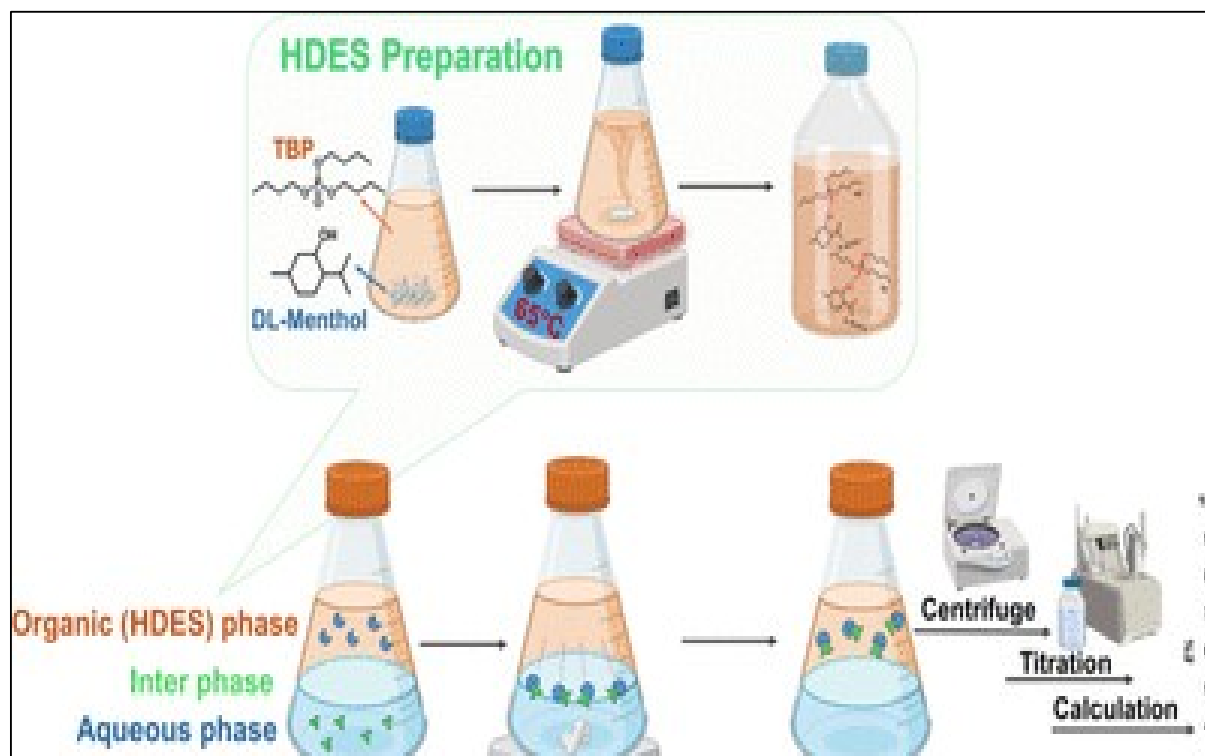
### Deep Eutectic Solvents (DESs)

Deep eutectic solvents represent an environmentally friendly class of solvents created by combining a hydrogen bond donor (HBD) with a hydrogen bond acceptor (HBA), producing a eutectic blend whose melting point is notably lower than that of the individual components (Abbott et al. 2008). These solvents are gaining recognition as viable substitutes for conventional organic solvents and ionic liquids due to their biodegradability, minimal toxicity, cost-efficiency, and straightforward synthesis that does not require extensive purification (Smith et al. 2014). DESs also possess unique characteristics such as low volatility and non-flammability, which broaden their application potential (Martins et al. 2019). Unlike ionic liquids, which are generally composed of discrete ion pairs, DESs arise from eutectic combinations of Lewis or Brønsted acids and bases, allowing for diverse ionic compositions. Their physical and chemical properties such as polarity, viscosity, and solvation capability can be finely adjusted by modifying the HBD and HBA constituents (Nam et al. 2023). The physicochemical characteristics of the resulting DESs such as viscosity, solubility, density, and melting point depend heavily on several factors: molar ratio of components, preparation temperature, presence of water, and the nature of the HBD and HBA used (Li et al. 2023). DESs have shown significant potential in a variety of domains, including catalysis, extraction, electrochemistry, and bioprocessing, especially in the eco-friendly separation of bio-based compounds such as organic acids, flavonoids, and renewable fuels (Aşçı & Lalikoglu 2021; van den Bruinhorst et al. 2018). Their sustainable nature and compatibility with renewable resources position DESs as ideal candidates for green chemistry innovations.

Reactive extraction of carboxylic acids using Deep eutectic solvents has gained attention as a sustainable and efficient alternative to conventional solvent systems. DESs, formed through hydrogen bonding between a hydrogen bond donor and acceptor, can chemically interact with carboxylic acids to form stable, extractable complexes (Wang et al. 2021). This facilitates high extraction efficiency and selectivity, particularly for bio-based acids such as glutaric, succinic, and

itaconic acid. In reactive extraction, DESs not only act as diluents but also actively participate in the extraction mechanism, enhancing the distribution coefficient ( $K_D$ ) and extraction efficiency ( $E\%$ ). In this approach, an extractant such as a tertiary amine like tri-*n*-octylamine (TOA) or phosphoric extractant like TOPO or TBP is typically dissolved in a DES composed of components like choline chloride (HBA) and decanoic acid or menthol (HBD). The amine reacts with the undissociated glutaric acid to form a stable acid amine complex, which is solubilized in the DES phase. The unique polarity and hydrogen bonding environment provided by DES enhances the solubility of this complex while maintaining low toxicity and volatility key criteria for green solvents. DES-based systems improve extraction efficiency ( $E\%$ ) and distribution coefficients ( $K_D$ ) compared to conventional organic solvents (Gautam & Datta 2022). They also offer tunability by varying the molar ratio and composition of the HBA and HBD, allowing fine control over selectivity and phase behavior. Moreover, DESs are often biodegradable, recyclable, and non-flammable, aligning well with sustainable separation goals. DESs such as choline chloride-urea or menthol-based systems have demonstrated strong affinity for carboxylic acids due to their tunable polarity and hydrogen bonding capabilities.

Experiments were conducted using a hydrophobic deep eutectic solvent (HDES) composed of DL-menthol (HBD) and tri-*n*-butyl phosphate (TBP, HBA), integrated in tri-*n*-octylamine (TOA) as a reactive extractant. HDES were prepared by combining menthol, serving as the hydrogen bond donor (HBD), with tributyl phosphate (TBP), acting as the hydrogen bond acceptor (HBA), in a closed glass vessel for 0.4, 0.6 and 0.8 mole fraction. The mixture was heated to approximately 80 °C and continuously stirred using a temperature-controlled magnetic stirrer until a transparent and homogeneous liquid was obtained. An aqueous solution of glutaric acid was prepared at a concentration of 0.195-1.133 mol. L<sup>-1</sup>. Equal volumes (3 mL each) of the aqueous glutaric acid solution and the organic phase comprising tri-*n*-octylamine (TOA) as the extractant and a hydrophobic deep eutectic solvent (HDES) based on menthol and tributyl phosphate (TBP) were added to an Erlenmeyer flask. The biphasic mixture was stirred in a temperature-controlled shaker at 298.15 K and 150 rpm for 20 minutes to attain equilibrium. After the extraction, the mixture was centrifuged at 4100 rpm for 5 minutes using a centrifuge to facilitate clear phase separation (Altunkaya et al. 2025). The aqueous phase was then separated and titrated with 0.1 N NaOH using phenolphthalein as an indicator a detailed experimental procedure is shown in Fig.8. The titration was performed to accurately determine the residual concentration of glutaric acid in the aqueous phase. The highest extraction efficiency was found to be 92.34 %. Hydrophobic DESs minimize water solubility issues and improve phase separation and reusability, making the system attractive for green and intensified separation processes (Shishov et al. 2017; Francisco et al. 2012).



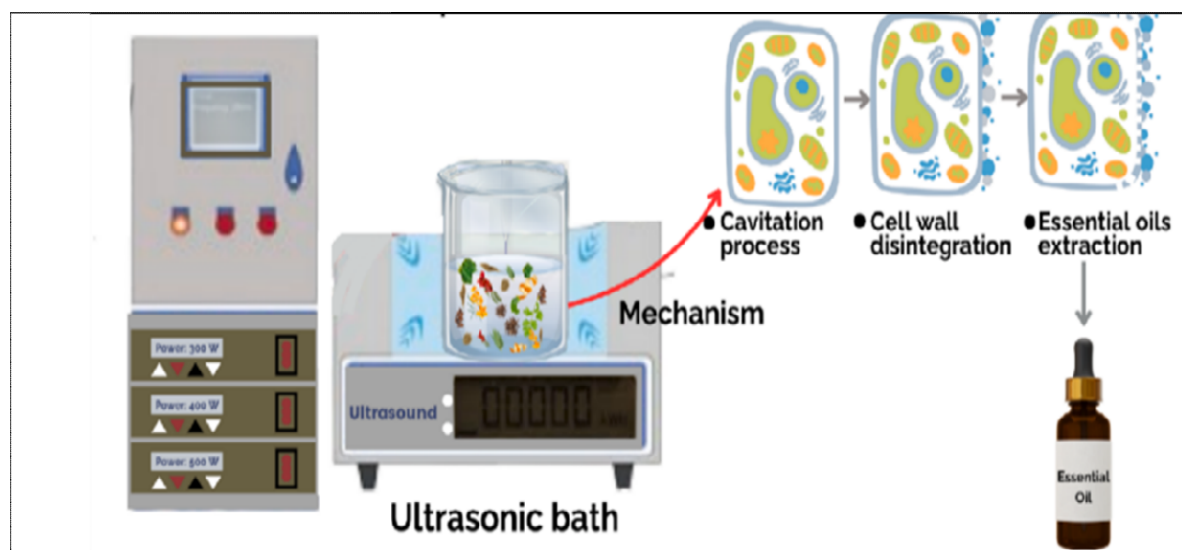
**Fig 8.** Experimental procedure for the Separation of carboxylic acid using DES  
(Altunkaya et al.2025)

### Ultrasound-Assisted Extraction (UAE)

Ultrasound-assisted extraction (UAE) is an advanced separation technique that utilizes ultrasonic waves to enhance the mass transfer between immiscible liquid phases. Ultrasonic waves improve liquid-liquid extraction by creating small high-energy zones in the liquids through a process called acoustic cavitation (Jadhav et al. 2023). Ultrasound-induced cavitation in extraction processes refers to the formation, growth, oscillation, and collapse of tiny gas bubbles in a liquid under the influence of ultrasound waves. This phenomenon is affected by the solvent's physical properties, such as viscosity, surface tension, and saturation vapor pressure. Cavitation occurs when the negative pressure during the rarefaction phase of ultrasound waves is sufficient to overcome the solvent's natural cohesive forces, creating a vacuum. The rapid pressure fluctuations caused by these sound waves lead to the formation and collapse of cavitation bubbles. Unlike solid particles, microbubbles enhance the liquid's compressibility, resulting in a reduction in viscosity.

This enhances the mixing of the two liquids and breaks the boundary layer between them, making it easier for the solute to move from one liquid to the other. As a result, the extraction process becomes faster and more efficient. The turbulence caused by the ultrasonic waves also helps the solvent to penetrate the liquid better and breaks up any solute clumps, increasing its ability to dissolve as shown in Fig.9. Additionally, the heat generated in these small zones can further improve the process for certain compounds (Kumar et al. 2021). The application of ultrasound generates acoustic cavitation, which creates localized high temperatures, pressures, and micro-

mixing effects. These phenomena improve solute diffusion and increase efficiency compared to conventional methods (Usman et al. 2012) .

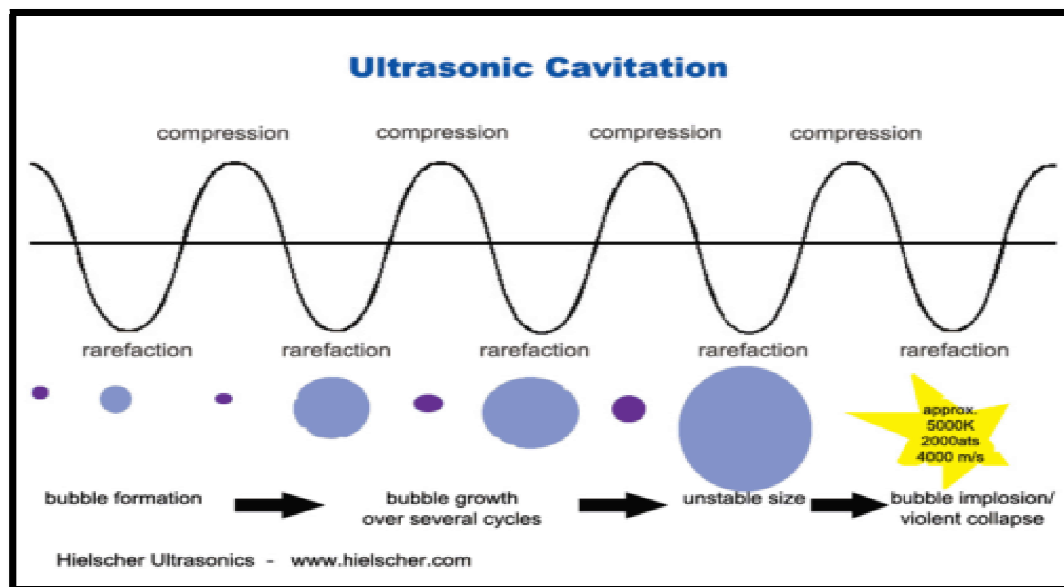


**Fig.9** Pictorial representation of Ultrasound-assisted extraction of essential oils

Ultrasound waves facilitate cell wall disruption and enhance mass transfer, leading to improved solubilization of glutaric acid in the extraction medium. This method is suitable for scale-up and synergizes well with solvent systems like DESs and ILs (Albero et al. 2019). Ultrasound-assisted extraction improves the efficiency of solute transfer between phases by inducing cavitation, which disrupts interfacial tension, enhances emulsification, and accelerates the mixing of immiscible liquids (Jha et al. 2017). Cavitation in extraction processes refers to the formation, growth, oscillation, and collapse of tiny gas bubbles in a liquid under the influence of ultrasound waves.

This phenomenon is affected by the solvent's physical properties, such as viscosity, surface tension, and saturation vapor pressure (Tiwari 2015). Cavitation occurs when the negative pressure during the rarefaction phase of ultrasound waves is sufficient to overcome the solvent's natural cohesive forces, creating a vacuum (Fig. 10, Bui et al. 20). The rapid pressure fluctuations caused by these sound waves lead to the formation and collapse of cavitation bubbles (Picó 2013). Unlike solid particles, microbubbles enhance the liquid's compressibility, resulting in a reduction in viscosity and an irreversible energy exchange, which do not occur with solid particles. The behavior and size of cavitation bubbles also depend on the ultrasound frequency. Low-frequency ultrasound (20–40 kHz) generates larger bubbles that collapse more violently, creating intense shear forces and high temperatures, which are ideal for disrupting cell walls and enhancing mass transfer in extraction processes. In contrast, high-frequency ultrasound (above 100 kHz) produces smaller bubbles that collapse less forcefully, making them more suitable for delicate extractions and fine

cavitation bubbles to form. Higher frequencies negatively impact cavitation since shorter rarefaction phases at increased frequencies make bubble formation more challenging. As a result, high-frequency ultrasound is considered non-destructive, as it prevents the occurrence of acoustic cavitation(Vázquez et al. 2013)



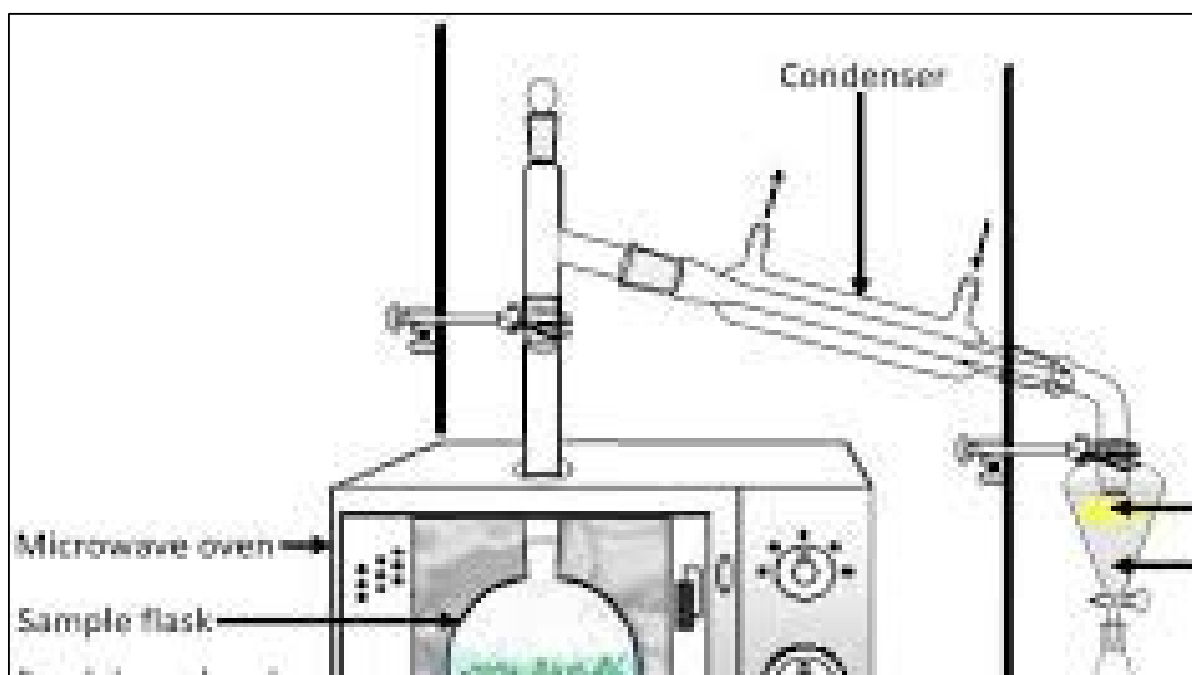
**Fig. 10** The formation of cavitation bubbles in UAE (Bui et al. 2020)

In our study the separation of glutaric acid from aqueous streams via ultrasound-assisted extraction using vegetable oils like sunflower oil and soyabean oil was studied. The initial concentration of glutaric acid was set between 0.19 and 1.14 mol/L, consistent with typical conditions in industrial downstream processes and fermentation broths. Experiments were performed in 100 ml Erlenmeyer flasks at a constant temperature of  $298.15 \pm 1$  K. Glutaric acid solutions were prepared by dissolving precise amounts of the acid in double-distilled water to achieve the desired initial concentrations. Each solution was mixed in a 1:1 volume ratio, combining 10 ml of the aqueous solution with 10 ml of the solvent (extractant). The flasks were placed in an orbital shaker incubator (Model: S-24BL, REMI India) at 250 rpm for 3 hours at 298 K, a duration determined to be sufficient for equilibrium based on preliminary tests. After shaking, the samples were treated in a laboratory-scale ultrasound sonication bath (Labman, India) operating at 40 Hz. The Erlenmeyer flasks were submerged in the sonication bath, which contained 2000 ml of tap water, and subjected to ultrasound treatment for 30 minutes at the same frequency. Phase separation was achieved by centrifuging the samples at 4000 rpm for 5 minutes using a REMI CENTRIFUGE-4C (India). A 2 ml sample of the aqueous phase was then analyzed using a UV-spectrophotometer (Shimadzu, UV-1800), with the maximum absorption wavelength ( $\lambda_{\text{max}}$ ) for glutaric acid recorded at 275 nm. This wavelength was used to determine the glutaric acid concentration in the aqueous phase, while the concentration in the organic phase was calculated

efficiency and distribution coefficient, with a correlation found between these parameters and the solvent's physicochemical properties. The distribution coefficient ( $K_D$ ) values for Glutaric acid across a concentration range of 0.19-1.14 mol/L were found to be between 0.354-0.686 for sunflower oil, and 0.258-0.429 for soyabean oil. The observed extraction efficiencies of sunflower oil (46.20 %) and soybean oil (34.20 %) with Ultrasound-assisted and for without ultrasound it was sunflower oil (31.31 %), and soybean Oil (22.65%) were recorded.

### Microwave-assisted extraction

Microwave-assisted extraction (MAE) is a widely used technique for isolating bioactive compounds from medicinal plants. It operates by applying microwave energy to heat the solvent-sample mixture, facilitating the release of target analytes from the plant matrix into the solvent (Kataoka 2019). This method offers several advantages due to the use of microwave radiation, a non-contact heat source. These benefits include enhanced heating efficiency, rapid energy transfer, minimized thermal gradients, selective energy absorption, elimination of certain process stages (Nour et al., 2021). A key strength of MAE lies in its ability to quickly elevate the temperature of the sample solvent system, making it particularly effective for the swift extraction of even heat-sensitive compounds. The performance of MAE is influenced by multiple variables such as the physicochemical properties of the solvent, the characteristics of the sample matrix, and the dielectric properties of the compounds being extracted (Fig. 11. Kusuma and Mahfud, 2016; Cavalluzzi et al. 2022).



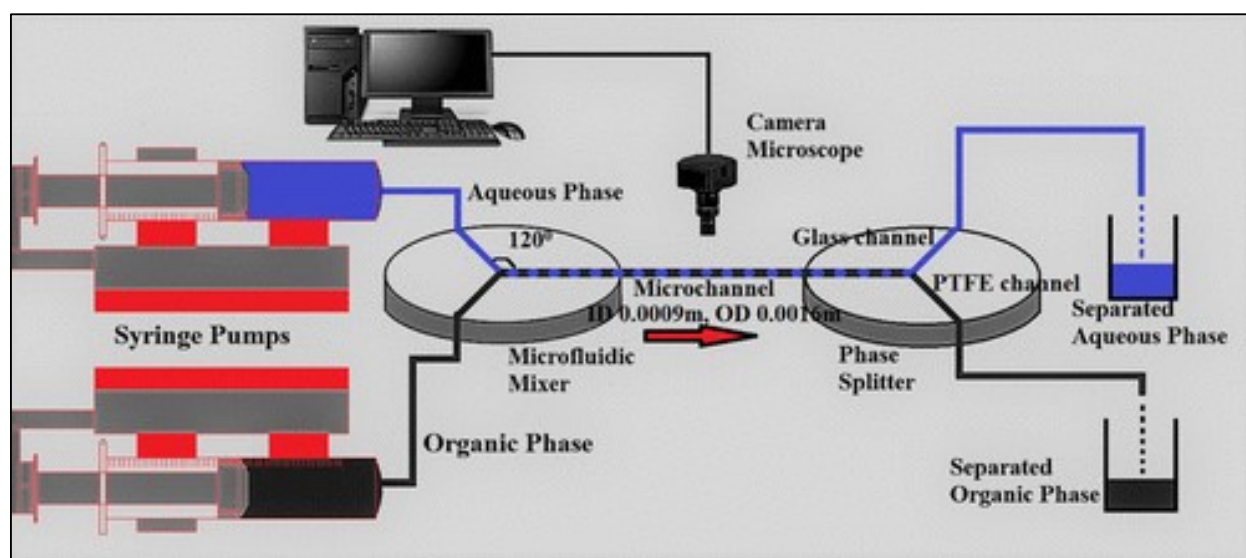
**Fig. 11** Schematic representation of Microwave assisted extraction (Kusuma and Mahfud, 2016)



Microwave assisted Extraction (MAE) of glutaric from aqueous media was been carried out using oleyl alcohol as a solvent at ambient conditions  $298 \pm 1$  K. Input power in terms of microwave irradiation (20 w) was given to the sample for 20 mins. Maximum extraction efficiency (68.56 %) was observed at 20 w respectively.

### Microfluidic and Inverted Coiled Systems

Microfluidic devices are highly efficient in providing higher mass transfer rates due to the enormous interfacial area created by the high surface-to-volume ratio. Droplet flow microfluidic devices can serve as an efficient process platform for the reactive extraction of various carboxylic acids from dilute aqueous solutions, but many of the process characteristics of these kinds of processes are not well studied, especially in very long microchannels (Fig. 12, Abraham et al. 2020). In literature, an effort was made to analyze the mass transfer behavior of very long microchannels during reactive extraction of citric acid from aqueous solutions of different concentrations in a uniform circular, 0.9 mm diameter droplet flow microfluidic contactor using tri-*n*-octylamine (TOA) in 1-decanol. The above complexation process was confirmed to be a kinetically controlled slow reaction. The devised microfluidic systems delivered higher efficiency than conventional contactors used for liquid–liquid extraction. It was also found that the residence time, TOA concentration, and interfacial area are the important factors that influence the extraction performance (Abraham et al. 2017).



**Fig.12** Schematic representation of Microfluidic reactive extraction system (Abraham et al.2020)

The inverted coiled flow inverter (ICFI) system represents another advanced and efficient approach to process intensification, particularly in multiphase mass transfer operations such as liquid-liquid and reactive extraction. Structurally, an ICFI comprises helically coiled tubular

reactors with regularly spaced inversions in curvature direction these abrupt bends generate periodic disturbances in the flow profile that significantly enhance mixing and mass transfer (Stankiewicz & Moulijn 2000). In such a design, the fluid experiences repeated stretching and folding, giving rise to secondary flows known as Dean vortices. These vortices disrupt the boundary layer, reduce axial dispersion, and promote radial mixing, which collectively result in more uniform distribution of the phases and increased interfacial area (Ravindra et al. 2007). Unlike traditional coiled flow reactors, ICFI systems introduce controlled chaotic advection without external energy input, thus achieving intensified mixing with minimal pressure drop (Patwardhan et al. 2016). In reactive extraction of dicarboxylic acids like glutaric acid, where phase interaction and complexation kinetics are critical, the ICFI offers substantial benefits. It can handle viscous and multiphase fluids such as those containing ionic liquids, DESs, or extractants like TOA and TBP in a more efficient manner than conventional batch or stirred systems. The enhanced contact time and phase intermingling within the coils ensure better extraction efficiency and conversion, even at lower residence times. Moreover, the modular and scalable nature of ICFIs enables seamless integration into continuous processing units, thereby supporting industrial applications in fine chemicals, pharmaceuticals, and biorefinery streams (Boodhoo & Harvey 2013). These systems are also ideal for coupling with heat exchange processes or in-line analytical tools, making them valuable in both research and production environments. Their capacity to achieve plug-flow-like behavior with improved dispersion characteristics allows for greater control over reaction kinetics and product separation, positioning them as a key innovation in sustainable separation technologies (Rathi et al. 2018).

## **Discussion**

Efficient and eco-friendly separation of glutaric acid from fermentation broth is vital for the sustainable production of bio-based chemicals. This investigation explores several green and intensified separation techniques, including the use of natural solvents, reactive extraction, ionic liquids, deep eutectic solvents, and enhanced processes like microwave- and ultrasound-assisted extraction. These methods address the drawbacks of conventional techniques such as high energy demands, toxicity, and environmental harm while improving extraction selectivity and overall yield. Critical factors such as solvent type, molar ratio, hydrogen bonding potential, and operating parameters significantly influence the extraction process. Experimental findings highlight the superior performance and reusability of solvents like TOA and menthol-based DESs, which contribute to cost-effectiveness and environmental sustainability. Innovative approaches such as microfluidic systems and inverted coiled flow extractors also present scalable alternatives for future applications. In summary, the study emphasizes the value of tailoring intensified separation strategies to specific needs for effective and sustainable glutaric acid recovery, promoting greener chemical processing technologies.

## **Conclusion**

The study of intensified sustainable approaches for glutaric acid separation demonstrates a significant advancement over traditional extraction methods. Techniques like reactive extraction, use of ILs, DESs, and assisted methods such as microwave and ultrasound not only enhance selectivity and yield but also reduce environmental burden. The integration of these technologies offers a scalable solution for the efficient and eco-friendly recovery of glutaric acid, facilitating its application in a broad spectrum of industries. The findings serve as a valuable guide for the selection and design of suitable separation processes tailored to specific industrial needs.

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## **Competing Interests**

The authors have no relevant financial or non-financial interests to disclose.

## **Authors Contributions**

All authors conceptualized the topic of the review and designed the structure. Ms. Ashwini S. Thakre drafted the complete manuscript. She conducted the literature review and synthesized the findings. Dr. Diwakar Shende, and Dr. Kailas Wasewar contributed to the critical revision of the manuscript. All authors approved the final version for submission.

## **Data Availability**

Data will be made available on request.

## **Declarations**

## **Conflicts of Interest**

The authors declare no conflict of interest to report regarding the present study.

## **References**

- Abraham E, Mukunthan Sulochana GN, Soundarajan B, Narayanasamy S (2017) Experimental investigation on microfluidic reactive extraction of citric acid using trioctylamine/1-decanol system in uniform and nonuniform circular microchannels. *Industrial & Engineering Chemistry Research* 56(38):10845–10855. A
- Abraham E, Prabhu A, Soundarajan B, Narayanasamy S (2020) Experimental study on influencing factors of microfluidic reactive extraction of citric acid using TOA in 1-decanol and flow schemes for performance improvement. *Industrial & Engineering Chemistry Research* 59(34):15343–15356.

- Albero B, Tadeo JL, Pérez RA (2019) Ultrasound-assisted extraction of organic contaminants. *TrAC Trends in Analytical Chemistry* 118:739–750.
- Almohasin JA, Balag J, Miral VG, Moreno RV, Tongco LJ, Lopez ECR (2023) Green solvents for liquid–liquid extraction: Recent advances and future trends. *Engineering Proceedings* 56(1):1–6.
- Antony FM, Wasewar KL (2022) Experimental investigation on recovery of bio-based protocatechuic acid using ionic liquids. *Journal of Chemical Technology & Biotechnology* 97(11):3144–3151.
- Athankar KK, Wasewar KL, Varma MN, Shende DZ (2015) Relative basicity approach for separation of  $\alpha$ -toluic acid with triglycerides of fatty acids by reactive extraction. *Journal of Industrial and Engineering Chemistry* 22:240–247.
- Athankar K, Wasewar K, Varma M, Shende D (2016) Reactive extraction of gallic acid with tri-n-caprylamine. *New Journal of Chemistry* 40:1–8.
- Athankar K, Wasewar K, Varma M, Shende D (2017a) Recovery of glutaric acid using tri-n-butyl phosphate: Effect of diluents and temperature. *Journal of Chemical Engineering & Process Technology* 8:1–5.
- Athankar K, Wasewar K, Varma M, Shende D (2017b) Recovery of glutaric acid using tri-n-butyl phosphate: Effect of diluents and temperature. *Journal of Chemical Engineering & Process Technology* 8:1–5.
- Bilgin M, Arısoy Ç, Kırbaşlar Şİ (2009) Extraction equilibria of propionic and butyric acids with tri-n-octylphosphine oxide/diluent systems. *Journal of Chemical & Engineering Data* 54(11):3008–3013.
- Blaga AC, Tucaliuc A, Kloetzer L (2022) Applications of ionic liquids in carboxylic acids separation. *Membranes* 12(8):1–21.
- Bodo E (2021) Modelling biocompatible ionic liquids based on organic acids and amino acids: Challenges for computational models and future perspectives. *Organic & Biomolecular Chemistry* 19(18):4002–4013.
- Dandekar P, Wasewar KL (2021) Experimental investigation on reactive extraction of vanillic acid with the help of tri-n-butyl phosphate in various diluents (decanol, kerosene, and soybean oil) at a constant room temperature of  $298.15 \pm 1$  K. *Journal of Chemical & Engineering Data* 66(2):999–1010.

- Datta D, Kumar S, Uslu H (2015) Status of the reactive extraction as a method of separation. *Journal of Chemistry* 2015(1):853789.
- De BS, Wasewar KL, Dhongde VR, Ingle AA, Mondal H (2018) Experimental and modeling of reactive separation of protocatechuic acid. *Chemical Engineering Research and Design* 132:593–605.
- Djukić-Vuković A, Mladenović D, Ivanović J, Pejín J, Mojović L (2019) Towards sustainability of lactic acid and poly-lactic acid polymers production. *Renewable and Sustainable Energy Reviews* 108:238–252.
- Doeker M, Hüttche V, Jupke A (2021) Reactive extraction for the recovery of primary amines from aqueous streams. *Separation and Purification Technology* 277:118229.
- Dutta A, Kininge MM, Priya, Gogate PR (2023) Intensification of delignification and subsequent hydrolysis of sustainable waste as banana peels for the HMF production using ultrasonic irradiation. *Chemical Engineering and Processing - Process Intensification* 183:10924.
- Garcia-Larez FL, Esquer J, Guzmán H, Zepeda-Quintana DS, Moreno-Vásquez MJ, Rodríguez-Félix F, Del-Toro-Sánchez CL, López-Corona BE, Tapia-Hernández JA (2024) Effect of ultrasound-assisted extraction (UAE) parameters on the recovery of polyphenols from pecan nutshell waste biomass and its antioxidant activity. *Biomass Conversion and Biorefin*
- Gautam K, Datta D (2022a) Recovery of nicotinic acid (niacin) using hydrophobic deep eutectic solvent: Ultrasonication facilitated extraction. *Chemical Data Collections* 41:100934.
- Gutiérrez A, Zamora L, Benito C, Atilhan M, Aparicio S (2022) Insights on novel type V deep eutectic solvents based on levulinic acid. *The Journal of Chemical Physics* 156(9):094504.
- Han DH, Hong WH (1996) Reactive extraction of lactic acid with trioctylamine/methylene chloride/n-hexane. *Separation Science and Technology* 31(8):1123–1135.
- Han YH, Park YL, Yang SY, Jung HR, Joo JC, Song BK, Lee SH, Park K, Ahn JO, Yang YH (2020) Selective extraction of glutaric acid from biological production systems using n-butanol. *Journal of Industrial and Engineering Chemistry* 82:98–104.
- Jacquemin J, Husson P, Padua AAH, Majer V (2006) Density and viscosity of several pure and water-saturated ionic liquids. *Green Chemistry* 8(2):172–180.

- Jadhav JJ, Jadeja GC, Desai MA (2023) Ultrasound-assisted hydrodistillation for extraction of essential oil from clove buds – A step towards process improvement and sustainable outcome. *Chemical Engineering and Processing - Process Intensification* 189:109404.
- Jha RR, Singh N, Kumari R, Patel DK (2017) Ultrasound-assisted emulsification microextraction based on a solidified floating organic droplet for the rapid determination of 19 antibiotics as environmental pollutants in hospital drainage and Gomti river water. *Journal of Separation Science* 40(13):2694–2702.
- Kar A, Bagde A, Athankar KK, Wasewar KL, Shende DZ (2017) Reactive extraction of acrylic acid with tri-n-butyl phosphate in natural oils. *Journal of Chemical Technology and Biotechnology* 92(11):2825–2834.
- Kertes AS, King CJ (1986) Extraction chemistry of fermentation product carboxylic acids. *Biotechnology and Bioengineering* 28(2):269–282.
- Keshav A, Keshav A, Wasewar KL, Chand S (2008) Reactive extraction of propionic acid using tri-n-butyl phosphate in petroleum ether: Equilibrium study.
- Keshav A, Wasewar KL, Chand S (2009) Extraction of acrylic, propionic and butyric acid using aliquat 336 in oleyl alcohol: Equilibria and effect of temperature. *Industrial and Engineering Chemistry Research* 48(2):888–893.
- Kumar A, Shende DZ, Wasewar KL (2019) Production of levulinic acid: A promising building block material for pharmaceutical and food industry. *Materials Today: Proceedings* 29:790–793.
- Kumar K, Srivastav S, Sharanagat VS (2021) Ultrasound assisted extraction (UAE) of bioactive compounds from fruit and vegetable processing by-products: A review. *Ultrasonics Sonochemistry* 70:105325.
- Kumar S, Wasewar KL, Babu BV (2008) Intensification of nicotinic acid separation using organophosphorous solvating extractants by reactive extraction. *Chemical Engineering & Technology* 31(11):1584–1590.
- Marták J, Schlosser Š (2006) Phosphonium ionic liquids as new, reactive extractants of lactic acid. *Chemical Papers* 60(5):395–398
- Marták J, Schlosser Š (2019) Influence of anion and cation structure of ionic liquids on carboxylic acids extraction. *Frontiers in Chemistry* 7:117.

- Mohadikar P, Kumar A, Wasewar K, Shinde DZ (2022) Experimental investigation using conventional and natural extractants for liquid-liquid extraction of glutaric acid. *Chemical Data Collections* 37:100790.
- Mungma N, Kienberger M, Siebenhofer M (2019) Reactive extraction of lactic acid, formic acid and acetic acid from aqueous solutions with tri-n-octylamine/1-octanol/n-undecane. *ChemEngineering* 3(2):43.
- Othman M, Ariff AB, Rios-Solis L, Halim M (2017) Extractive fermentation of lactic acid in lactic acid bacteria cultivation: A review. *Frontiers in Microbiology* 8:2285.
- Pandey S, Kumar S (2020) Reactive extraction of gallic acid from aqueous solution with tri-n-octylamine in oleyl alcohol: Equilibrium, thermodynamics and optimization using RSM-rCCD. *Separation and Purification Technology* 231:115904.
- Parrilla Vázquez MM, Parrilla Vázquez P, Martínez Galera M, Gil García MD, Uclés A (2013) Ultrasound-assisted ionic liquid dispersive liquid-liquid microextraction coupled with liquid chromatography-quadrupole-linear ion trap-mass spectrometry for simultaneous analysis of pharmaceuticals in wastewaters. *Journal of Chromatography A* 1291:19–26.
- Pehlivanoğlu N, Uslu H, Kirbaşlar Şİ (2010) Extractive separation of glutaric acid by Aliquat 336 in different solvents. *Journal of Chemical & Engineering Data* 55(9):2970–2973.
- Pehlivanoğlu N, Uslu H, Kirbaşlar Şİ (2009) Experimental and modeling studies on the extraction of glutaric acid by trioctylamine. *Journal of Chemical & Engineering Data* 54(12):3202–3207.
- Picó Y (2013) Ultrasound-assisted extraction for food and environmental samples. *TrAC Trends in Analytical Chemistry* 43:84–99.
- Politzer P, Murray J (2007) Quantitative approaches to solute-solvent interactions. In: *ChemInform* Vol. 37, pp. 1–63.
- Shimizu K, de Freitas AA, Burba CM (2022) Cation-anion and cation-cation interactions in mixtures of hydroxy-functionalized and aprotic ionic liquids. *J Ionic Liquids* 2:100022.
- Smith EL, Abbott AP, Ryder KS (2014) Deep eutectic solvents (DESs) and their applications. *Chem Rev* 114:11060–11082.
- Sprakel LMJ, Schuur B (2019) Solvent developments for liquid-liquid extraction of carboxylic acids in perspective. *Sep Purif Technol* 211:935–957.

- Srivastava S, Pandey VK, Fatima A, V MS, Pandey S, Singh R, Dar AH, Dhillon B (2024) A literature review on process intensification: an innovative and sustainable food processing method. *Appl Food Res* 4:100363.
- Tiwari BK (2015) Ultrasound: a clean, green extraction technology. *TrAC Trends Anal Chem* 71:100–109.
- Uslu H, Inci I (2009) A study on glutaric acid extraction by tridodecylamine: equilibria and models. *Chem Eng Technol* 32:1951–1957.
- Usman MR, Hussain SN, Asghar HMA, Sattar H, Ijaz A (2012) Liquid-liquid extraction of acetic acid from an aqueous solution using a laboratory scale sonicator.
- Wang J, Zhang S, Ma Z, Yan L (2021) Deep eutectic solvents eutectogels: progress and challenges. *Green Chem Eng* 2:359–367.
- Wang Y, Li Y, Wang J, Li Z, Dai Y (2001) Extraction equilibria of monocarboxylic acids with trialkylphosphine oxide. *J Chem Eng Data* 46:
- Wasewar K (2012) Reactive extraction: an intensifying approach for carboxylic acid separation. *Int J Chem Eng Appl* 3:249–255.
- Wasewar K, Keshav A (2010) Physical extraction of propionic acid. *Int J Res Rev Appl Sci* 3:
- Wasewar KL, Heesink ABM, Versteeg GF, Pangarkar VG (2004) Intensification of conversion of glucose to lactic acid: equilibria and kinetics for back extraction of lactic acid using trimethylamine. *Chem Eng Sci* 59:2315–2320.
- Wasewar KL, Pangarkar VG, Heesink ABM, Versteeg GF (2003) Intensification of enzymatic conversion of glucose to lactic acid by reactive extraction. *Chem Eng Sci* 58:3385–3393.
- Wasewar KL, Shende DZ (2011) Equilibrium for the reactive extraction of caproic acid using tri-n-butyl phosphate in methyl isobutyl ketone and xylene. *J Chem Eng Data* 56:3318–3322.
- Wasewar K, Shende D (2010) Extraction of caproic acid using tri-n-butyl phosphate in benzene and toluene at 301 K. *J Chem Eng Data* 55:
- Wasewar K, Shende D, Keshav A (2011) Reactive extraction of itaconic acid using tri-n-butyl phosphate and aliquat 336 in sunflower oil as a non-toxic diluent. *J Chem Technol Biotechnol* 86:319–323.