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Liquid–liquid extraction of volatile fatty acids from anaerobic bioprocesses: Solvent systems, selection framework, and sustainability

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ABSTRACT

The valorisation of organic waste through anaerobic digestion (AD) and arrested methanogenesis (AM) offers a renewable route for producing volatile fatty acids (VFAs), key intermediates for bio-based chemicals. However, VFA accumulation inhibits microbial activity, and their recovery from dilute, complex fermentation broths remains a major economic challenge. Liquid–liquid extraction (LLE) has emerged as a promising recovery strategy due to its ability to selectively transfer VFAs into an organic phase under mild conditions while reducing product inhibition.

This review critically evaluates solvent systems for VFA extraction, including conventional extractants (oxygen-bearing solvents, organophosphorus compounds, and reactive amines) and emerging alternatives such as ionic liquids (ILs), deep eutectic solvents (DESs), hydrophobic deep eutectic solvents (HDESs), and bio-based solvents. Reactive amines demonstrate superior performance for dilute short-chain VFAs due to strong acid–base interactions, whereas emerging solvents offer improved tunability and sustainability, but face challenges related to cost and viscosity. The effects of key process parameters, including pH, temperature, and solvent-to-feed (S/F) ratio, are analysed, highlighting their role in controlling extraction efficiency. A decision-making framework is proposed to guide solvent selection based on feed characteristics, acid type, and process constraints. Overall, solvent selection is identified as a multi-objective optimisation problem integrating performance, economics, and sustainability.

1. Introduction

Biogas plants represent a demonstrated and mature renewable energy technology, with a high technology readiness level (TRL 8–9) across Europe. Anaerobic digestion (AD) converts biomass into biogas and digestate [1,2]. Recent studies have investigated arrested methanogenesis (AM) as an alternative strategy to repurpose conventional AD systems for VFA production rather than methane generation alone. AM operates by deliberately interrupting the AD process before methanogenesis, thereby shifting the system toward acidogenic fermentation and facilitating the accumulation of VFAs [3,4]. VFAs are value-added platform molecules for the synthesis of fuels, solvents, polymers, and other bio-based chemicals [5–9]. The recovery of these intermediates enables the transition from conventional waste treatment systems to integrated biorefineries while improving resource efficiency and overall economic performance [10–12]. As a consequence, the primary bottleneck in such systems shifts from product formation to downstream separation, making efficient VFA recovery a critical determinant of process viability. The synergistic integration of AD with VFA co-production is illustrated in Fig. 1.

Abbreviations: AD, Anaerobic digestion; AM, Arrested methanogenesis; COSMO-RS, Conductor-like screening model for real solvents; DEE, Diethyl ether; DES, Deep eutectic solvents; HBA, Hydrogen-bond acceptor; HBD, Hydrogen-bond donor; HDES, Hydrophobic DES; (2-MeTHF), 2-Methyltetrahydrofuran; ChCl, Choline chloride; KD, Distribution coefficient; EE, Extraction efficiency; S/F, Solvent-to-feed ratio; LCA, Life-cycle assessment; MD, Molecular dynamics; RDF, Radial distribution function; LLE, L liquid-liquid extraction iquid-liquid extraction; MIBK, Methyl-isobutyl ketone; TBP, Tri-n-butyl phosphate; TOA, Tri-octylamine; TOPO, Tri-n-octyl phosphine oxide; TRL, Technology readiness level; VFAs, Volatile fatty acids; OLR, Organic loading rate; CPME, Cyclopentyl methyl ether; TBAB, Tetraoctylammonium bromide; IL / ILs, Ionic liquid(s); TEA, Techno-economic assessment; HES, Hydrophobic eutectic solvent; NADES, Natural deep eutectic solvents; TOMAC, Methyltrioctylammonium chloride.

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Fermentation broths usually contain VFAs at low concentrations, often in the range of a few grams per litre [14,15], in complex aqueous matrices containing salts, biomass residues, and other soluble organics [16–18]. Because of these dilute and multicomponent conditions, product recovery can account for a major fraction of total process cost and energy demand [19,20]. Various separation techniques have been investigated for VFA recovery, including liquid-liquid extraction (LLE) [21], distillation, adsorption [22], membrane-based separations [23], pervaporation, and electrodialysis [24].

Among these, LLE has attracted particular attention as a primary recovery step because it can extract VFAs from dilute aqueous streams into an organic phase under mild operating conditions, thereby reducing product inhibition and lowering the burden on subsequent purification steps [17,26]. In this context, "mild conditions" generally refer to operation at near-ambient temperatures (≈20–40 °C), atmospheric pressure, and slightly acidic pH (≈2–4), which favour the undissociated and thus more extractable form of VFAs while avoiding excessive chemical severity [27].

Importantly, LLE is not intended to replace conventional separation methods such as distillation, but rather to act as a pre-concentration step. Following extraction, VFAs are transferred into an organic phase, enabling subsequent recovery through distillation or alternative solvent regeneration techniques such as pH-swing back-extraction or moderate temperature shifts (<50 °C).

This approach significantly reduces the energy demand of downstream separation, as distillation is performed on a concentrated VFA stream rather than on dilute aqueous broths, where energy requirements are prohibitively high. To further limit solvent usage, solvent-to-aqueous phase ratios are typically maintained within 0.5:1 to 2:1 (v/v), while process intensification strategies enable short residence times ranging from seconds to minutes [28]. Consequently, integrating LLE with downstream recovery processes enhances overall process efficiency and sustainability. Fig. 2 compares direct distillation with extraction-assisted recovery (LLE followed by distillation), illustrating how prior phase transfer of VFAs into an organic solvent significantly reduces the overall energy requirements.

The efficiency of LLE depends strongly on solvent selection. Conventional oxygen-bearing solvents, organophosphorus extractants, and high-molecular-weight amines have all been investigated for VFA extraction, while ionic liquids (ILs), deep eutectic solvents (DESs), hydrophobic deep eutectic solvents (HDESs), and bio-based solvents have emerged as promising alternatives with improved tunability and, in some cases, comparatively low environmental impact [8,19,29,30]. However, the literature remains fragmented: many studies report extraction performance for individual solvent systems, but fewer works provide a critical comparison across solvent classes while simultaneously considering solvent regeneration, process integration, and sustainability metrics.

Accordingly, this review focuses specifically on LLE as a recovery strategy for VFAs from anaerobic and acidogenic bioprocesses. The aim is not to comprehensively review all available downstream technologies, but rather to critically examine the solvent systems used in LLE, the process variables governing extraction performance, and the environmental and economic considerations that affect their practical implementation. Special attention is given to comparing conventional and emerging solvent classes, identifying key criteria for solvent selection, and highlighting research needs for scalable and sustainable VFA recovery.

Bibliometric trends further demonstrate rapidly increasing research interest in VFA recovery and extraction technologies for integrated biorefinery applications. A literature survey using the ScienceDirect database in May 2026 indicated that more than 5357 research articles related to "volatile fatty acid", "VFA", and "extraction" have been published since 2021, reflecting growing interest in downstream VFA recovery. Within this field, approximately 416 publications addressed ionic-liquid-based extraction systems, whereas 61 focused on deep eutectic solvent (DES)-based extraction systems, highlighting increasing attention toward emerging solvent platforms. In addition, approximately 491 research articles related to VFA extraction, together with life-cycle assessment/analysis (LCA), demonstrate growing emphasis on

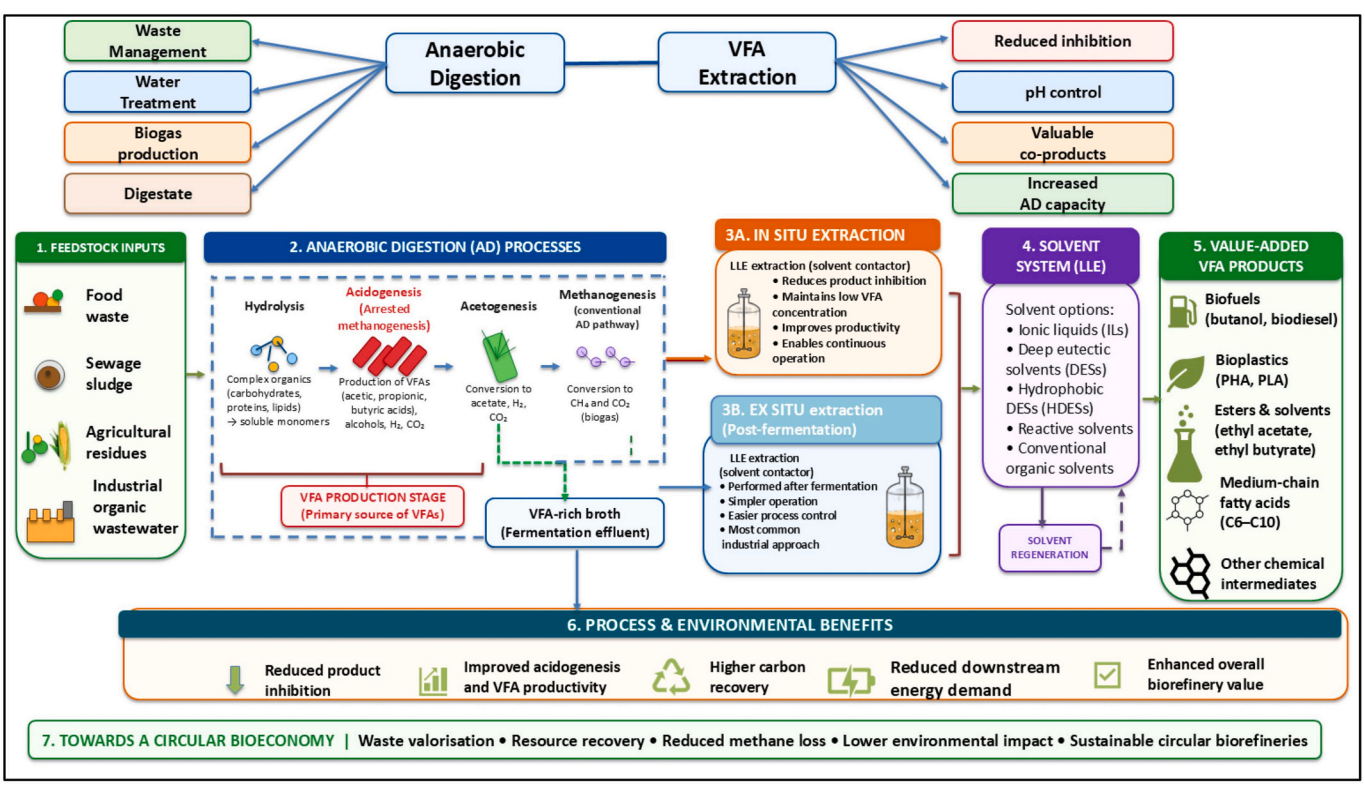

Fig. 1. Integrated AD and VFA co-production pathway for waste valorisation and resource recovery.

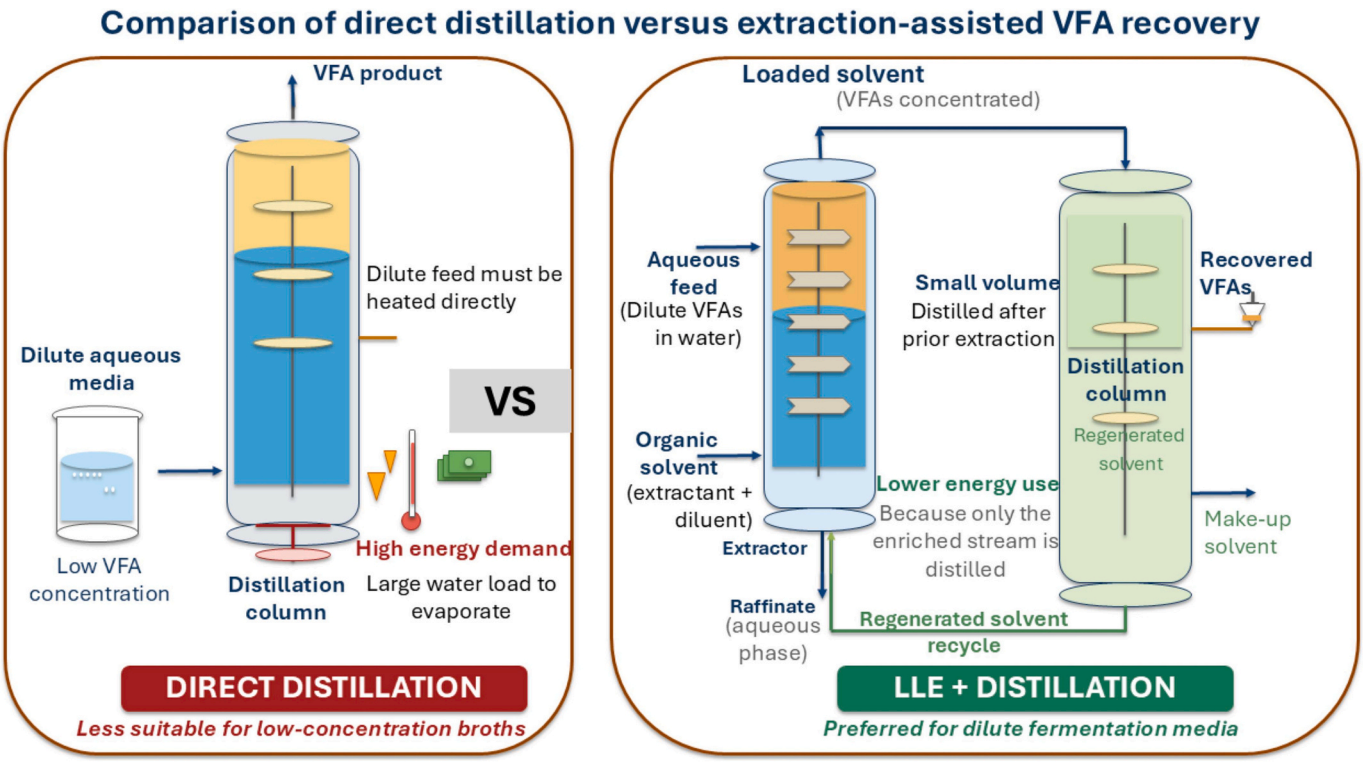

Fig. 2. Schematic of comparison of direct distillation versus extraction-assisted VFA recovery.

sustainability and techno-economic analysis (TEA) of VFA recovery systems. These trends indicate a transition toward integrated solvent design, process intensification, and sustainability-oriented VFA biorefinery research.

1.1. Fundamentals of LLE and solvent selection for VFA recovery

Amid the growing interest in sustainable biorefineries, the efficient separation of VFAs from fermentation broths has become a critical challenge in downstream processing. In LLE, an aqueous VFA-containing feed is contacted with an immiscible organic solvent, allowing VFAs to partition between phases based on their distribution coefficient (KD), influenced by solvent properties, pH, temperature, and acid structure. This selective transfer enables separation from water, salts, and biomass, facilitating downstream purification. Extraction performance is typically assessed using the KD and extraction efficiency (EE%), which quantify solute partitioning and recovery, respectively, and allow comparison of different solvent systems. Although KD and EE are widely used metrics, they do not capture process-level limitations such as solvent regeneration, phase separation, and integration with fermentation systems.

VFA's extraction is highly sensitive to system pH, particularly in integrated fermentation–extraction set-ups. High methanogenic activity is generally sustained at pH levels between 6.5 and 7.2 [1,11,31]. Because VFAs are weak acids, their speciation is pH-dependent: at low pH, they remain undissociated and more hydrophobic, enhancing extraction into organic solvents, while at high pH they dissociate into carboxylate ions, reducing extractability. Thus, pH control is critical for effective LLE performance in VFA recovery. In addition to pH, LLE efficiency is strongly influenced by the physicochemical properties of the extractant. An effective solvent should exhibit a high KD and selectivity for VFAs, low miscibility with water, and a favourable viscosity to enable efficient mass transfer and phase separation. It should also be low in toxicity, environmentally acceptable, easily regenerable and recyclable to support sustainable and cost-effective operation. Because no single solvent simultaneously satisfies all these criteria, many extraction systems employ mixtures of extractants and diluents. In such systems, the active extractant provides strong interactions with VFAs (for example, through hydrogen bonding or acid–base complexation), while the diluent improves phase behaviour, reduces viscosity, and enhances mass transfer.

The following sections provide a critical overview of these solvent systems, comparing their extraction mechanisms, reported performance, and practical limitations for the recovery of VFAs from anaerobic bioprocesses.

2. Extractant systems for LLE of VFAs

Organic solvents employed for the LLE of VFAs can generally be classified according to their chemical structure and extraction mechanism. These solvent systems can broadly be divided into two major categories: conventional extractants and emerging green solvent systems. These solvent classes differ not only in extraction mechanism but also in their suitability for dilute systems, process integration, and scalability.

Conventional extractants include oxygen-bearing hydrocarbons such as alcohols and ketones [32], phosphorus-based extractants such as Tri-n-butyl phosphate (TBP) and tri-n-octyl phosphine oxide (TOPO) [13], and reactive amines such as tri-octylamine (TOA) and Alamine 336 [33]. These solvents have been extensively investigated due to their availability, relatively low cost, and established extraction performance. However, concerns about solvent volatility, toxicity, and environmental impact have spurred growing research interest in alternative solvent systems.

In response to these limitations, a range of next-generation solvents has been explored in recent years, including ILs, DESs, HDESs, and bio-based solvents. These systems offer advantages such as tunable physicochemical properties, negligible vapor pressure, and potentially improved environmental compatibility [34]. Fig. 3 illustrates the main solvent classes used in LLE of VFAs.

The extraction mechanism varies across solvent classes. Non-reactive

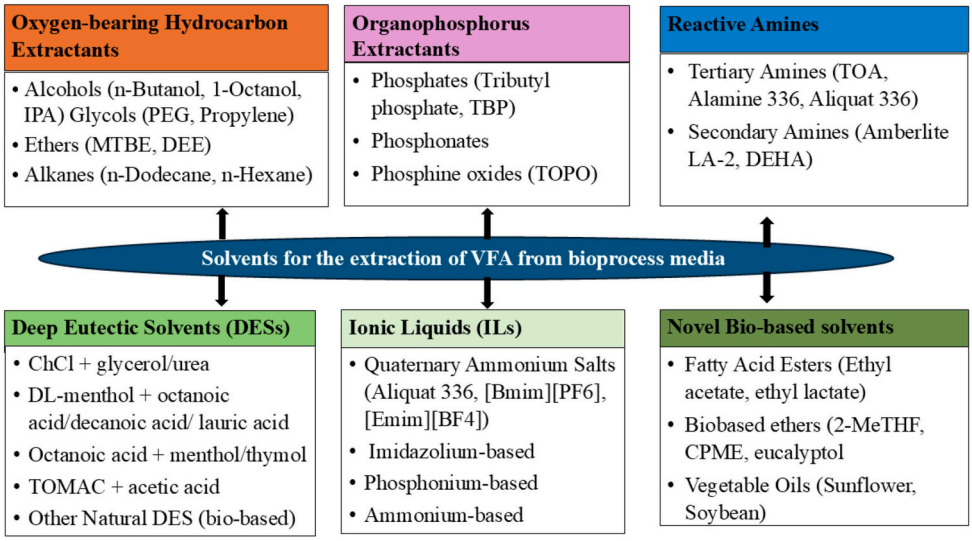

Fig. 3. Classification of solvents used in LLE of VFAs.

solvents extract VFAs primarily through physical partitioning and hydrogen-bonding interactions, while reactive extractants such as tertiary amines form acid–base complexes with the carboxylic acids, resulting in significantly higher KDs. Organophosphorus extractants generally rely on donor–acceptor interactions between the phosphoryl oxygen and the hydroxyl group of the acid, leading to intermediate extraction performance between physical and reactive systems. A comparison of the principal extractant classes used in LLE of VFAs is presented in Table 1.

In many LLE systems for VFA recovery, extraction performance depends not only on the active extractant but also on the nature and proportion of the accompanying diluent phase. Reactive amines, organophosphorus extractants, and some viscous IL systems are commonly combined with alcohols, ketones, hydrocarbons, or vegetable oils to improve phase separation, reduce viscosity, and enhance mass-transfer characteristics. The composition of the solvent system strongly influences KD, EE, solvent loading, and overall process operability. In general, polar diluents improve solvation of acid–extractant complexes, whereas nonpolar diluents primarily improve hydrodynamics and phase disengagement. Therefore, optimisation of extractant–diluent composition is essential for balancing extraction performance, regeneration feasibility, and industrial applicability. The following subsections discuss the most widely studied extractant systems in greater detail.

2.1. Conventional oxygen-bearing solvents

Conventional oxygenated solvents such as alcohols, ketones, and ethers, such as Methyl isobutyl ketone (MIBK), 1-octanol, 1-decanol, and diethyl ether (DEE), are among the earliest extractants used for VFA recovery. They rely on physical solubility and hydrogen-bonding interactions with the carboxyl group (C═O or —O—), extraction governed mainly by liquid–liquid equilibrium rather than chemical reaction [39].

However, these solvents often exhibit limited extraction performance, particularly for short-chain VFAs such as acetic and propionic acids, which have low KDs in dilute systems. Nonetheless, they can be effective for selectively recovering longer-chain VFAs - for example, Jänisch et al. [31] investigated the extraction of VFAs from biogas plant hydrolysates using DEE and MIBK. They reported efficient recovery of non-polar acids such as butyric, valeric, and caproic acids. In another study, ethyl acetate was demonstrated as an effective oxygen-bearing solvent for LLE of VFAs from fermentation broth, achieving high

Table 1
Comparison of major extractant classes for LLE of VFAs, highlighting their suitability for recovery from dilute aqueous streams and potential for selective separation.

Extractant Category	Representative solvents	Extraction Mechanism	Key advantages and limitations	Best application	Ref
Conventional oxygen-bearing solvents	Alcohols (n-butanol, 1-octanol), ethers, methyl tert-butyl ether, glycols	Physical partitioning	✔ low cost, simple operation ✖ limited selectivity, solvent losses, water co-extraction	Recovery of medium- to long-chain VFAs (C4–C6); use as diluents in reactive extraction systems	[31,35]
Non- oxygenated hydrocarbons / aromatics	n-hexane, n-dodecane, toluene, xylene	Physical partitioning	✔ inexpensive, low viscosity ✖ poor affinity for VFAs, toxicity (aromatics)	Diluent phase only; not suitable as a primary extractant	[36]
Phosphorus-bonded oxygen-bearing extractants	TBP, phosphonates, TOPO	Solvation/ complexation	✔ higher affinity than simple solvents ✖ cost, possible water co-extraction	Intermediate extraction systems; moderate concentration feeds; acidic conditions	[26]
Reactive amines (secondary/tertiary)	TOA, Alamine 336, amberlite LA-2	Reactive extraction (acid–base complexation)	✔ very high KD ✖ requires diluent, emulsion risk, viscosity	Dilute short-chain VFAs (C2–C3); industrial LLE systems; continuous extraction	[27]
ILs	Aliquat 336, imidazolium-based ILs	Physical + specific interactions	✔ negligible vapor pressure, tunable properties ✖ high cost, viscosity, scale-up issues	Selective extraction and process intensification; niche or advanced systems	[2]
DES	ChCl-urea, ChCl-glycerol	Hydrogen bonding network	✔ low cost, biodegradable (NADES) ✖ high viscosity, limited industrial data	Green solvent systems: Moderate-performance sustainable extraction	[37,38]
Bio-based solvents	Vegetable oils, fatty acid esters (ethyl oleate)	Physical + weak interactions	✔ renewable, low toxicity ✖ lower capacity for short-chain acids, higher viscosity	Sustainable extraction of hydrophobic VFAs (C4–C6); biocompatible systems	[35]

recovery efficiencies, particularly at low pH conditions. Maximum recoveries of ~93% for butyric acid and ~ 73% for propionic acid were obtained at pH 2.5, highlighting the strong dependence of extraction on acid protonation. The study also confirmed that equilibrium can be reached within ~30–40 min, supporting the feasibility of ethyl acetate for efficient VFA recovery [40].

These solvents are also frequently used as diluents in reactive extraction systems, where they improve phase separation and reduce the viscosity of active extractants such as TOA or TBP [32]. Overall, these solvents remain attractive for low-cost extraction processes, but their relatively low extraction capacity and limited selectivity often necessitate the use of more advanced solvent systems.

2.2. Organophosphorus extractants

Organophosphorus extractants such as TBP and TOPO extract VFAs through solvation and donor–acceptor interactions between the phosphoryl group and the carboxylic acid. They form solvated complexes that enhance partitioning into the organic phase, placing them in an intermediate class of extractants. Their performance is improved by specific molecular interactions but remains strongly dependent on pH and diluent selection [41].

Compared with conventional oxygen-bearing solvents [36,42], organophosphorus extractants generally exhibit higher KDs and improved selectivity toward carboxylic acids, particularly under acidic conditions. EE is strongly influenced by operating parameters such as pH and extractant concentration. For example, Alkaya et al. [43] demonstrated that VFA extraction using TOPO in kerosene was significantly higher at pH 2.5 compared with pH 5.5, reflecting the importance of maintaining acids in their undissociated form. Similarly, Xing et al. [44] reported that the KD for butyrate decreased markedly from ~4.5 at pH 3 to ~1.5 at pH 5, while propionate and acetate exhibited lower values, further highlighting both the strong pH dependence and the chain-length-dependent selectivity of the extraction process. A summary of reported extraction studies employing organophosphorus extractants under different operating conditions is presented in Table 2.

Organophosphorus extractants are typically used in combination with organic diluents such as kerosene, MIBK, vegetable oils or alcohols to improve phase behaviour and reduce solvent viscosity. Despite their favourable extraction properties, these solvents may present limitations due to water co-extraction, sensitivity to process conditions, relatively higher cost and lower biodegradability compared with emerging green solvents.

2.3. High-molecular-weight aliphatic amines

High-molecular-weight aliphatic amines, such as TOA, Alamine 336, and Aliquat 336, represent one of the most effective extractant classes for recovering VFAs from dilute aqueous streams. These extractants operate via a reactive extraction mechanism, in which the amine forms an acid–base complex with the carboxylic acid, producing an ion-pair species that is soluble in the organic phase. This mechanism significantly enhances acid partitioning into the solvent phase and enables high EE even at relatively low acid concentrations. The stability of the acid–amine complex depends strongly on factors such as amine basicity, diluent polarity, and acid dissociation behaviour [46]. Tertiary amines are generally preferred because they exhibit lower water solubility and greater chemical stability compared with primary and secondary amines. Because high-molecular-weight amines are inherently viscous and exhibit limited phase separation when used alone, they are typically employed with diluents such as alcohols or vegetable oils to reduce viscosity, enhance mass transfer, improve phase disengagement, and stabilise the acid–amine complex in the organic phase. Several studies have reported high EE using amine-based solvent systems. The reactive extraction of butyric acid using Alamine 336 in oleyl alcohol achieved an EE of approximately 91% [48].

Babu and Venkata [49] reported that partitioning of propionic acid between the aqueous and organic phases reaches equilibrium within the concentration range of 0.009 to 0.055 kmol/m^3 with an optimal TOA concentration of 40%, yielding a KD of 16.7 and a maximum EE of 43.82%, while separation performance varied with extractant and acid concentrations. Similarly, Oh et al. [50] demonstrated high EE (~95%) for butyric acid using 10 wt% Alamine 336 in oleyl alcohol, with subsequent alkaline stripping, recovering ~90% of the acid, confirming the effectiveness of tertiary amine-based systems. In addition to amine-based extractants, alternative solvent systems have been explored for

Table 3
Comparison of reactive extractant–diluent systems for VFA extraction.

Extractant system	Broth/feed matrix	Acid extracted	Extraction metric reported (KD, EE%)	Ref
Alamine 336 + 1-octanol	Aqueous propionic acid solution	C3	KD:16.7, EE:43.82	[49]
TOA + soybean oil	Aqueous propionic acid / fermentation-relevant dilute feed	C3	KD: 0.73, EE:42.75	[33]
TOA + rice bran oil		C3	KD: 0.66, EE: 40	[33]
TOA (continuous CLEANS process)	Real food-waste anaerobic fermentation broth	C2–C6	KD: 44.5, EE: 81.3	[21]
Aliquat 336 + butyl acetate	Leached-bed reactor leachate from food-waste acidogenesis	C2	KD: 2.46, EE: ~38–75	[46]
Aliquat 336 + MIBK		Lactic acid	KD:~3.0, EE: ~38–75	[46]
TBP + oleyl alcohol / lamp oil / canola oil	Wastewater AD broth	Mixed VFAs	EE: TBP + oleyl alcohol: ~56–57%, TBP+ lamp oil: 57–58%, TBP + canola oil: 54–55% (all values at pH 3.9)	[13]
TOA + oleyl alcohol / lamp oil / canola oil		Mixed VFAs	EE: TOA + oleyl alcohol: ~82%, TOA + lamp oil: ~33%, TOA+ canola oil: ~48% (all values at pH 3.9)	[13]
TOPO + oleyl alcohol/ lamp oil/ canola oil		Mixed VFAs	EE: TOPO+oleyl alcohol: ~60%, TOPO+lamp oil: ~80–82%, TOPO+ canola oil: ~75–76% (all values at pH 3.9)	[13]

Table 2
Summary of VFAs extraction employing organophosphorus extractants with different diluents under different pH conditions.

Solvent	Diluent system	Acid Extracted	KD	EE (%)	pH	Ref
TBP	Sunflower oil, petroleum ether, n-heptane, toluene	C3	1.1–1.8	53–64	<4.7	[45]
20 wt% TOPO in kerosene	Kerosene	C2, C4	2.07	67	2.5	[43]
20 wt% TOPO in kerosene	Kerosene	C3	0.48	32	5.5	[43]
TBP	1-decanol +kerosene	C3	Up to 5.9	85	2.4–3.5	[42]
TBP	Oleyl alcohol, canola oil, lamp oil	C2–C6	~0.5–2.5	40–75	~2–4	[13]
TOPO	Oleyl alcohol, canola oil, lamp oil	C2–C6	~2.0–5.0	60–90	~2–4	[13]

performance and cost considerations. A comparison of representative extraction systems employing amine-based solvents is presented in Table 3.

In Table 3 above, the EEs reported by Morison et al. [13] are at pH 3.9, where VFAs are predominantly in the undissociated form, yielding maximum extraction performance. EEs decrease significantly at higher pH values between 5.6 and 6.8. The data from the above table confirm that reactive extraction systems provide significantly higher KD values than physical systems, particularly for short-chain acids.

Although amine-based systems provide excellent extraction performance, they may also present operational challenges such as emulsion formation, increased solvent viscosity, and the need for suitable diluents to stabilise the acid–amine complexes.

3. Emerging green solvents for VFA extraction

In recent years, scientific research has increasingly focused on aligning separation technologies with sustainability and green engineering principles. In the context of VFA recovery from anaerobic bioprocesses, the use of environmentally benign solvents has gained considerable attention as a means of reducing the environmental burden and energy intensity associated with conventional organic solvents. Consequently, solvent systems such as ILs, DES/HDES, and bio-based solvents have emerged as promising alternatives to conventional extractants discussed in Section 2 in LLE processes. These solvent classes are often referred to as "designer solvents" because their physicochemical properties can be tuned by modifying their molecular composition. Such tunability allows optimisation of extraction performance, solvent stability, and environmental compatibility, which are critical considerations for downstream processing of fermentation-derived products [51].

The extraction behaviour of emerging solvent systems such as DESs, HDESs, and ILs is strongly influenced by the relationship between solvent structure, hydrophobicity, and pH-dependent VFA speciation. HDES systems demonstrated improved extraction performance under acidic conditions, particularly for longer-chain VFAs, where hydrophobic interactions became more significant.

In contrast, dissociation into carboxylate ions (R–COO$^-$) at higher pH increases aqueous-phase affinity, thereby reducing KD and EE values. In addition, extraction performance generally improves with increasing VFA chain length because longer-chain acids exhibit lower water solubility and stronger hydrophobic interactions with organic solvent phases. Consequently, extraction in emerging solvent systems is governed not only by solvent acidity/basicity, but also by the combined effects of intermolecular interactions, solvent hydrophobicity, and acid-speciation equilibrium [38,52,53].

3.1. Deep eutectic solvents (DES and HDES)

DESs are mixtures of two or more components forming a low-melting liquid phase due to hydrogen bonding between hydrogen-bond donors (HBDs) and hydrogen-bond acceptors (HBAs) [54]. These systems often contain strongly functionalized components, enabling enhanced solubility and facilitating their use as liquid extractants even when individual constituents are solid at room temperature [55,56]. In VFA extraction, DESs primarily operate through hydrogen-bond interactions between the solvent components and the carboxyl group of the acids, with additional electrostatic and van der Waals interactions contributing to stabilisation of the extracted species [37]. Their ease of synthesis, low volatility, tunable properties, and broad liquid range make them attractive alternatives to conventional solvents [54,57,58]. However, their environmental performance and EE depend strongly on the nature of the constituent components.

A key limitation of conventional DESs is their partial miscibility with water, which can reduce EE and complicate phase separation. To address this, HDESs have been developed as water-immiscible systems composed of hydrophobic components such as fatty acids, terpenoids, or quaternary ammonium salts. These systems offer improved phase separation and enhanced extraction performance for VFAs, particularly for more hydrophobic acids [59].

As summarised in Table 4, menthol–fatty acid-based HDES systems show moderate EEs for acetic acid in single-stage operation (≈27–40%), which can be significantly improved in multi-stage processes (up to ~88%) [60]. Similarly, HDES systems based on octanoic acid combined with menthol or thymol demonstrate high EEs (up to ~98%) for C2–C5 acids, highlighting the importance of hydrophobicity and solvent composition [53].

Additional studies further support the versatility of HDES systems for organic acid recovery. Van Osch et al. [38] reported that HDES systems based on fatty acids and quaternary ammonium salts effectively extract short-chain acids such as acetic, propionic, and butyric acids. Likewise, van den Bruinhorst et al. [55] demonstrated stable extraction performance using hydrophobic eutectic mixtures (e.g., dihexylthiourea–TOPO), although strong intermolecular interactions within the solvent may reduce the availability of active extraction sites. More recent studies have explored alternative HDES formulations, including amide-based systems combined with terpenoids, achieving moderate KD ≈ 2–3 [61], and decanoic acid–lidocaine systems with improved performance (KD > 5) under acidic conditions [62]. In addition, menthol-based HDES systems have demonstrated stable extraction performance with real fermentation broths, achieving KDs in the range 4–6 for C4–C5 acids over multiple cycles [56]. In situ DES systems, such as Methyltrioctylammonium chloride (TOMAC)-based mixtures, have also shown high EEs (>90%) for butyric and valeric acids, further highlighting the potential of tailored eutectic systems for targeted VFA recovery.

Overall, DES- and HDES-based solvent systems provide a flexible platform for solvent design, where extraction performance can be tuned through careful selection of components and molar ratios. While challenges such as viscosity and mass-transfer limitations remain, these systems offer significant opportunities for process optimisation and integration, particularly in applications requiring selective recovery of VFAs from complex fermentation media.

3.2. Ionic liquids

ILs are molten salts composed entirely of ions that remain liquid at or near ambient temperature. These solvents typically consist of a stabilised organic cation and an organic or inorganic anion, resulting in unique physicochemical properties such as adjustable polarity, negligible vapor pressure, and high thermal stability [64]. Due to their tunable properties through careful selection of cation–anion combinations, ILs are often referred to as designer solvents [58].

Several mechanisms have been proposed for the extraction of VFA using ILs. Martak and Schlosser investigated the extraction of lactic acid using phosphonium-based ILs and reported that [P666,14][Phos] achieved KDs greater than 40, primarily through hydrogen-bond interactions with undissociated acid molecules [2]. Similarly, Reyhanitash et al. [52] investigated the extraction of VFAs from fermented wastewater using phosphonium-based ILs such as [P666,14]Cl, [P666,14]Br, [P666,14][Phos], and [P666,14][N(CN)2] under extraction conditions of 20 ± 1 °C and a S/F ratio of 3/5 using artificial fermented wastewater containing approximately 1 wt% VFAs at pH values between 2.8 and 6.0. Their results suggested that the extraction process occurs through a combination of anion-exchange and hydrogen-bonding mechanisms, in which chloride or bromide ions are partially replaced by VFA anions. Among the investigated ILs, [P666,14][Phos] exhibited the highest extraction performance with KD values up to 17.0 and EE up to 94% for acetic acid at pH 2.8, while multi-stage extraction enabled combined VFA loadings of approximately 10 wt% and recovery streams approaching ~65 wt% VFAs. Phosphonium-based ILs containing long alkyl chains, such as the [P666,14] family, generally exhibit improved

Table 4
Summary of DES-, HDES-, and HES-based solvent systems for VFA extraction.

Solvent class	Components of DES / HDES	Molar ratio	Target acid(s)	EE (%)	Ref
HDES	DL-menthol + octanoic acid	2:1	C2	29.9	[60]
HDES	DL-menthol + decanoic acid	2:1	C2	28.5	[60]
HDES	DL-menthol + lauric acid	2:1	C2	27.2	[60]
HDES	DL-menthol + lauric acid	1.5:1	C2	40.5 (single stage)	[60]
HDES	DL-menthol + lauric acid	1.5:1	C2	88 (multi-stage)	[60]
HES	Octanoic acid + menthol	1:1	C2–C5	15.7/60.4 /82.0 /91.3	[53]
HES	Octanoic acid + thymol	1:2	C2–C5	35.5/73.1/82.1/89.0	[53]
In situ DES	TOMAC + acetic acid	7:3	C2	65.28	[63]
In situ DES	TOMAC + acetic acid	7:3	C3	84.96%	[63]
In situ DES	TOMAC + acetic acid	7:3	C4, C5	92.04 / 95.81%	[63]

extraction performance because increased hydrophobicity reduces water miscibility and enhances partitioning of undissociated VFAs into the organic phase. The extraction performance of these ILs is summarised in Table 5.

These results show that lower pH values significantly improve EE, since a larger fraction of the acids remains in the undissociated form. Additional studies have explored the integration of ILs with other separation or reaction processes. For example, Singh et al. [64] investigated hydrophobic ILs such as [P666,14][DBP] and [P666,14]Cl for VFA extraction coupled with enzymatic esterification, reporting high extraction capacity and good solvent stability. Other studies have demonstrated the compatibility of ILs with biological systems. Cull et al. [66] investigated the use of ILs in extractive fermentation processes, while Smirnova et al. [67] demonstrated their application in the extraction of amino acids from fermentation broths. Fig. 4 illustrates the principle of LLE and membrane-assisted in-situ separation of VFAs from fermentation broth. In conventional LLE, VFAs are transferred from the aqueous fermentation medium into an organic extractant phase through phase partitioning. The CLEANS process further enhances EE by promoting emulsification between the aqueous and organic phases, thereby increasing the interfacial contact area and mass transfer rate. Subsequent membrane-based phase separation enables continuous recovery of the extracted VFAs while recycling the aqueous stream back to the fermentation system.

Aoki et al. [68] investigated the use of gas–liquid–liquid slug flow systems to enhance mass transfer in LLE, demonstrating that the introduction of gas slugs could significantly increase the maximum stable flow rate in microchannel extraction systems. Although ILs exhibit excellent extraction performance and tunable properties, their large-scale application may be constrained by high synthesis cost, viscosity, and potential esnvironmental persistence.

Table 5
Summary of usage of various ILs for VFA extraction and their performance.

IL	Target acid(s)	Extraction metric reported	Ref
[P666,14][Phos]	C2	pH 2.8:- KD: 17, EE: 94% pH 4.6:- KD: 1.2, EE: 55%	[52]
[P666,14][cl]	C2	pH 2.8:- KD: 3.7, EE: 79% pH 4.6:- KD: 3.4, EE:77%	[52]
[P666,14][Br]	C2	pH 2.8:- KD: 2.2, EE: 69% pH 4.6:- KD: 1.4, EE: 58%	[52]
[P666,14][N(CN)$_2$]	C2	pH 2.8:- KD: 1.8, EE: 64% pH 4.6:- KD: 0.7, EE: 41%	[52]
[P666,14][Phos]	C2–C6	pH 2.8:- KD: 17, EE: 94% pH 4.6:- KD: 1.2, EE: 55%	[13]
[P666,14][cl] + dodecane	C2, C4	pH 6:- EE = 38.4–49.9% (C2); EE: 66.0–92.1% (C4)	[44]
[P666,14][Phos] + dodecane	C2, C4	pH 3:-EE: ≈ 89.8% pH 6:-EE ~ 14.6%	[44]
[P666,14][DBP]	C2–C6	Extraction capacity ≈ 842.8 mg VFA/g IL	[64]
[P666,14]-based ILs (mixed anions)	C2	Partition ratio ≈ 1.0 (cl/DCA); ≈0.23 (BF$_4$/Tf$_2$N)	[65]

3.3. Bio-based solvents for VFA extraction

Bio-based solvents have emerged as promising alternatives for LLE of VFAs due to their renewable origin, lower toxicity, and improved environmental compatibility, offering sustainable options for downstream processing of fermentation-derived products. These solvents can be broadly classified into several categories, including fatty acid esters (e.g., ethyl acetate, ethyl lactate), bio-based ethers (e.g., 2-methyltetrahydrofuran (2-MeTHF), cyclopentyl methyl ether (CPME), and eucalyptol (1,8-cineole)), and vegetable oils/lipid-based solvents, which are often used as diluents in reactive extraction systems.

Fatty acid esters such as ethyl acetate and ethyl lactate have been widely investigated for VFA extraction due to their favourable partitioning behaviour and relatively low cost. For instance, Fioravante et al. [40] demonstrated that ethyl acetate can achieve high EEs (>90% for C4 and > 70% for C3) under acidic conditions, highlighting its effectiveness for short-chain VFA recovery. Similarly, López-Porfiri et al. [17] identified ethyl lactate as a promising green solvent based on thermodynamic screening and Conductor-like screening model for real solvents (COSMO-RS) analysis, showing favourable solvent–acid interactions and phase separation characteristics.

Bio-based ethers such as 2-MeTHF, CPME, and eucalyptol (1,8-cineole) have also attracted attention due to their hydrophobicity, low water miscibility, and improved phase separation. López-Porfiri et al. [17] reported that these solvents exhibit favourable thermodynamic behaviour for organic acid extraction. Türk et al. [32] demonstrated that 2-MeTHF provides higher EE in physical extraction, whereas CPME enhances reactive extraction performance when combined with extractants such as TBP. These solvents are particularly effective for medium to long-chain VFAs, where hydrophobic interactions dominate the extraction mechanism. Vegetable oils and lipid-based solvents, including soybean oil, rice bran oil, and canola oil, are primarily employed as diluents in reactive extraction systems.

While bio-based solvents offer clear environmental and operational advantages, their performance also provides opportunities for further optimisation. For example, their relatively higher viscosity and moderate affinity for short-chain VFAs highlight their potential for process intensification through solvent modification, blending, or integration with reactive extraction systems. Such approaches can enhance mass transfer, improve selectivity, and expand their applicability across a wider range of VFA systems. Overall, bio-based solvents represent a flexible and sustainable platform for solvent design, particularly when tailored to specific acid characteristics and process conditions [33].

3.4. Comparative physicochemical, environmental, and economic characteristics of solvent systems

In addition to extraction performance, the practical applicability of solvent systems for VFA recovery is influenced by physicochemical, environmental, and economic characteristics, including viscosity, polarity, boiling point, biodegradability, production source, and solvent cost. As discussed in Sections 2–4, these properties affect extraction

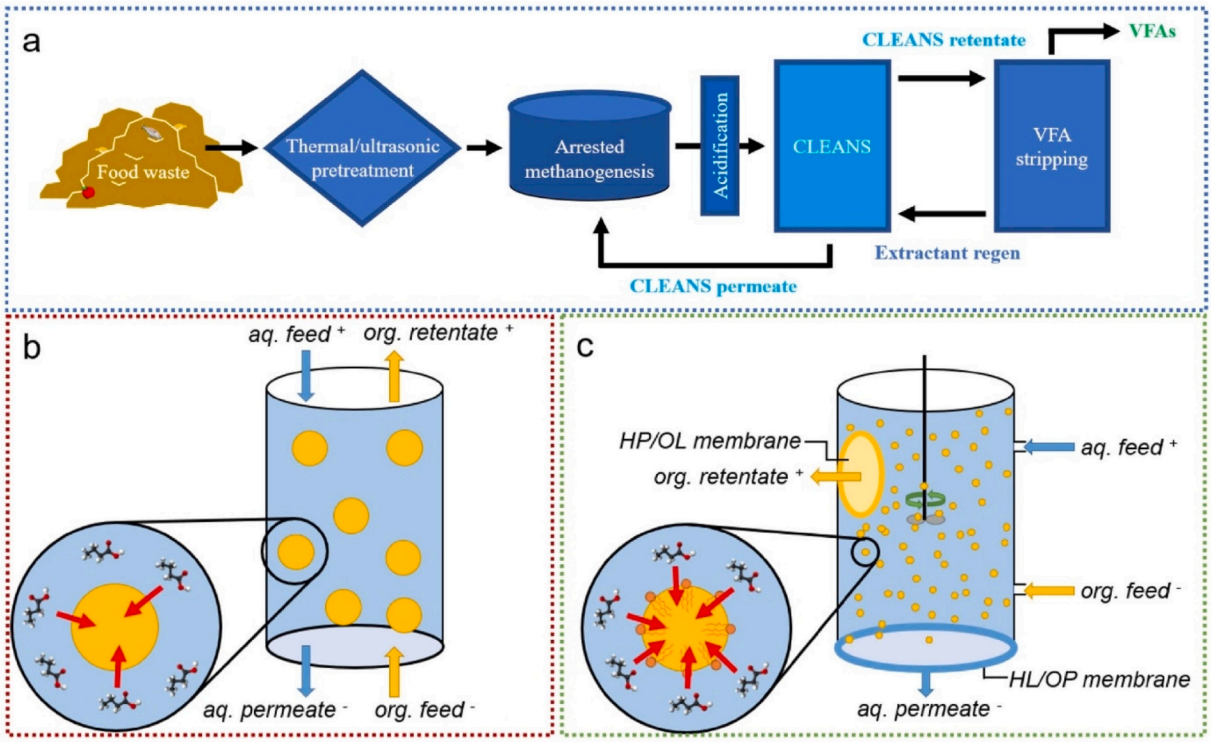

Fig. 4. LLE and in-situ separation of VFAs from fermentation broth - Integrated VFA production and recovery process using the CLEANS system: (a) process flow diagram; (b) conventional liquid–liquid extraction (LLE); (c) CLEANS process schematic. Reproduced from [21] permission from Elsevier.

behaviour, phase separation, regeneration requirements, process operability, and scale-up feasibility. Environmental considerations such as biodegradability and persistence, together with economic factors associated with solvent make-up, regeneration, and recycling, further influence the suitability of solvent systems for industrial implementation.

For emerging solvent systems such as ILs and DESs, industrial implementation is influenced not only by solvent cost but also by the scalability of solvent production. Although these solvents offer tunable properties and promising extraction performance, large-scale preparation may be constrained by synthesis complexity, purification requirements, control of solvent composition, and limited commercial manufacturing infrastructure compared with conventional solvents. Consequently, production scalability remains an important consideration when evaluating their industrial applicability.

Therefore, comparative evaluation of these characteristics is important for identifying solvent systems that provide an appropriate balance between EE, regeneration feasibility, environmental considerations, and economic viability. Table 6 summarises the key physicochemical, environmental, and economic characteristics of representative solvent systems discussed in this review.

3.5. Computational approaches for solvent screening and extraction mechanism analysis

In recent years, computational approaches have increasingly been integrated with experimental studies to improve understanding of extraction mechanisms and accelerate solvent selection for VFA recovery systems. Among these approaches, COSMO-RS has been widely employed to predict solvent–acid affinity, phase equilibrium behaviour, KD, and relative extraction performance before experimental validation. López-Porfiri et al. [17] used COSMO-RS screening to evaluate green solvents for organic acid recovery and demonstrated that solvents such as ethyl lactate, CPME, and 2-MeTHF exhibited favourable thermodynamic interactions and phase-separation behaviour for carboxylic acid extraction. Similarly, Benabid et al. [57] applied COSMO-RS and molecular reactivity analysis to hydrophobic DES systems and showed that solvent polarity and hydrogen-bonding characteristics strongly influence extraction compatibility and solvation behaviour. These studies demonstrated that computational screening can significantly reduce experimental solvent-selection requirements by rapidly evaluating large numbers of candidate solvents before laboratory testing. Beyond screening existing solvents, COSMO-RS can also be employed as a predictive solvent-design tool. By evaluating hypothetical solvent structures and component combinations prior to synthesis, COSMO-RS enables identification of promising IL, DES, and bio-based solvent candidates with favourable thermodynamic properties. This capability reduces experimental trial-and-error efforts and supports rational design of next-generation extraction solvents tailored for specific VFA recovery applications.

In parallel, molecular dynamics (MD) simulations and density functional theory calculations have increasingly been used to investigate hydrogen-bonding interactions, diffusion behaviour, solvent microstructure, and acid–extractant complex formation at the molecular level. Liu et al. [61] combined MD simulations with experimental studies for amide-based DES systems and demonstrated that hydrogen-bond networks and intermolecular interactions strongly govern extraction performance and diffusion behaviour of carboxylic acids. Matsumoto et al. [62] further investigated hydrophobic eutectic mixtures containing terpenoids and decanoic acid and reported that intermolecular interactions and solvent hydrophobicity significantly affected extraction selectivity and phase behaviour. More recent studies on hydrophobic DES systems for VFA recovery also showed that increasing fatty-acid chain length enhances hydrophobic interactions and modifies solvent microstructure, thereby improving extraction selectivity and stability of the organic phase [58]. In addition, computational analyses using radial distribution functions and interaction-energy calculations demonstrated that hydrogen bonding and van der Waals interactions are dominant factors governing EE in DES- and IL-based systems.

These molecular-level descriptors can provide mechanistic interpretation of experimentally observed liquid–liquid equilibrium

Table 6
Comparison of physicochemical, environmental, and economic characteristics of representative solvents.

Solvent	Viscosity (mPa·s, 25 °C)	Polarity (log P)	Boiling point (°C)	KD or EE	Source of production	Biodegradability	Approximate bulk cost(€ kg^{-1})*
Conventional oxygen-bearing solvents							
Ethyl acetate	0.45	0.3	77	EE ≈ 73% (C3), 93% (C4)	Petrochemical/ bio-derived	Readily biodegradable	~0.9–1.8
MIBK	0.59	1.3	117	EE ≈ 50–80% for C4–C6	Petrochemical	Moderately biodegradable	~2.3–2.8
DEE	0.2–2	1.0	34.6	EE ≈ 60–85%	Petrochemical / bioethanol dehydration	Biodegradable	~1.8–3.7
1-octanol	7.4	3.0	195	KD ≈ 2–10 (with reactive systems)	Petrochemical / oleochemical	Biodegradable	~2.8–4.6
1-Decanol	11–14	4.1	232	KD ~5.9 with TBP systems	Petrochemical / oleochemical	Biodegradable	~3.7–5.5
Organophosphorus extractants							
TBP	3.4	3.99–4.01	289	KD ≈ 1.1–5.9; EE ≈ 53–85%	Petrochemical phosphate ester	Low biodegradability	~2.8–5.5
TOPO	~80–100	9.54	~390	KD ≈ 2–5; EE ≈ 60–90%	Petrochemical phosphine oxide synthesis	Poor biodegradability	~18–37
Reactive amine							
TOA	~80–120	8.0	~365	KD ~ 44.5;EE ≈ 33–82%	Petrochemical amine synthesis	Poorly biodegradable	~7–14
Alamine 336	~100–150	1.45	>300	EE ≈ 95% for C4	Petrochemicaltertiary amine mixture	Limited biodegradability	~9–18
Aliquat 336	~1500–2500	7–9.5	Decomposes at >200	KD ≈ 2.46–3.0; EE ≈ 38–75%	Petrochemical	Poor biodegradability	~14–23
ILs							
[P666,14][Phos]	~300–500	≈5–8	Nonvolatile	KD ~ 17; EE ~ 94%	Synthetic IL	Poor biodegradability (21–33% after 300 d)	>45–90
[P666,14]cl	~250–400	Hydrophobic IL	Nonvolatile	KD ≈ 3.4–3.7; EE ≈ 77–79%	Synthetic IL	Poor biodegradability	>37–74
[P666,14][DBP]	~350–600	6–9	Nonvolatile	Extraction capacity ≈842.8 mg VFA g^{-1} IL	Synthetic IL	Limited biodegradability	>74–110
DES/HDES systems							
ChCl–urea	~750–900	≈ − 1.29 to −1.50	Nonvolatile	Moderate extraction	ChCl + urea	Biodegradable	~1.8–4.6
ChCl–glycerol	~300–500	ChCl= -4.99& glycerol = −1.76	Nonvolatile	Moderate extraction	ChCl + glycerol	Biodegradable	~1.8–5.5
Menthol–lauric acid	~20–50	Menthol = 3.15–3.4& glycerol =4.6	Low volatility	EE ≈ 27–88%	Natural terpene + fatty acid	Biodegradable	~4.6–9
Octanoic acid–menthol	~15–30	Octanoic acid = 3.05 and menthol 3.15	Low volatility	EE ≈ 15.7–91.3%	Bio-based fatty acid + terpene	Biodegradable	~4.6–11
Octanoic acid–thymol	~15–25	Octanoic acid = 3.05& thymol 3.3–0.3.4	Low volatility	EE ≈ 35.5–89.0%	Bio-based fatty acid + terpene	Biodegradable	~4.6–11
Bio-based / green solvents							
2-MeTHF	0.46	0.9	80	Good extraction for medium-chain VFAs	Biomass-derived (furfural route)	Biodegradable	~2.8–5.5
CPME	0.47	1.6	106	Improved reactive extraction performance	Petrochemical/ partially bio-based	Moderate biodegradability	~4.6–7.4
Ethyl lactate	2.7	~ − 0.07 to 0.7	154	Favourable solvent–acid interactions	Fermentation-derived	Readily biodegradable	~3.7–7.4
Vegetable oils	~50–80	10–20	>300	EE ≈ 40–48% with TOA systems	Renewable vegetable oils	Highly biodegradable	~0.9–2.8

Note: Approximate solvent costs correspond to industrial bulk-scale commodity prices estimated from market-analysis databases such as ICIS, Intratec, and Procurement Resource; values vary depending on purity, supplier, region, production scale, and market conditions.

behaviour. For example, stronger hydrogen-bond interactions, lower solvent–acid interaction energies, and higher Radial Distribution Function (RDF) peak intensities generally indicate stronger affinity between VFAs and solvent molecules, which may promote acid partitioning into the organic phase. Consequently, these microscopic properties can often be associated with higher KD values, improved EE, and enhanced extraction selectivity. Although direct quantitative correlations remain challenging, combining MD simulations with thermodynamic modelling and experimental measurements provides valuable insight into structure–property–performance relationships governing VFA extraction [61].

Overall, recent studies increasingly combine COSMO-RS, MD simulations, thermodynamic modelling, and experimental validation to establish structure–property–performance relationships for emerging solvent systems and support rational solvent selection for VFA recovery.

4. Process engineering and operational considerations for LLE-based VFA recovery

In addition to selecting appropriate solvent systems, the efficiency of LLE for VFA recovery is strongly influenced by operating conditions. Parameters such as pH, temperature, S/F ratio, ionic strength, and mixing intensity significantly affect phase equilibrium, mass transfer, and overall extraction performance [49]. Control and optimisation of these variables are therefore essential for achieving efficient and stable VFA separation from fermentation broths. To systematically evaluate their impact, this section discusses the effects of key operating parameters.

4.1. Influence of operating parameters on VFA extraction performance

Effect of pH: pH governs the equilibrium between undissociated (R–COOH) and dissociated ($R–COO^-$) forms, with extraction favoring the undissociated species; consequently, EE is higher at low pH (≈2–4) and decreases as pH increases [35,52]. However, biological constraints must also be considered, as acidogenic pathways typically operate at pH ≈ 5–6, whereas methanogenic microorganisms require near-neutral conditions (≈6.8–7.5). Therefore, when the objective is VFA production, a staged approach can be adopted in which fermentation is maintained under acidogenic conditions, followed by controlled pH reduction (≈2–4) prior to extraction. In practice, pH adjustment is commonly achieved through acid addition (e.g., H_2SO_4 or HCl) or CO_2 dosing to shift the equilibrium toward the undissociated form [27,52]. Such process decoupling enables efficient VFA recovery while maintaining biological stability.

Effect of temperature: Temperature influences LLE by affecting solvent properties. Although increasing temperature can enhance mass transfer by reducing viscosity and improving diffusion, its overall effect on VFA extraction is governed by equilibrium behaviour. In reactive systems, the extraction process is exothermic; therefore, extraction performance generally decreases with increasing temperature. Eda et al. [69] showed that both KD and EE decline as temperature increases from 293 to 323 K, primarily due to increased partitioning of acids into the aqueous phase and reduced strength of complex formation. This trend is observed for short-chain VFAs such as acetic, propionic, and butyric acids, with smaller variations for more hydrophobic acids. Consequently, while moderate temperatures may aid mass transfer, higher temperatures reduce extraction performance and increase energy demand, highlighting the need for careful optimisation.

Effect of S/F ratio: The S/F ratio is a critical parameter governing EE and solvent capacity in LLE. Increasing S/F generally enhances VFA recovery due to greater solvent availability; however, excessive solvent use reduces solvent utilisation efficiency and increases operational costs, necessitating optimisation. Singh et al. [64] reported that IL: feed ratios in the range of 0.1–1.0 significantly affect extraction performance, with higher ratios (≥0.25) achieving >90% recovery for longer-chain VFAs, while lower ratios (0.1–0.125) maximise solvent loading (≈188–197 mg VFA g^{-1} IL). Similarly, Reyhanitash et al. [52] demonstrated that at an S/F of 3/5, high-capacity ILs such as [P666,14][Phos] can achieve VFA loadings of ~10 wt% and concentrate dilute feeds (~0.25 wt%) to ~65 wt% streams, outperforming conventional TOA-based systems. These findings highlight that optimal S/F selection must balance EE, solvent loading, and process economics.

Effect of ionic strength and broth composition: Fermentation broth composition affects VFA extraction, as salts, proteins, and suspended solids influence phase behaviour and efficiency. Reyhanitash et al. [52] showed that salts like potassium chloride can alter ionic equilibrium and promote undissociated acids, enhancing EE. However, impurities may also cause emulsification and phase instability, especially with reactive or viscous solvents, posing challenges for scale-up.

Effect of mixing and contact time: Efficient mixing and adequate contact time are crucial in LLE, as increased interfacial area enhances mass transfer and accelerates extraction. However, excessive mixing can cause stable emulsions, hindering phase separation and requiring a balance in process design. Advanced approaches, such as membrane contactors and intensified flow systems, have shown improved mass transfer and stable operation at higher flow rates [16].

Scale-up challenges and process intensification in LLE systems: Scale-up of LLE systems for VFA recovery is additionally influenced by solvent viscosity, emulsification, mass-transfer limitations, and equipment compatibility. Conventional oxygenated solvents typically exhibit low viscosities (~1–5 mPa·s), whereas ILs and DES/HDES systems may exceed 50–500 mPa·s, reducing diffusivity, slowing phase disengagement, and increasing pumping energy requirements. In real fermentation broths, suspended solids, proteins, and extracellular polymeric substances can stabilise emulsions, particularly in reactive amine systems, leading to solvent loss and operational instability. These limitations can reduce the performance of mixer-settlers and extraction columns at an industrial scale, thereby motivating the development of intensified systems such as membrane contactors, centrifugal extractors, and slug-flow microreactors to improve interfacial mass transfer and process stability [70,71].

Integrated process optimisation: Because key operating parameters are interdependent, effective VFA extraction requires simultaneous optimisation of multiple variables, including pH, temperature, S/F ratio, and solvent composition. Xing et al. [44] systematically evaluated IL concentration (2–10%), S/F (1/2–2/1), pH (3–6), and feed concentration (2–10 g L^{-1}), demonstrating that extraction performance is governed by their combined effects. Under optimised conditions (10% [P666,14][Cl] in dodecane, S/F = 2:1, pH ≈ 6, and VFA concentration ≈ 10 g L^{-1}), EEs of ~49.9% for acetic acid and up to ~92.1% for butyric acid were achieved.

These findings highlight that optimisation is inherently multi-parametric and must be tailored to the target acid and feed characteristics rather than based on a single variable. At a broader scale, process optimisation is also critical for economic feasibility, as downstream recovery represents a major cost contribution in VFA production systems [35]. Therefore, process design should follow a decision-oriented approach in which operating conditions are selected based on acid chain length, feed composition, and desired trade-offs between EE, solvent utilisation, and energy demand. Beyond process parameters, solvent selection must also be guided by environmental and economic constraints to ensure scalable and sustainable VFA recovery.

4.2. Solvent regeneration, recyclability, and scale-up considerations

Following VFA extraction, regeneration and recycling of the solvent phase are essential for process sustainability, economic feasibility, and industrial scale-up [23,27]. In LLE systems, the loaded organic phase must be regenerated to recover the extracted acids and enable solvent reuse over multiple extraction cycles. The regeneration strategy depends on the solvent type, extracted VFAs, and the strength of solvent–acid

interactions. Among the available approaches, pH-swing back-extraction (alkaline stripping) is the most widely used technique for reactive amine and organophosphorus systems because it enables high regeneration efficiency under mild conditions [41]. In this process, extracted undissociated acids are converted into water-soluble carboxylate salts using alkaline solutions such as NaOH or KOH. For example, Alamine 336 in oleyl alcohol achieved ~95% EE with ~90% acid recovery during alkaline stripping [50], while TOA-based systems reported KD values up to 16.7 and EE up to 43.8% after regeneration [49]. However, this method increases chemical consumption and generates salt-containing streams that may require additional treatment.

Thermal regeneration through distillation is commonly applied to volatile oxygenated solvents such as ethyl acetate, MIBK, DEE, and octyl acetate, where VFAs are recovered based on boiling-point differences [31,40]. Octyl acetate systems achieved 99% overall recovery and 99.8 wt% product purity after solvent recycle through heat-integrated distillation [50]. Similarly, ethyl acetate extraction achieved ~93% recovery for butyric acid and ~ 73% for propionic acid after solvent recovery [40]. Although distillation facilitates solvent recycling and high-purity product recovery, the associated energy demand can become significant for dilute fermentation broths, making energy integration and solvent selection critical for industrial implementation.

Temperature-swing regeneration has also been investigated for reactive extraction systems, where increasing temperature from 293 to 323 K weakens acid–extractant interactions and reduces EE, thereby promoting acid release from the solvent phase [69]. However, regeneration through temperature variation is often incomplete and may reduce overall process efficiency because reactive extraction of VFAs is generally exothermic.

For emerging solvents such as ILs, DESs, and HDESs, regeneration is more challenging because of their low volatility and high viscosity [54]. IL-based systems such as [P666,14][DBP] achieved extraction capacities up to ~842.8 mg VFA g^{-1} IL, while integrated esterification-assisted regeneration reached conversion efficiencies up to 83.7% for C6 acids [64]. However, the viscosity of ILs and DESs can exceed 50–500 mPa·s, compared with ~1–5 mPa·s for conventional solvents, resulting in reduced mass-transfer rates, slower phase separation, and higher pumping energy during scale-up. Consequently, membrane-assisted recovery, vacuum stripping, and reactive conversion strategies have gained attention to reduce energy demand and improve solvent recyclability [16,23].

Regeneration performance is further affected by the complexity of real fermentation broths containing salts, proteins, suspended solids, and biomass residues, which can increase emulsification, prolong phase separation, and reduce solvent stability during repeated cycles [21]. These issues become more significant during scale-up, where stable emulsions, increased solvent losses, and reduced interfacial mass transfer can limit continuous operation in mixer-settlers and extraction columns. Therefore, industrial implementation requires not only high EE, but also robust solvent recyclability, low regeneration energy, rapid phase disengagement, and long-term stability under realistic fermentation conditions. The main regeneration and recycling strategies reported for VFA extraction systems are summarised in Table 7.

5. Environmental and economic considerations in LLE of VFAs

Environmental and economic considerations play a critical role in evaluating solvent systems for LLE of VFAs from anaerobic bioprocesses. Beyond EE, solvent selection must consider regeneration energy, solvent stability, recyclability, environmental persistence, and compatibility with integrated biorefinery systems [24]. Recent studies have shown that downstream separation and purification remain major contributors to the overall economic and environmental burdens of VFA biorefineries because of the high energy demand associated with solvent recovery, product concentration, and chemical consumption [24,35].

5.1. Life-cycle and techno-economic analysis

LCA and TEA are increasingly employed to evaluate the sustainability of integrated VFA production and recovery systems. However, relatively few studies have specifically assessed the environmental and economic performance of LLE-based VFA recovery. Available

Table 7
Regeneration and recycling strategies for solvent systems used in LLE-based VFA recovery.

Regeneration technique	Solvent system	VFAs extracted	No. of solvent recycles / EE per cycle	Ref
pH-swing back-extraction (alkaline stripping)	Alamine 336 (10 wt%) in oleyl alcohol	C4	~95% EE with ~90% recovery during alkaline stripping and solvent reuse after regeneration	[50]
	TOA + oleyl alcohol/ kerosene /1-decanol	C3	KD up to 16.7 with EE up to 43.82%; regenerated reactive extraction solvent retained extraction performance after alkaline stripping	[49]
Distillation / thermal regeneration	Octyl acetate	C4	99% overall recovery with 99.8 wt% product purity after solvent recycle through heat-integrated distillation	[50]
	Ethyl acetate, MIBK, and DEE	C3-C6	Ethyl acetate achieved ~93% butyric acid and ~ 73% propionic acid extraction after thermal recovery; MIBK and DEE enabled efficient solvent reuse for hydrophobic VFAs	[40]
Temperature-swing regeneration	TOA and TBP based reactive extraction systems	C2-C4	Increasing temperature from 293 to 323 K reduced KD and EE by weakening acid–extractant interactions, enabling partial thermal regeneration	[69]
	Phosphonium IL systems ([P666,14]-based ILs)	C2	Temperature-sensitive extraction equilibrium enabled thermal release of acids from the IL phase during regeneration	[2]
Vacuum stripping /	Ethyl acetate and MIBK	C2-C4	Reduced-pressure regeneration minimised thermal degradation and improved solvent recovery efficiency for volatile solvent systems	[27]
	Volatile oxygenated solvent systems	C2-C6	Vacuum-assisted recovery improved downstream separation and reduced energy demand compared with direct atmospheric distillation	[24]
Membrane-assisted regeneration	IL-integrated extraction systems	C2-C6	Continuous membrane-assisted regeneration reduced solvent consumption and improved energy efficiency	[23]
	DES- and HDES-integrated extraction systems	C2 and C4	Membrane contactors enabled continuous solvent regeneration with lower energy demand and improved process stability	[16]
Reactive conversion/ esterification-assisted regeneration	[P666,14][DBP] hydrophobic IL	C2–C6	Extraction capacity ≈842.8 mg VFA g^{-1} IL with esterification conversion up to 83.7% for hexanoic acid	[64]
	Hydrophobic IL–enzyme systems	C6 and mixed VFAs	Integrated esterification enabled simultaneous product upgrading and solvent regeneration	[64]
Gas stripping	Volatile solvent systems	C2-C6	Continuous stripping-assisted regeneration improved downstream recovery efficiency and reduced solvent loading	[24]
	Integrated fermentation–recovery systems	C2-C6	Steam/gas stripping enhanced VFA recovery while improving process integration in fermentation systems	[35]

assessments indicate that energy consumption, chemical usage, and process integration are major contributors to the overall sustainability of VFA biorefineries. Elginoz et al. [72] demonstrated that reactor heating and NaOH addition were significant contributors to environmental burdens during VFA production from dairy wastewater, while Gracia et al. [73] reported increased global warming impacts with prolonged fermentation times because of higher energy consumption. Although these studies primarily evaluated VFA production systems, they demonstrate that operational parameters such as heating demand, pH control, hydraulic retention time, and chemical consumption can significantly influence the environmental performance of integrated VFA production and recovery platforms.

From a recovery perspective, LLE offers an important sustainability advantage by functioning as a pre-concentration step prior to downstream purification. As discussed in Section 1 and illustrated in Fig. 2, extraction-assisted recovery transfers VFAs from dilute fermentation broths into a concentrated organic phase before final product purification. This approach reduces the volume of water requiring thermal treatment and can substantially decrease the energy demand associated with direct distillation of dilute aqueous streams. Because distillation energy consumption increases markedly with decreasing product concentration, pre-concentration through LLE has the potential to improve both economic and environmental performance by reducing heat requirements, lowering associated greenhouse-gas emissions, and decreasing operating costs [27,50].

From a solvent perspective, conventional organic solvents are often associated with volatility, solvent losses, emissions, and safety concerns, motivating the development of alternative solvent systems including ILs, DESs, and bio-based solvents. However, low volatility alone does not guarantee improved environmental performance because solvent behaviour depends strongly on molecular structure, biodegradability, toxicity, and environmental persistence.

For example, phosphonium-based ILs exhibit high extraction efficiencies and distribution coefficients for organic acids [52,74], but Sydow et al. [75] reported only 21–33% biodegradation of $[P_{66614}]Cl$ after 300 days, indicating potential long-term environmental persistence despite negligible vapor pressure. Moreover, biodegradation rate alone does not fully describe environmental fate because degradation products and intermediate compounds may exhibit different mobility, persistence, or ecotoxicity compared with the parent solvent. Therefore, environmental assessment of emerging solvents should consider both biodegradation behaviour and the potential impacts of degradation products.

In contrast, DESs and bio-based solvents generally exhibit improved biodegradability and lower volatility, although their environmental performance remains dependent on constituent composition and operating conditions. Singh et al. further demonstrated that hydrophobic IL systems integrated with in situ enzymatic esterification improved extraction capacity while reducing downstream processing requirements [64]. These findings highlight that solvent selection should simultaneously consider extraction performance, environmental fate, and long-term process sustainability.

In integrated anaerobic digestion and acidogenic fermentation systems, solvents must also exhibit low microbial toxicity because residual solvent accumulation can inhibit microbial activity, alter metabolic pathways, and reduce process stability. Therefore, solvent systems should be evaluated not only as extraction media but also as integral components of coupled biological and separation processes.

From a techno-economic perspective, downstream recovery and purification often represent a substantial fraction of the total cost of fermentative VFA production systems [27,28]. Solvent selection, therefore, influences operating expenditure through solvent make-up requirements, energy consumption, solvent losses, and recycling efficiency. Solvents exhibiting high extraction efficiencies may not necessarily provide favourable economics if recovery and recycle operations are energy-intensive. Conversely, systems with moderate extraction performance may become economically attractive when low-cost solvents, efficient recycle, and reduced utility demand are achieved. For example, Oh et al. [50] demonstrated that extraction-assisted recovery using octyl acetate achieved approximately 99% recovery of C4 acids with 99.8 wt% product purity at a recovery cost of approximately USD 0.23 kg^{-1} through heat-integrated solvent recycling. Similarly, Li et al. reported net greenhouse gas emissions of approximately −0.4 kg CO_2-eq kg^{-1} VFA for an integrated food-waste fermentation–microbial electrosynthesis platform because of avoided methane emissions and simultaneous production of value-added chemicals [50,76]. These findings indicate that energy demand, solvent management, and process integration are key techno-economic drivers governing industrial implementation of VFA recovery systems.

Overall, quantitative environmental and economic assessments specifically focused on LLE-based VFA recovery remain limited. As emerging solvent systems such as ILs, DESs, HDESs, and bio-based solvents continue to be developed, there is considerable scope for future research to systematically evaluate their environmental and economic performance using integrated LCA and TEA methodologies. Consequently, combining LCA, TEA, and process simulation tools such as Aspen Plus, SimaPro, and openLCA will be essential for developing multi-criteria optimisation frameworks capable of identifying solvent systems that minimise environmental impacts while maintaining economic feasibility and industrial scalability.

5.2. Conceptual framework for solvent selection in LLE of VFAs

The environmental and economic considerations discussed above necessitate a systematic framework for solvent selection in LLE of VFAs. Accordingly, Fig. 5 presents a literature-informed, decision-oriented framework that integrates key parameters governing extraction performance, including feed characteristics, acid chain length, and pH-dependent speciation, together with economic and environmental constraints.

Fig. 5 also includes an illustrative example showing how the proposed framework can be applied to guide solvent selection for recovery of mixed VFAs from a food-waste fermentation broth. The example is intended solely to demonstrate the sequential decision-making process and is derived from the synthesis of the literature discussed throughout this review rather than from a single experimental study.

Within this framework, solvent selection is primarily guided by the physicochemical properties of the target acids, particularly chain length and aqueous solubility, as well as the operating conditions of the fermentation broth. Short-chain VFAs (C2–C3), which remain highly soluble in water, generally require reactive extraction systems to achieve effective recovery, whereas medium- to long-chain VFAs (C4–C6) exhibit greater hydrophobicity and can be recovered using physical or hybrid extraction approaches. Consequently, the choice of extraction strategy is dictated by acid characteristics rather than solvent class alone.

The framework further incorporates the influence of pH, which governs acid speciation and determines the suitability of physical versus reactive extraction. Under acidic conditions, where undissociated acids dominate, both physical and reactive extraction systems can be effective, while at near-neutral pH, reactive systems are generally preferred to compensate for reduced extractability. This highlights the importance of integrating upstream process conditions with downstream separation requirements.

Beyond extraction performance, solvent selection is governed by process-level constraints, including regeneration strategy, energy demand, phase behaviour, solvent-to-feed ratio, and biocompatibility in integrated AD or AM systems. These factors often determine the practical feasibility of a solvent system, even when intrinsic extraction performance is favourable.

Accordingly, the framework adopts a multi-criteria, decision-oriented approach in which solvent selection is performed sequentially

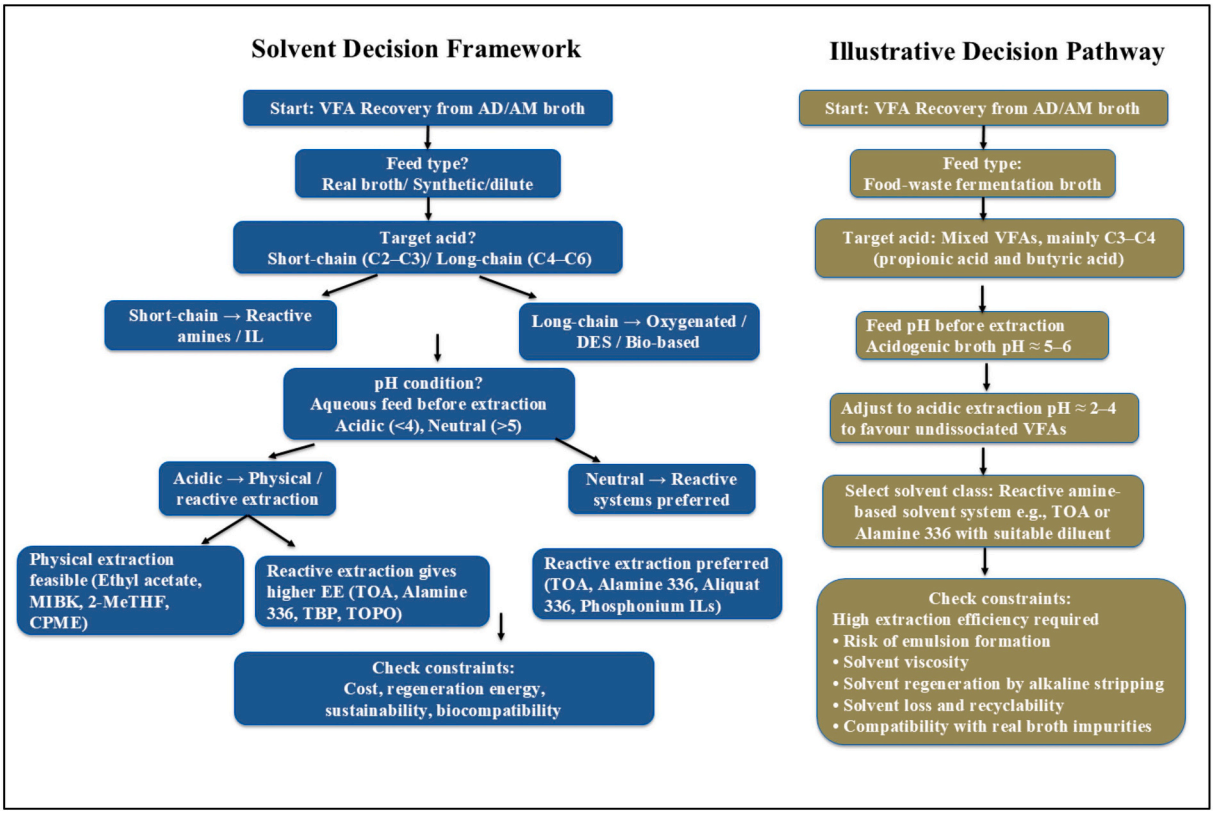

Fig. 5. Decision-making framework for solvent selection in LLE of VFAs from anaerobic bioprocesses together with an illustrative example demonstrating its application for mixed VFA recovery from a food-waste fermentation broth.

based on acid properties, feed characteristics, operating conditions (e.g., pH and concentration), and finally economic and environmental constraints. This structured evaluation enables identification of solvent systems that are both technically effective and scalable under realistic process conditions.

Overall, the framework emphasises that efficient VFA recovery through LLE requires integrated optimisation of solvent properties, operating conditions, and process constraints, providing a practical basis for the design of sustainable and economically viable recovery systems.

6. Conclusion and future recommendations

The recovery of VFAs from AD, AM, and related fermentation processes represents an important step toward the development of integrated waste-based biorefineries and circular bioeconomy systems. This review demonstrates that LLE is a promising and versatile approach for VFA recovery from dilute and complex aqueous streams because it enables selective separation under mild operating conditions while reducing product inhibition in biological systems. Among the solvent systems evaluated, reactive amine-based extractants consistently exhibit high extraction performance for dilute short-chain VFAs because of strong acid–base complexation mechanisms that significantly enhance KD. Organophosphorus extractants provide intermediate extraction performance with improved selectivity under acidic conditions, whereas conventional oxygen-bearing solvents are more suitable for recovery of hydrophobic, longer-chain VFAs. Emerging solvent systems such as ILs, DESs, and HDESs further provide opportunities for tunable extraction performance and reduced solvent volatility solvent design flexibility, and potential environmental compatibility. However, important limitations remain, including solvent viscosity, regeneration energy demand, emulsification, solvent cost, and limited industrial-scale validation. Future progress will therefore depend on integrated optimisation of solvent design, regeneration strategy, process intensification, and sustainability assessment to enable economically viable and scalable VFA recovery systems.

The analysis of process parameters highlights that extraction performance is strongly governed by pH-dependent VFA speciation, solvent composition, temperature, and S/F ratio. In addition, practical implementation of LLE systems is influenced by solvent regeneration requirements, viscosity, emulsification tendency, phase disengagement, and compatibility with real fermentation broths containing salts, proteins, suspended solids, and biomass residues. Similarly, solvent systems exhibiting excellent EE may still face challenges associated with solvent persistence, operational stability, and downstream energy consumption. These findings demonstrate that solvent selection for VFA recovery cannot be based solely on EE, but must also consider regeneration feasibility, environmental impact, process integration, and industrial operability.

From a broader process perspective, LLE-based VFA recovery systems exhibit important strengths including high extraction selectivity, compatibility with dilute fermentation broths, and potential integration with anaerobic biorefineries.

Future research should therefore focus on the rational design of solvent systems with improved selectivity, lower viscosity, and enhanced recyclability, together with development of low-energy regeneration strategies and intensified extraction configurations. Greater emphasis is also needed on evaluating solvent performance under realistic fermentation conditions to better understand long-term operational stability, solvent loss, and phase behaviour during continuous operation. In addition, integration of computational solvent design, membrane-assisted recovery, in situ extraction systems, and process-level LCA/TEA analysis will be important for accelerating the development of sustainable VFA recovery technologies. Overall, advancement of LLE-based VFA recovery will require a transition from isolated solvent-screening studies toward integrated process-oriented approaches combining solvent design, extraction engineering,

regeneration strategy, and sustainability evaluation to support industrial implementation of VFA biorefineries.

Declaration of competing 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 paper.

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Data availability

No data was used for the research described in the article.

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Further reading

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