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Review/Derleme

Fermentative Organic Acid Production and Separation

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Abstract

Anaerobic digestion processes offer several benefits over aerobic ones such as higher organic loading rates and energy production in the form of methane. Recently, production of valuable fermentation intermediates instead of methane has gained a significant interest due to low calorific value and storage difficulties of methane. Organic acids, which are produced via anaerobic fermentation, can be subsequently removed/recovered via separation processes such as solvent extraction, chemical precipitation, adsorption, and electrodialysis. Chemical precipitation is not feasible for the short-chain fatty acids due to their high solubility at varying pH values. Solvent extraction is feasible for organic acid removal, however yields highly polluted waste. Adsorption processes are expensive, non-specific and not as efficient as other separation techniques. Membrane processes such as electrodialysis seem to be the most promising separation technique for the organic acid removal, however, more research needs to be conducted on the optimization of electrodialytic processes to reduce problems such as polarization, membrane fouling, and back diffusion.

Keywords: Adsorption, fermentation, electrodialysis, extraction, chemical precipitation, VFAs separation

Fermentatif Organik Asit Üretimi ve Ayrılması

Özet

Anaerobik çürütme işleminin, aerobik işlemlere göre, metan formunda enerji üretimi ve yüksek organik yük uygulanabilirliği gibi çeşitli avantajları vardır. Düşük kalorifik değeri ve depolama zorlukları gibi sebeplerden dolayı metan üretimi yerine değerli fermentasyon ara ürünlerinin üretimi son zamanlarda yoğun ilgi görmeye başlamıştır. Anaerobik fermentasyon ile üretilen organik asitler; solvent ekstraksiyonu, kimyasal çöktürme, adsorpsiyon ve elektrodiyaliz gibi ayırma yöntemleri kullanılarak ayrılabilir ve geri kazanılabilir. Kısa-zincirli uçucu yağ asitleri, değişik pH değerlerinde yüksek çözünürlük gösterdiklerinden, kimyasal çöktürme ile ayrılmaları uygun değildir. Solvent ekstraksiyonu organik asitlerin ayırılması için uygundur, fakat işlem sonucu yüksek kirlilikte atık oluşmaktadır. Adsorpsiyon prosesleri, diğer ayırma yöntemlerine göre daha pahalı, verimsiz ve daha az seçicidir. Membran prosesi olan elekrodiyaliz, organik asit ayırmak için en ümit verici yöntem olarak gözükmektedir. Fakat, elektrodiyaliz işlemlerinde karşılaşılan kutuplanma, membran kirlenmesi ve geri yayınım gibi problemlerin azaltılması ve prosesin iyileştirilmesi için daha fazla araştırma yapılması gerekmektedir.

Anahtar Kelimeler: Adsorpsiyon, fermentasyon, elektrodiyaliz, ekstraksiyon, kimyasal çöktürme, uçucu yağ asidi ayırma

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Introduction

Anaerobic digestion process is considered to be one of the most efficient waste and wastewater treatment technology, therefore, it has been widely used for the treatment of high- and low- strength carbohydrate-rich wastes such as municipal sludge, municipal solid waste, organic industrial wastes including fruit and vegetable processing wastes, packing-house wastes, agricultural wastes, food processing wastewaters etc [1; 2]. Anaerobic digestion offers number of significant advantages such as low sludge production, low energy requirement, high organic loading rates, and energy production in the form of methane. However, due to low calorific value and storage difficulties of methane, production of valuable fermentation intermediates such as organic acids may have wider applications.

Fatty acids are organic acids with one or more carboxylic acid groups [3]. Volatile fatty acids (VFAs) such as acetic, propionic, isobutyric, butyric, isovaleric, caproic acids contain a single carboxyl group (-COOH) and non-volatile fatty acids such as oxalic, succinic, and malonic acids contain two carboxyl groups. These two groups of organic acids can be observed in fermentation broths. VFA production via anaerobic digestion can be difficult due to its inhibitory effects on the process. Undissociated VFAs can freely permeate the cell membrane lowering pH within the cell [4]. Accumulation of certain VFAs may alter the anaerobic digestion process, causing reactions to became thermodynamically unfavorable, which may result in changes of the pathway of certain reactions [5]. Therefore, in order to prevent the inhibition, optimize the VFA production, and recover VFAs as valuable commodity chemicals, VFAs should be removed from the anaerobic digestion process. In a conventional anaerobic process, acetic acid and hydrogen is removed from the system by methanogens, which enhances the overall VFA production and utilization. Therefore, in order to maximize the VFA production without the production of methane, VFAs and hydrogen should be continuously separated from the system by other means [6; 7; 8].

In this review, organic acid production and separation techniques such as chemical precipitation, solvent extraction, adsorption and electrodialysis are discussed. Integrated fermentation and organic acid removal techniques are not included in this review.

Anaerobic Digestion

Anaerobic digestion (AD) is a natural process in which a variety of different species from two entirely different biological kingdoms, Bacteria and Archaea, work together to convert organic wastes through a variety of intermediates into methane gas [9]. The consortia of microorganisms involved in the overall conversion of complex organic matter to one-carbon compounds representing the most oxidized (CO_2) and most reduced (CH_4) begins with the bacteria that hydrolyze complex organic matter (carbohydrates, proteins and fats) into simple monomers, such as monosaccharides, amino acids and fatty acids [10].

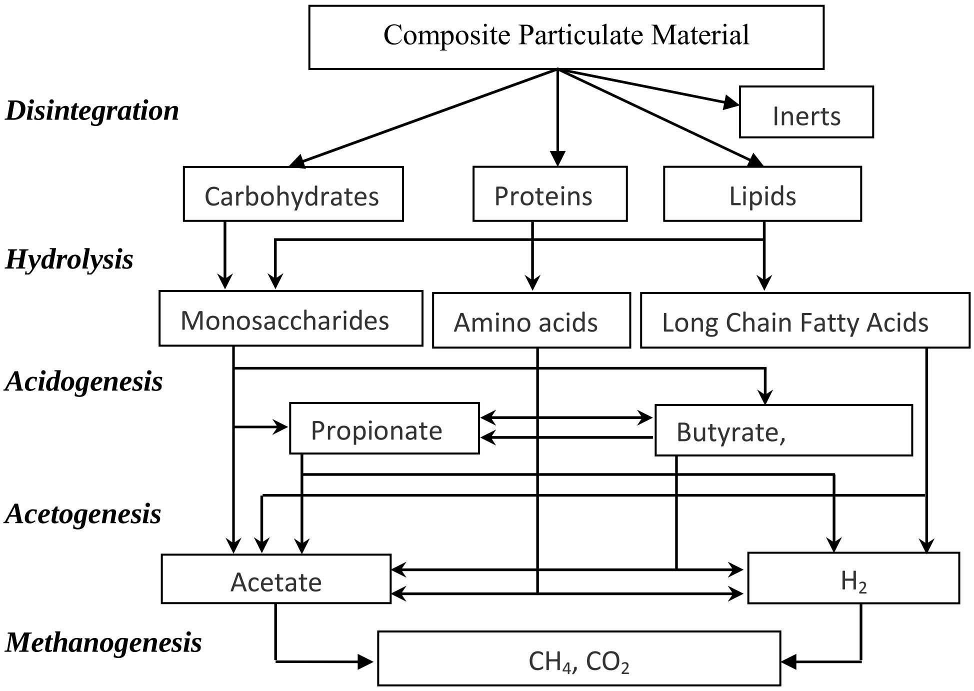

Figure 1. Carbon flow in a typical anaerobic degradation processes [2].

The monomers are then utilized by fermenting bacteria producing organic acids and molecular hydrogen as the dominant intermediate products. The organic acids are then partially oxidized by other fermenting bacteria producing additional hydrogen and acetic acid, which then are used by methanogens and converted to methane (Figure 1). The term fermentation was first used by Pasteur to define respiration in the absence of free molecular oxygen. Fermentation is a form of respiration performed by facultative anaerobes and strict anaerobes, which involves transformation of organic compounds to various organic and inorganic compounds [10]. During fermentation, a portion of the organic compound gets oxidized while the other portion is reduced. Through these oxidation-reduction reactions, fermentative bacteria obtain energy and produce various compounds with different oxidation states. Fermentation of soluble carbohydrates results in the production of ethanol, acetate, H_2 and CO_2 in the absence of methanogens [1]. The major end products of fermentation of amino acids are short-chain fatty acids, succinate, aminovalerate, and H_2 [1].

The biological production of methane is carried out by a group of strictly anaerobic Archaea, called methanogens. In natural anaerobic environments, methanogens catalyze the terminal step of organic matter degradation to CO_2 and CH_4. Methanogenesis takes place in the absence of oxygen or other electron acceptors. Methanogens are phylogenetically diverse and they have the ability to utilize few simple compounds, such as single-carbon compounds ($HCOO^-$, CO_2, CO, methanol, methylamine, methylmercaptan, etc.); and acetyl substrates (acetate) [11]. Therefore, methanogens depend on other microorganisms for the production of substrate(s).

In general, the beneficial product formation through AD has been focused on methane only. However, AD must not be seen just as a biogas production process. In addition to the production of biogas, AD process can be used to generate valuable intermediate products, such as high commercial value organic acids (acetic, butyric, propionic, etc.) or chemical solvents (ethanol, butanol, methanol, etc.) [12]. Considering low calorific value and storage difficulties of methane, production of intermediate fermentation products can be more beneficial.

Anaerobic fermentation process can be used for a wide range of waste types due to rapid expansion of new reactor designs in recent years [13]. Anaerobic fermentation of high-solids organic wastes and wastewaters yield high organic VFA production and have been achieved by a wide variety of anaerobic digester designs such as plug flow, continuously stirred tank reactor, and leach-bed reactor, anaerobic sequencing batch reactor, upflow sludge bed reactor, and anaerobic filters [14; 15]. Produced VFAs can be extracted and converted to valuable commodity products, moreover can be used as a carbon source for biological nutrient removal [16], bio-polymer production [17] or bio-electricity production using microbial fuel cells (MFCs) [18].

Organic Acid Separation

Removal of organic acids such as mono- (acetic, propionic acid etc.) and di-carboxylic acids (succinic, oxalic acid etc.) from fermentation broths is necessary to prevent inhibition, optimize organic acid production, and recover organic acids as valuable commodity chemicals. Organic acid separation from fermentation broths can be achieved by chemical precipitation, solvents extraction, adsorption and electrodialysis. In recent years, integrated fermentation and organic acid recovery/removal processes raised an interest.

Chemical Precipitation

The classical industrial method for the isolation of carboxylic acids is the precipitation with calcium hydroxide ($Ca(OH)_2$) or calcium oxide (CaO) [19; 20]. Following the addition of $Ca(OH)_2$ or CaO; (1) the precipitate is filtered off and the cake is treated with sulfuric acid leading to a preferential precipitation of $CaSO_4$ and (2) the free organic acid in the filtrate is purified via ion exchange or active carbon adsorption and evaporated to yield the crystals of the acid [21]. The calcium salts of many carboxylic acids such as fumaric, citric and lactic acids have low solubilities in water and thus chemical precipitation has been used for the separation of these carboxylic acids [3]. However, the acid crystallization step is challenging and the yields are low. In addition, short chain organic acids have similar characteristics in solution at room temperature (Table 1); therefore, it is not easy to remove target organic acid from a fermentation broth. Either in salt or free acid form; formic, acetic, and lactic acid have perfect solubility in water at pH 1-14 and temperature values above $0^{o}C$ [20]. Therefore, it is very difficult to remove low molecular weight acids via precipitation.

Table 1. Key physicochemical properties of different short-chain carboxylic acids [37].

CARBOXYLIC ACID	**PROPERTIES** *							
	M (g/mol)	pKa	COD (mg/L)	T_{bp} (°C)	γ^{o}_{100}	p^{o}_{100} (kPa)	α	T_{mp} (°C)
Formic $C_1H_2O_2$	46.0	3.75	347	100.6	0.78	99.30	0.8	8.9
Acetic $C_2H_4O_2$	60.1	4.75	1070	117.9	1.23	56.74	0.7	16.7
Propionic $C_3H_6O_2$	74.1	4.87	1510	141.2	5.60	24.32	1.3	-20.7
Butyric $C_4H_8O_2$	88.1	4.81	1820	163.3	24.0	9.12	2.3	-5.2
Valeric $C_5H_{10}O_2$	102.2	4.82	2040	185.8	70.3	2.63	2.5	-34.0
Caproic $C_6H_{12}O_2$	116.2	4.88	2200	205.7	204	1.42	2.9	-3.0

*: M, Molar mass; pKa, Acid dissociation constant; COD, Chemical oxygen demand; T_{bp}, Boiling point; γ^{o}_{100}, Activity coefficient at infinite dilution at 100°C; $p^{o}_{100,}$ Vapor pressure at 100°C; α, Relative volatility; T_{mp}, Melting point

Recently, recovery of di-carboxylic acids such as succinic acid from fermentation broths has gained an increased attention. Li et al. (2010), studied succinic acid removal through direct crystallization and modified calcium precipitation methods (Figure 2). In both methods, the fermentation broth was centrifuged and was mixed with activated carbon (%20 w/v) to remove color and protein impurities, then suspension was filtered and treated either with method I or II (Figure 2). [20]. Succinic acids solubility is strongly dependant on the pH and temperature of the solution and therefore, direct crystallization is achieved by decreasing pH and temperature [20]. Li et al.(2010), achieved 70% succinic acid recovery yield and 90 % purity via direct purification method whereas the yield was 52% (92% purity) when the modified calcium precipitation method was used. Acetic and propionic acids in a fermentation broth can also be precipitated as calcium magnesium acetate (CMA) or calcium magnesium propionate (CMP), which can be used as a road de-icer, as an alternative to sodium chloride [22; 23]. CMA and CMP can be produced within the fermenter without affecting the VFA production [22]. The product CMA and CMP in the clear liquid can be recovered by evaporation [22].

Solvent Extraction

Solvent extraction can be achieved using three extractants; (1) carbon-bonded oxygen-bearing (hydrocarbon) extractants, (2) phosphorus-bonded oxygen-bearing (organophosphorus) extractants, and (3) high-molecular weight aliphatic amines [21]. The main difference between oxygen-bearing (carbon, phosphorus) and nitrogen-bearing extractants in the extraction of carboxylic acids is the behavior of the acid proton during the transfer from an aqueous to an organic solution [24]. In oxygen-bearing extraction systems, extractability is measured through the acid strength in the aqueous solution and the hydrogen bond strength in the organic solution [24]. Acid extracted via nitrogen-bearing amine extractants loses its acid properties and becomes an ammonium salt, therefore the extractability is measured as the extent of ion pair association between alkyl ammonium cation and acid radical [24].

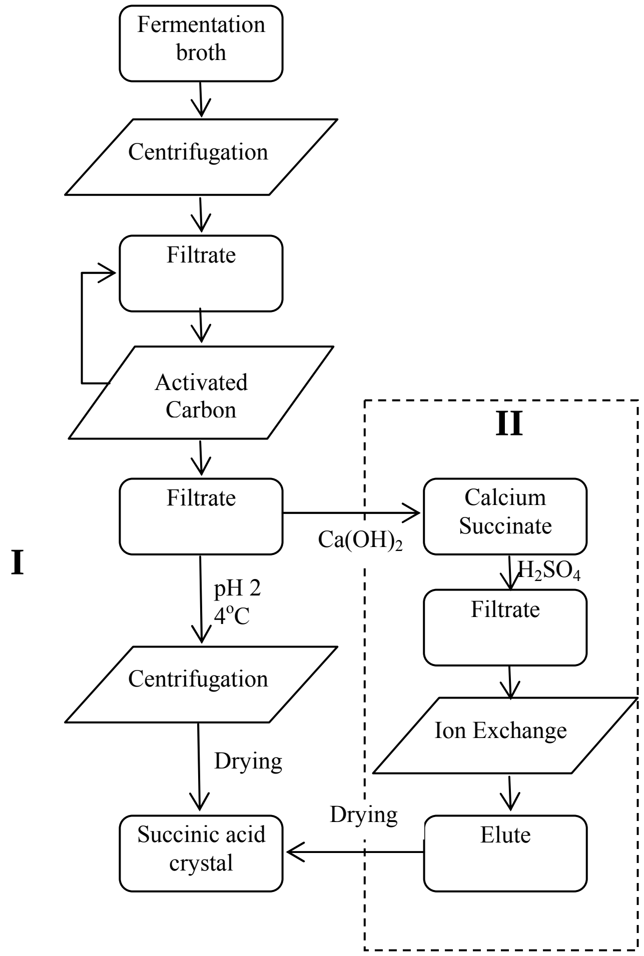

Figure 2. Diagram of succinic acid recovery processes, (I) direct crystallization and (II) modified calcium precipitation [20].

Carbon-bonded oxygen-donor extractants are more soluble in water compared to that of other groups of extractants [25]. Carbon-bonded oxygen-donor extractants are not used for the carboxylic acid extraction due to their low efficiency compared to other two extractant categories [24], therefore, further discussion will not be included in this review.

Phosphorus-bonded oxygen donor extractants have a stronger Lewis base group than carbon-bonded oxygen-donor extractants [24]. In addition, organophosphorus extractants are more water immiscible and extractable than carbon-bonded oxygen donor extractants [24]. Therefore, weak organic acids are extracted by organophosphorus extractants more effectively than carbon-bonded oxygen donor extractants under similar conditions [21; 24; 25]. Most commonly used organophosphorus compounds for carboxylic acid extraction are trioctylphosphine oxide (TOPO), tributylphosphate (TBP), and di-2-ethylhexylphosphoric acid (DEHPA) [21; 26; 27]. Among these extractants, TOPO seems to be the most effective one especially for the extraction of acetic acid [21]. The extraction process involves the centrifugation of the fermentation broth, mixing different ratios of TOPO:kerosene with the supernatant, and extraction of the carboxylic acid. The optimum condition found for the extraction of carboxylic acids are 20% (w/w) TOPO:kerosene mixture at pH 2.5, which enables 80 % total VFA recovery [26; 27]. The VFA recovery efficiency for VFAs were in the decreasing order of; valeric acid (~98%)> butyric acid (~82%) > propionic acid (~73%) > acetic acid (~62%) when TOPO:kerosene mixture of 20% (w/w) is used at pH 2.5 [26].

Extraction of proton bearing organic or inorganic compounds from aqueous media by aliphatic amines in water immiscible organic solvents has been widely applied [21; 24]. In order to extract low concentration of carboxylic acids; long chain aliphatic amines, secondary (ditridecyl amine, Amberlite LA-2 in methyl isobutyl ketone), and tertiary amines (tricaprylyl amine, Alamine 336 in di-isobutyl ketone) have been widely used due to their low solubility in water and high distribution coefficients for carboxylic acids [3; 24]. Tributyl amine (TBA) is a tertiary amine, which belongs to the class of trialkylamines and it has been used for the extraction of acetate [28]. TBA is immiscible in water, however the TBA:Acetic acid (TBA:HAc) complex is water soluble [28]. When a dilute aqueous solution of calcium acetate is mixed with TBA at neutral pH under a constant CO_2 purging, 2 mols of TBA:HAc and 1 mole of $CaCO_3$ precipitate is formed [28]. TBA:HAc complex is then extracted via chloroform or alcohols such as butanol, pentanol, hexanol, or octanol. After the extraction, esterification and distillation processes yield acetate ester [28]. Highest esterification yield of 93.6 % was obtained for acetate when hexanol with H_2SO_4 catalyst was used with TBA [28]. One of the disadvantages of amine based extractants is the need for low pH to convert acid to its undissociated form, therefore the pH needs to be adjusted before the extraction [24].

Solvent extraction processes are expensive and yields highly polluted waste [19]. In addition, fermentation broth's pH needs to be adjusted in order to achieve best extraction conditions and the solvent needs to be regenerated in order to decrease the cost.

Adsorption

Adsorption of a certain chemical from a solution is strongly affected by the polarity and the porosity of the adsorbent [29]. The effect of porosity of adsorbent depends on the dimensions of adsorbent and the adsorbate molecules. In other words, the size of the adsorbate in relation to adsorbent determines the adsorption process. Polar adsorbents will tend to strongly adsorb polar adsorbates and weakly non-polar adsorbates [29]. The carboxylic group (-COOH) gives a polar character to the low molecular carboxylic acids and the aliphatic group (R-) contributes to non-polar character thus making carboxylic acids both polar and non-polar [29].

Adsorption of VFAs has been studied with activated carbon [7; 29; 30], modified and unmodified montmorillonite clays [29], commercial adsorbents [7; 31], and anionic exchange resins [3; 7; 30; 31]. Activated carbon shows higher adsorption capacity to VFAs due to its higher surface area when compared to modified and unmodified montmorillonite clays [29]. Activated carbon is a non-polar adsorbent whereas clays are polar adsorbents, therefore as the chain number of VFAs increase polarity of adsorbate decreases and thus adsorption capacity of activated carbon increases [29]. Activated carbon shows limited adsorption capacity for smaller-sized, low molecular weight VFAs due to its large pore size [7].

Anion exchange resins are widely studied adsorbents for carboxylic acids such as acetic, lactic, and formic acids [3]. The main disadvantages of resins are their low adsorption capacity for carboxylic acids (100 mg/g resin) and the requirement of other chemicals for the acidification of the broths. In addition, presence of other ions such as SO_4^{2-} and Cl^- can reduce the adsorption efficiency due to competition for active sites in the resin [3]. Commercial anion exchange resin adsorbents such as Cellufine A-200, DIAION WA21J, DOWEX SBR has better adsorption capacity for low molecular weight fatty acids such as acetic and formic, due to their smaller pore sizes compared to that of activated carbon [7; 31]. However, in general adsorption processes are expensive, non-selective and not as efficient as the other separation processes.

Electrodialysis

Electrodialysis (ED) is an electrochemical separation process by which electrically-charged species are transported from one solution to another by using anion-cation exchange membrane and/or bipolar membrane in a direct current field. There are at least five elements complementary to an electrodialysis applications (Figure 3): (a) a direct current supply, which provides an effective means to reinforce ion transport, (b) electrodes, where oxidation/reduction reactions on the cathode and anode attain the transformation from ionic conduction to electron conduction, thus provide original driving force for ion migration, (c) ion exchange membranes such as monopolar membranes (anion and cation selective) and bipolar membranes (composition of anion and cation selective layer), (d) solvents, which make continuum for ion transport by filling the space between electrodes and membranes, (e) electrolytes, the current carriers between anode and the cathode [32].

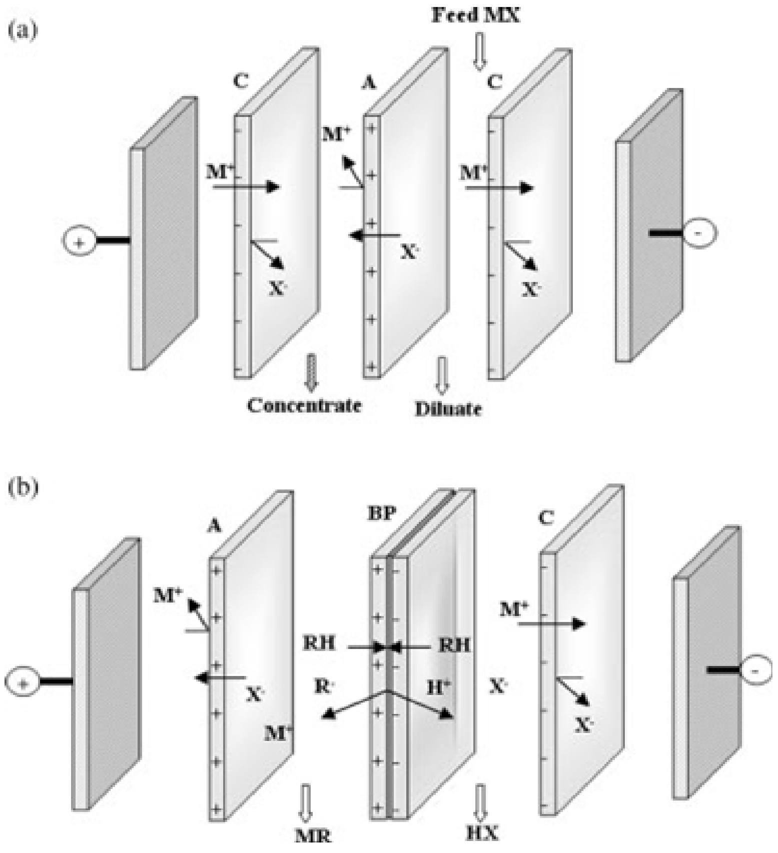

Figure 3. Schematic of Electrodialysis (a) and bipolar electrodialysis (b) units. A: Anionic membrane, C: Cationic membrane, BP: Bipolar membrane, M+: Cation, X-: Anion **[33].**

Electrodialysis process can be integrated to: (a) chemical unit operations such as ion exchange, adsorption, electrolysis, extraction, stripping; (b) pressure driven membrane processes such as microfiltration, nanofiltration, ultrafiltration, reverse osmosis; or (c) biochemical unit processes such as fermentation and membrane bioreactors [33]. Feed stream going into the ED unit is called the diluent and the product stream coming out of the ED unit is called the concentrate.

Acetate separation was achieved in synthetic acetate and calcium magnesium acetate (CMA) solutions at near neutral pH values at current densities of 87 and 174 A/m^2, respectively [34]. A bench-top electrodialysis unit with 20 cation exchange membranes (CEM) and 20 anion exchange membranes (AEM) was used (Table 2). Acetate recoveries more than 90% was achieved in all stages of the experiment (Table 2). However, the authors suggests that increasing residence time in ED units causes back diffusion of acetate from the product to feed stream [34]. Therefore, Chukwu and Cheryan (1999) suggest that more stages and higher current densities should be used to increase acetate recovery efficiency rather than increasing the residence time. Propionic acid separation from fermentation broth via bipolar electrodialysis was also achieved with more than 85% efficiency (Table 2) [35].

Generally, proton leakage, water transport from diluents to concentrate, concentration polarization due to increase of resistance as a result of depletion of ions in the diluents seems to be problems associated with electrodialysis process. Weier et al. (1992) demonstrated that it is possible to recover acetate and propionate from fermentation broths with ~75% efficiency using two-cell pair electrodialysis unit with continuous recycle (Table 2). Recovery of light carboxylic acids (C1-C6) at dilute solutions (0.2-0.4 w% total concentration) was studied in a four compartment ED unit and the recovery percentage of VFAs were higher than 84% (Table 2) [37]. Lactic acid accumulation in fermentation systems causes inhibition, its separation via electrodialysis unit from a kitchen garbage fermentation broth has been achieved with 89.5% efficiency (Table 2) [39]. Although separation of organic acids in synthetic solutions and fermentation has been achieved using electrodialytic processes; high membrane cost, membrane fouling, back diffusion, polarization are the main problems preventing wide spread use of electrodialysis processes. Therefore, more research needs to be conducted on the optimization of electrodialytic processes.

Table 2. Electrodialysis processes.

Application	Medium	Electrodialysis unit characteristics	Power Supply	Recovery	Ref.
Acetic acid separation	Synthetic solution	Bench-top monopolar ED Unit (Medimat 220, Ionics Inc.) Effective membrane area: 0.46 m^2 (20 CEM, 20 AEM) Current density: 87 A/m^2 and 174 A/m^2 Electrode Streams: 0.2 N Sodium sulfate at pH 2	TCR 80 S13, electronic measurement Inc, Neptune) 0-80V, 0-15 amps	>90%	[34]
Propionic acid separation	Fermentation broth	Bipolar ED unit Electrodes: platinum coated titanium sheets Effective membrane area: 20 cm^2 (2 BPM, 1 AEM, 1 CEM) Electrode Streams: 1 M Na_2SO_4 Current density: 500 A/m^2	Not reported	>85%	[35]
Propionic and acetic acid separation	Fermentation broth	Bench-top electrodialysis unit (Medimat 5, Ionics Inc.) Two cell pair: Alternating CEM and AEM separated by tortuous-path polyethylene spacers Electrode stream: 0.05M Na_2SO_4	Fixed-voltage power supply 11 V, 100mA-800 mA	~75%	[36]
Light carboxylic acid (C1-C6) separation	Synthetic solution	In-house designed electrodialysis unit Electrodes: ruthenium oxide activated Ti mesh as anode and stainless steel mesh as cathode Effective membrane area 100 cm^2 (2 CEM, 1 AEM) Electrode stream: 0.05M H_2SO_4	Fixed voltage power supply (Philips PE 1649), 25-55 V.	Formic, 99%; Acetic, 91%; Propionic, 88%; Isobutyric, 84%; Butyric, 89%; Valeric, 88%	[37]
Lactic acid separation	Kitchen garbage fermentation broth	Mono-polar electrodialysis unit (HIT instrument factory, T-1) 12 compartment with alternating CEM and AEM Electrodes: Titanium plated with ruthenium Electrode stream: 1 M H_2SO_4	Not reported	89.5%	[38]

Conclusions

Removal of organic acids such as mono- and dicarboxylic acids from fermentation broths is necessary to prevent inhibition, optimize organic acid production, and recover organic acids as valuable commodity chemicals. Chemical precipitation, solvents extraction, adsorption and electrodialysis processes have been used to remove organic acids/VFAs from fermentation broths. Chemical precipitation can be achieved via crystallization of organic acid using $Ca(OH)_2$, CaO, or Calcium-Magnesium salts. However, acid crystallization step for the short-chain carboxylic acids (formic, acetic and lactic acids) is challenging due to similar characteristics of these acids at room temperature. Formic, acetic, and lactic acid have perfect solubility in water at pH 1-14 and temperature values above 0^oC, therefore it is not feasible to remove these acids by chemical precipitation. Chemical precipitation method can be applied to dicarboxylic acids such as succinic acid successfully. Among three extractant groups, phosphorus-bonded and aliphatic amine extractants are the feasible ones for the carboxylic acid removal. Trioctylphosphine oxide (TOPO) is found to be the most effective phosphorus-bonded extractant especially for the acetic acid removal. Removal of low concentration carboxylic acids has been achieved by secondary and tertiary amines. However, solvent extraction process is costly and yields highly polluted waste. Adsorptive separation of organic acids via activated carbon, clay, and anionic exchange resins have been studied. However, in general adsorption processes are expensive, non-selective, and not as efficient as other separation techniques. Recovery of light carboxylic acids (C1-C6) at dilute solutions (0.2-0.4 w %) has been achieved with high efficiencies using electrodialysis. However, high membrane cost, membrane fouling, back diffusion, polarization are the main problems preventing wide spread use of electrodialysis processes. Electrodialysis processes seems to be the most promising separation technique for the removal of organic acids, however, more research needs to be conducted on the optimization of electrodialytic processes.

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