A Glimpse of the World of Volatile Fatty Acids Production and Application: A review

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ABSTRACT
Sustainable provision of chemicals and materials is undoubtedly a defining factor in guaranteeing economic, environmental, and social stability of future societies. Among the most sought-after chemical building blocks are volatile fatty acids (VFAs). VFAs such as acetic, propionic, and butyric acids have numerous industrial applications supporting from food and pharmaceuticals industries to wastewater treatment. The fact that VFAs can be produced synthetically from petrochemical derivatives and also through biological routes, for example, anaerobic digestion of organic mixed waste highlights their provision flexibility and sustainability. In this regard, this review presents a detailed overview of the applications associated with petrochemically and biologically generated VFAs, individually or in mixture, in industrial and laboratory scale, conventional and novel applications.

1 Introduction

One of the megatrend topics of nowadays, sustainable living, involves leading a life that has as little impact as possible on the environment. Sustainability, which can be divided into three categories: economic, social, and environmental/ecological, can be defined as developing and maintaining the strategies taken for the development of economic prosperity and welfare in a way that does not harm people or the planet. To ensure the sustainability of natural resources, using them efficiently and taking necessary measures are a matter of special importance for the world today. In this context, considering environmental sustainability as a goal for the 21st century, the transition from a linear economy to a circular economy including resource recovery, reuse, and recycling is essential. Considering that the volume of waste generated all around the world is expected to increase continuously in the upcoming years due to the increasing population, it is crucial to find out feasible waste management routes not only to handle but also to valorize waste. Thanks to the adaptation capabilities of bioengineering, environmentally benign and sustainable production approaches are now in hand that provide us with the ability to convert large diversity of organic residuals and waste streams to value-added resources, returning nutrient to production and application cycle in a circular manner [1]. Volatile fatty acids (VFAs) (eg acetic, propionic, and butyric acids) are among the essential chemical building blocks used extensively from food and pharmaceutical industries all the way to plastic production and wastewater treatment. Although VFAs can be generated from both processing petrochemical derivatives and bioconversion of organic matter, the sustainability in their production and application should be maintained. Therefore, in order to provide a better understanding of the role of VFAs in the material and chemical market, organic waste management, and economic and technical developments, this review paper highlights the details of VFA production and application.

There are different types of VFAs based on their different properties. VFAs (also known as low
molecular weight organic acids) include a group of aliphatic monocarboxylic acids with two to six carbon atoms (C2 to C6): acetic (C2\text{\text{HAc}}), propionic (C3\text{\text{HPr}}), iso-butyrlic (iC4\text{\text{iHBu}}), n-butyrlic (C4\text{\text{HBu}}), iso-valeric (iC5\text{\text{iHVA}}), n-valeric (C5\text{\text{HVA}}), iso-caproic (iC6\text{\text{iHCA}}), and n-caproic (C6\text{\text{HCA}}) acids. As carboxylic acids, VFAs are weak acids (pKa = 4.75) [2] that do not donate protons very well. In general, they partially dissociate into H+ cations and \text{RCOO}^- anions in neutral aqueous solvents such as water. An acid dissociation constant (Ka), which is expressed by using the logarithmic measure of the constant (Ka), is then called pKa and is more commonly used in practice. pKa is a quantitative measure of the strength of an acid in solution. The smaller the pKa value, the stronger the acid (pKa < 3). Usually during VFA production through acidogenic fermentation, VFA production decreases when pH drop below the pKa value of VFAs since most microorganisms can not survive the extremely acidic pH (< 3). Previous studies suggested that slightly acidic to neutral pH (5.5–7.0) facilitated the best VFA yield during acidogenic fermentation [3–6]. VFAs are polar molecules, which make them soluble in water and form hydrogen bonds with water. These acids tend to have a strong odor [7].

Conventionally, VFAs as a part of commercial pure chemicals are mainly synthesized from fossil-based (petroleum-based) resources through petrochemical pathways [8,9]. Although high yielding and relatively fast, production of VFAs from non-renewable petroleum-dependent sources and technologies will eventually be hindered by the overexploitation and depletion of the planet’s limited fossil resources. Furthermore, these petrochemical production pathways such as oxidation and carboxylation depend upon the chemical synthesis processes, which may involve inmoderate use of energy, labor force, and coproduction of various derivatives/by-products that are an issue of concern [10–13]. Since the application areas of both individual and mixed VFAs have increased, research works on alternative production processes have been intensified. Due to constantly rising environmental awareness and the scarcity of global petroleum sources, economically feasible new alternative production methods have emerged, e.g. anaerobic digestion (AD) of organics accompanied by VFA recovery [14]. VFAs are the main intermediates generated in the fermentative stages (acidogenesis and acetogenesis) of the AD process. Although individual VFAs can be biologically produced using single microorganism assimilation pure organic streams (different sugary and starchy material), through the AD approach, using a mixed microbial culture, the generated mixed organic residuals and wastes can be evaluated as feedstock for the sustainable production of VFA at significantly lower in price compared to pure substrates [15]. Therefore, the production and recovery of VFAs, especially from renewable biomass with mixed consortia of microbial fermentation, have attracted more and more attention, recently. Various fermentation processes have been developed for the bacterial/microbial production of VFAs starting from commercially available sugars to inexpensive raw materials or waste streams such as primary sludge, waste activated sludge, food waste, animal manure, and agricultural rejects [11,12,16,17]. In the past years, many studies have been carried out considering different types of organic waste and operating conditions to maximize VFAs production through AD [9]. Besides controlling the operating conditions, different pretreatment methods (physical, ultrasonic, thermal, chemical, and thermochemical) have been employed to enhance acidification and suppress methane production during AD [18–23]. However, it should be noted that what is obtained from AD of mixed residual streams is an effluent with a mixture ofVFAs (differing in VFA composition and content) along with released or unutilized macro and micronutrients. These effluents are quite complex both in chemical composition and fluid properties, which makes the necessary downstream processes like recovery, purification, and separation of VFAs for the individual VFA applications technically and economically difficult [24]. Aside from the applications that each individual VFA has, their mixture and the outflowing nutrients can also be marketed as presented in this review.

The aim of this article is to present an overview of different approaches for the production of VFAs, both petrochemical and biological approaches, along with the many common applications for both individual and mixed VFAs to
emphasize on their role in defining the sustainability of future societies. The range of applications presented include from conventional industrial scale utilization purposes for VFAs to novel usages proposed and applied at laboratorial research stage. In addition to the applications of the mixed VFAs solution produced from waste and residual streams, alternative applications of other constituents in the anaerobic digestion effluent have been highlighted.

2 The production and applications of the individual volatile fatty acids

The individual VFAs are produced generally through conventional thermochemical processes as well as single (pure) culture bioconversion processes. Synthetic production of VFAs has been carried out from petrochemicals derivatives and almost 90% of total market demand of VFAs is met through these petroleum-based products. The rest is met by alternative bio-based production routes, including oxidative and anaerobic fermentation. These methods are reported to have lower productivities and to be much less viable economically compared to synthetic methods [10,25]. However, the rapidly depleting fossil resources, requirement of the high amount of energy and chemicals, associated greenhouse gas emissions and carbon footprints, and generation of huge amount of waste associated with conventional process force the industry to shift focus to environmentally benign bio-based methods [26,27]. As presented in Figure 1, produced from either approaches, the great industrial appeal for VFAs is due to their diverse applications. In this section, an overview of the production approaches and applications affiliated with each of the VFAs is thoroughly reviewed.

2.1 Acetic acid

Acetic acid (CH₃COOH), also known as ethanoic acid, is the most used organic acid and one of the most commercially significant VFAs [28]. According to a new report by Expert Market Research, the global acetic acid market reached a volume of 17.28 million tons in 2019 and is projected to reach a volume of around 24.51 million tons by 2025. Acetic acid market attained a value of 8.6 billion USD in 2019 which is expected to grow at a compound annual growth rate (CAGR) of around 5.75% to reach 12 billion USD in the forecast period of 2020–2025 [E. M. 29].

The production of acetic acid from oil and natural gas use chemical catalysis of acetaldehyde, methanol, butane, or ethylene [30,31]. Regarding the biological production routes, a number of microbial strains have been investigated for the production of acetic acid, including Acetobacter, Thermoanaerobacter, Acetomicrobium, Acetothermus, and Clostridium [32–34]. The bacteria from genus Acetobacter can utilize a variety of commercial sugars such as glucose, ribose, mannose, melibiose, trehalose, arabinose, galactose, and xylose for the industrial production of acetic acid [35]. The free sugars are converted into acetate through the glycolysis pathway [36] and the optimization of the operating parameters is carried out to enhance the production of acetic acid from sugars [35]. Since the cost of these commercial sugars is quite high, researchers are looking for the novel and readily available carbon sources to make the process more economical. Ravinder et al. (2000) [37], used Clostridium lentocellum SG6 to produce 30.98 g/L of acetic acid utilizing paddy straw as the substrate while a very high amount of acetic acid (96.9 g/L) was obtained after the concentration using cheese whey as the carbon source for Acetobacter aceti fermentation [38]. The production of acetic acid has been improved by applying various fermentation strategies, for example, microaerobic fermentation, pH-controlled fed batch fermentation, and a fibrous bed bioreactor [39–41].

Acetic acid has a wide range of commercial applications in polymer industry, chemical industry, electronic industry, and the food industry [11]. For example, in food industry, it is used both as a solvent and food product preparation [42,43]. It is the main compound in vinegar, which is 5–20% acetic acid. Additionally, it can be used as a preservative, acidity regulator, and a flavor component in food and beverage industry [10]. Another major global use of acetic acid is the production of terephthalic acid (TPA) which only is followed by the primary application in the food industry. The main uses of TPA can be counted as the production of polyethylene terephthalate
(PET) packaging fibers, clothing, plastic bottles, and films. Similar to the usage volume of acetic acid in TPA production, the use of acetic acid to form acetate esters used as solvents for inks,
Propionic acid (CH\(_3\)CH\(_2\)CO\(_2\)H) is a colorless pungent organic acid and can be manufactured through both chemical and fermentation processes. The market of propionic acid generated a revenue of 1.2 billion USD in 2018 and is expected to reach 1.6 billion USD by 2026. The market is projected to grow at a CAGR of 3.5% from 2019–2026 [51].

Chemically, propionic acid is synthesized using petroleum resources with a yearly production of 995 million USD [52]. The synthesis is carried out by the hydroxyacarbonylation of ethylene catalyzed by rhodium or nickel carbonyl [30]. The eco-friendly biosynthesis of propionic acid is carried out mainly utilizing the bacteria from genus Propionibacterium. Several strains such as P. acidipropionici, P. freudenreichii, P. shermanii, and P. thoenii were used to produce propionate from hexoses and pentoses [53]. Glycerol, which is cheap and widely available, was found to be a good carbon source for propionic acid production compared to commercial sugars. Propionic acid being of much higher commercial value than glycerol, using later as a precursor is economically favorable process. Glycerol was consumed by mutant strain of P. acidipropionici (ACK-Tet) as carbon source with high acid productivity at 0.71 g/g compared to that of glucose (0.35 g/g) [52]. A high yield of 68.5 g/L was obtained on Jerusalem artichoke hydrolyzate in immobilized cell fibrous fed bioreactor using the same strain [54], while only 8.2 g/L propionate was obtained in batch fermentation using sugarcane molasses [53]. Beside sugarcane molasses, cheese whey, and hemicellulose hydrolyzed corn meals were also used as cheap carbon sources for propionate production with relatively good yields [55,56]. Much like butyric acid, propionic acid fermentation is also sensitive to end product inhibition even at the low concentration of 10 g/L. Genetic engineering has been explored to prepare more propionate tolerant strain of P. acidipropionici resulting in improved production of propionic acid (by 25%) compared to the wild strain [57].

The applications of propionic acid range from being directly used as building block chemicals for several industries, preservative in food industry, animal feed [58–65], and grain preservation [66,67], as flavors, esters, and herbicides [68], in plastics and petrochemicals manufacturing to pharmaceutical industry [69,70].

### 2.3 Butyric acid

Butyric acid (CH\(_3\)CH\(_2\)CH\(_2\)CO\(_2\)H) is a oily-colorless carboxylic acid that exhibits an unpleasant smell, has a pungent taste, and is usually found in the milk of farm animals. The derivatives of butyric acid are also called butanoic acid. The global butyric acid derivative market is estimated to grow at CAGR of above 6.8% over the forecast time frame 2019–2026 and reach a market value of around 170 million USD by 2026 [71].

The industrial scale production of butyric acid is carried out via chemical synthesis. It involves butyaldehyde oxidation which is obtained from propylene (derived from crude oil) by a process called oxo-synthesis [72]. Chemical synthesis using propylene as a precursor remains a preferred
method for its low production cost and easier availability of propylene compared to other chemicals.

\[
\begin{align*}
\text{H}_2^\circ + \text{CO} + \text{CH}_3\text{CH} &= \text{H}_2^\circ \\
\rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{CHO} &\rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{H}
\end{align*}
\]

This is a preferred production approach because of the lower production cost and availability of propylene as the precursor. Butyric acid, known to be found naturally in milk, contains 3 to 5 mmol in 100 g milk, while up to 30 mmol in 100 g cheese [73]. Butyric acid can also be extracted from butter where its concentration ranges from 2–4%, however, the process is not as cost effective as the chemical approach [74]. Although currently expensive, the biological production of butyric acid is carried out through fermentation, which is preferred for being eco-friendly with lower carbon footprints [25]. Butyric acid has been produced using a number of different microorganisms, eg Butyrivibrio, Butyribacterium, Clostridium, Eubacterium, Fusobacterium, Megasphaera, and Sarcina [36]. Of these, industrial scale production of butyric acid has been carried out by the different strains of bacteria Clostridium because of their high productivities and capability of using different carbon sources like hexoses and pentoses. The most productive strains are C. butyricum [75,76], C. tyrobutyricum [77,78], and C. thermobutyricum [79]. C. tyrobutyricum can tolerate the high concentration of butyric acid that alleviates the end product inhibition which is a common problem with butyric acid production [74]. However, it can only ferment specific carbohydrates such as glucose, xylose, fructose, lactate, etc., while C. butyricum can utilize a wider variety of additional carbon sources like molasses, lignocelluloses, glycerol, cheese whey permeate, etc. [75]. A very high concentration of butyric acid, ie 60.4 g/L was achieved from Jerusalem artichoke hydrolyzate using C. tyrobutyricum ZJU 8235 via fed batch fermentation (immobilized cells) [80]. Comparable yield of butyric acid was obtained using C. tyrobutyricum CIP 1–776 from glucose in the same fermentation mode while batch mode of fermentation experienced yield reduction (45 g/L) [81]. C. butyricum S-21 produced 18.6 g/L of butyric acid using lactose in batch mode [82] while 10 g/L using sucrose in extractive batch [83]. The results show higher production of butyrate in fed batch mode. The production was also affected by the addition of acetate in continuous mode [84], by the nutrient medium including nitrogen source and trace elements especially iron and phosphate [25].

The butyric acid and its derivatives have numerous applications in food, pharmaceutical, perfume, and polymer industry. Butyric acid is also used as a precursor of biofuel like ethyl and butyl butyrate [11,36]. The butyric acid derivatives are the salt and esters of butyric acid. These salts include potassium butyrate, calcium butyrate, and magnesium butyrate with the main segment as sodium butyrate. Of these, sodium and calcium butyrate are substantially in high demand and predominantly used in animal feed products. The controlled release of butyrate in animal colon is achieved by offering butyric acid derivative to animal in micro-encapsulated form. Butyric acid salts are mainly used to boost animal colon and gastrointestinal health and increase the overall meat yield from the animal [85–93]. Other butyric acid esters like methyl, ethyl, and amyl butyrate are usually aromatic and therefore applied as the flavoring and fragrance agents in food, cosmetic, and beverage industries [94,95]. In the polymer industry, butyric acid is used for the synthesis of cellulose acetate butyrate (CAB) which is a butyryl polymer with many attractive properties [96]. Low-molecular-weight esters of butyric acids, such as methyl butyrate, have mostly pleasant aromas or tastes [97], while in the healthcare industry, butyric acid is used as a component of anticancer prodrug [98].

### 2.4 Iso-butyric acid

Iso-butyric acid, also known as dimethyl acetic acid, has a special smell. Iso-butyric acid is similar to butyric acid, mainly used to produce the corresponding esters, as raw materials for the synthesis of flavors. The global market for iso-butyric acid is expected to grow at a healthy CAGR during the forecast period of 2018–2023 and the key players are Eastman Chemical Company (US), OXEA GmbH (Germany), Beijing Huamaoyuan Fragrance Flavor Co., Ltd., Inc. (China), etc. [99]. Iso-butyrate is one important aliphatic ester used as a modifier or fixative in flavor industry, which is used as
reminiscent of apple, banana, and pineapple flavor. It is occasionally used as a fruity modifier in lipstick perfumes, in flavor compositions for imitation of apple, apricot, banana, butter, cherry, ginger, etc. 100, used iso-butyric acid with n-butanol to synthesis of butyl iso-butrylate by esterification. Novozym SP 435 was found to be the most efficient catalyst offering a conversion of 56% at 30°C in 6 h and proved to be a more popular method because of its higher efficiency, lower costs, and higher purity product than the traditional chemical synthesis and extraction methods [100]. There are also reports showing that iso-butyric acid can be isomerized to butyrate by syntrophic acid oxidizing bacterium Syntrophothermus lipocalidus [101]. This means that iso-butyric acid can be applied as carbon source for pure culture of oxidizing bacterium Syntrophothermus lipocalidus for bioenhancement. Iso-butyric acid (0.2 M) was reported to be used for the synthesis of isobutyl isobutyrate with a yield of 195 mM through direct esterification with isobutyl alcohol [102]. Iso-butyric acid and isomyl alcohol were used to synthesize isoamyl iso-butyrate in n-hexane, achieving the maximum ester yield of 2.2 M applying the following condition: enzyme/substrate ratio, 19.6 g/mol; substrate concentration, 2.5 M; reaction time, 18 h; and temperature, 26.5°C [103]. Isoamyl isobutyrate is valuable and highly-demanded flavor compound of commercial importance and widely used in the food, beverage, cosmetic and pharmaceutical industries. It is a natural flavor ester extracted from plant sources. It was also observed that fatty acid esters, synthesized by enzymes such as lipase, often have better odor and flavor characteristics compared to similar esters produced by conventional means that are often in short supply or expensive. However, it should be considered that flavor quality and quantity vary from region to region.

2.5 Valeric acid

Valeric acid, or pentanoic acid, is a straight-chain alkyl carboxylic acid with the chemical formula CH₃(CH₂)₃COOH. The global valeric acid market achieved a value of USD 15.06 billion in 2020 driven by the continuously growing demand from the food and beverage and cosmetic industry. Supported by the ongoing research activities, the cosmetics market is expected to grow at a CAGR of 5.3% in the forecast period of 2021–2026. Dow Chemical Company, Otto Chemie Pvt. Ltd. and Perstorp group are some of the key industry players [E. M. 104]. Valeric acid is mainly used as a chemical intermediate to manufacture flavors and perfumes, synthetic lubricants, agricultural chemicals, and pharmaceuticals. It is also used as a flavoring aid in foods. Valeric acid is considered safe as a food additive by the World Health Organization. Valeric acid is considered to be a rather suitable model for a qualitative and quantitative examination of adsorption properties of porous sorbents, because, on one hand, the solubility of valeric acid in water is sufficiently high and, on the other hand, it adsorbs readily on hydrophobic surfaces owing to its C4-aliphatic chain. Besides, valeric acid does not form micelles even in rather concentrated aqueous solutions. Polyhydroxalkanoates (PHA) can be formed by 3-hydroxybutyrate (HB), 3-hydroxyvalerate (HV), 3-hydroxyhexanoate (HH), and 4-hydroxybutyrate (4HB) monomers [105]. As reported odd-numbered VFAs (propionic and valeric acids) promote the synthesis of hydroxy valerate (HV) [106]. Beyond cosmetics, some of the applications of valeric acid are in the production of the following:

- Synthetic valerate: Valeric acid can undergo esterification reaction with alcohols to form valerate, which is often used in food flavors and daily flavors.
- Synthesis of 1,2-pentanediol: 1,2-pentanediol is a key intermediate in the preparation of the fungicide propiconazole. It is also an important application in the pharmaceutical, surfactant, polyester fiber, and other industries. It is a very versatile organic chemical raw material and intermediate.
- Preparation of valeric anhydride: Valeric anhydride is an intermediate in chemical synthesis, pharmaceutical raw materials and biopharmaceuticals.
- Preparation of lubricating oil: Using technical-grade pentaerythritol and monobasic mixed carboxylic acid and dicarboxylic acid as raw materials, through esterification reaction, synthetic base oil can be prepared with high viscosity index, viscosity, and low pour point.
2.6 Iso-valeric acid

Iso-valeric acid is a C5, short-branched-chain saturated fatty acid exuding a strong pungent cheesy or sweaty smell. When it is highly diluted, iso-valeric acid has a sweet fruity aroma and a lingonberry-like aroma. It has a role as a plant metabolite and mammalian metabolite. Iso-valeric acid is seen as the primary cause of the flavors added to wine. Small amounts of iso-valeric acid in wine adds a smoky, spicy, or medicinal smell [107], but an excess of iso-valeric acid in wine is generally seen as a defect, as it can smell sweaty, leathery, or like a barnyard [108]. Iso-valeric acid is a clear colorless liquid that is a natural volatile fatty acid found in a wide variety of plants and essential oils, which is an important raw material for the production of fragrance iso-valerate [109,110]. Iso-valeric acid is used not only in cheese, baked foods, meat products, and cream/fruit flavors but also in the preparation of medicines, spices, condiments, etc. As early as 1997, iso-valeric acid was used to synthesize β-hydroxyisovaleric acid, which is a 3-hydroxy monocarboxylic acid that can be used as indicator of biotin deficiency [111]. In addition, iso-valeric acid is used to produce bromo isovaleryl urea, which is a sedative and hypnotic [112,113]. In addition, iso-valeric acid can also be used as a pharmaceutical synthesis intermediate [114], such as for the synthesis of bromisovaler and the preparation of meso diisopropyl succinic acid [115]. Other studies have shown that adding 6 g/d of iso-valeric acid can promote the growth performance, growth axis hormone receptor mRNA, and serum indicators of calves before weaning [116]. It is worth noting that iso-valeric acid is found to be associated with isovaleric acidemia, which is an inborn error of metabolism [117]. Therefore, the applied dosage and concentration of iso-valeric need to be strictly controlled.

2.7 Caproic acid

Caproic acid, also known as hexanoic acid, is the carboxylic acid derived from hexane with the chemical formula CH₃(CH₂)₄COOH. It is a colorless oily liquid with a pungent smell, found in oils and animal fats [118]. Conventionally, caproic acid is produced from food materials though recently it has been produced by carrying out the fermentation by the reverse β-oxidation of lactic acid. This lactic acid was generated from low value lignocellulosic biomass [119].

Application examples of this organic acid are as follows: plasticizers [120,121], antimicrobials [122,123], flavor additive [124,125], and additive in animal feed [126]. It was predicted that the global market of caproic acid will reach 1.25 billion USD in 2020. The primary use of caproic acid is in manufacturing of its esters for artificial flavors, and in manufacturing of hexyl derivatives, such as hexylphenols [127,128]. In addition, caproic acid is widely used for parenteral nutrition in individuals requiring supplemental nutrition and is being more widely used in foods, drugs, and cosmetics (nontoxic) [123,124,126]. It is safe for human dietary consumption up to levels of 1 g/kg. Caproic acid is found to be associated with medium chain acyl-CoA dehydrogenase deficiency, which is an inborn error of metabolism. As a volatile fatty acid, caproic acid has been identified as a fecal biomarker of Clostridium difficile infection [122]. Furthermore, caproic acid was reported to be applied to prevent the aerobic deterioration of silages prepared from Italian ryegrass or cocksfoot (dry matter 16.3–34.5%) after opening, with dose of 50 mmol/kg grass at ensiling or 10 mmol at ensiling and 10 mmol at opening in that order [129]. In recent years, there are a few researches showed that caproic acid is possible precursor applied in production of biofuels and used as fuel precursors [130]. The global caproic acid market is projected to reach $252.8 million by 2027 growing at a CAGR of 5.6% over the analysis period 2020–2027 [131].

3 The production and applications of mixed VFA solutions

The three most common mixed VFAs produced from anaerobic digestion of waste streams are acetic, propionic, and butyric acids. The individual VFA production through thermochemical and pure culture processes leads to higher productivity with minimum generation of side products, though the process is expensive because of the high cost of raw materials and requirement for
sterile operating conditions [36,132]. VFAs are also produced as a valuable intermediate products of anaerobic digestion of organic-rich waste streams for, eg municipal, agricultural, and industrial residues using a consortium of microorganisms [10]. Contrary to the pure culture processes, the mixed culture fermentation is cost effective as it has no requirement for individual pure microbial strains and can be carried out in a non-sterile environment with more flexibility in operating parameters. The process is also flexible to consume a variety of organic substrates and hence can be fed with different waste streams as mentioned above without a dependency on edible carbon resources [133,134]. Anaerobic digestion in large scale from a wide range of organic residues and waste streams is a well established process that has ubiquitously applied [135–138]. The whole process is eco-friendly and sustainable as it offers better organic waste management by decreasing the amount of waste and further valorizing it into a variety of value-added end products supporting a circular economy. The process of anaerobic digestion for the production of mixed VFA has been explored in past and is well documented in the previous studies [6,132,139–143] and therefore this section will focus mainly on the applications of the mixed VFA. The overview of the process is well represented in Figure 2.

As presented in Figure 2, mixed VFAs solutions produced by mixed culture fermentation have multiple novel applications like the production of bioplastics (PHA), biofuels, eg hydrogen and bio-butanol, microbial oil, methane, etc. and as an important carbon source in biological nutrient removal (BNR) processes which are discussed in detail in the following sections.

### 3.1 Polyhydroxyalkanoates (PHA)

Polyhydroxyalkanoates are completely biodegradable polymers that can be biologically synthesized using renewable resources [9] like waste derived low cost VFA. These environmentally benign plastics have long been considered as the best alternative for traditional petrochemical derived plastic as they possess similar characteristics [144]. PHAs are intracellular granules that are synthesized by bacteria for energy storage and are thermoplastic esters of 3-, 4-, 5-, and 6-hydroxyalkanoic acids [145]. Despite of having a broad range of applications in various industries as well as their

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**Figure 2.** An overview of mixed VFA production from organic waste, adapted from [132].
mechanical, structural, and thermal properties, PHA production costs are 5–10 times higher than conventionally produced plastics [146], leaving their commercialization limited to only high-end applications. The industrial production of PHAs is usually carried out using pure microbial culture. The PHA content obtained in this process is quite high but the requirement of sterilization, need of refined sugar substrate, and downstream processing increase the production cost [147]. Fifty percent of the overall production cost is imparted by the cost of carbon source [148], therefore, waste derived VFAs are promising economically feasible option for this purpose. Previous studies suggest that PHA can be produced by more than 90 genera of gram-positive and gram-negative bacteria both under aerobic and anaerobic conditions using several carbon sources, out of which VFAs are favored as they are the direct metabolic precursors of PHAs [149,150]. In recent years the mixed microbial cultures (MMCs) have been used to reduce the production cost of PHAs. A number of microorganisms such as Alcaligenes eutrophus, Bacillus megaterium, Pseudomonas oleovorans, Azotobacter beijerincki, Rhizobium, and Nocardia can consume VFAs as carbon sources to produce PHAs [151]. Additionally, producing PHA by MMCs have no sterility demands making it way more cost-effective than pure microbial culture, reducing the production cost by more than 50% [152].

Here, PHAs are produced by a three-step process in which the first step is the acidogenic fermentation that transforms the organic waste in to VFAs followed by the selection of PHA accumulating cultures and finally PHA is accumulated in batch conditions [153–156]. The operating efficiency and complexity of the final step affect greatly on the MMCs PHA production applications [157]. The operational conditions of the cultivation reactor can be optimized to increase the PHA content obtained from mixed culture [158,159] like by feeding the appropriate VFA type [160,161].

The VFAs produced by the acidogenic fermentation are more suitable for the synthesis of PHA than the pure acid mixtures where the ratio of even numbered to odd numbered VFA can be controlled [162]. The monomers 3-hydroxybutyrate (HB), 3-hydroxyvalerate (HV), 3-hydroxyhexanoate (HH), and 4-hydroxybutyrate (4HB) can be used to synthesize the PHA [105]. The production of hydroxybutyrate (HB) is facilitated by even numbered VFA (acetic and butyric acids), while the synthesis of hydroxyvalerate (HV) is promoted by odd-numbered VFA (propionic and valeric acids) [106]. As per reports, the uptake of acetate and propionate in their mixtures is related directly to the ratio of HB and HV [105] and this is why the composition of VFAs needs to be regulated in acidification process so that the PHA with desired performance can be obtained [162].

A number of studies have investigated the PHA production and wastewater treatment at the same time. Primary sludge (PS) and waste activated sludge (WAS) can be utilized as carbon source for PHA production [163–165] via acidogenic fermentation during anaerobic fermentation. The PHA content of 51% was obtained from WAS with a productivity rate of 2.19 g/L h) [166]. Additionally the mixed bacteria cultures are a cost effective way to produce PHA compared to traditional method, since the sterilization step is not needed and hence integration of PHA production and wastewater treatment may help address the problem of high cost of PHA production by traditional methods [167]. Study data from German WWTP showed that theoretically possible production of bioplastics in Germany amounts to more than 19% of 2016 worldwide biopolymer production [167].

### 3.2 Biofuel

The rising concern about the depleting fossil fuels along with the environmental concerns associated with their excessive application is pushing the society to seek sustainable alternatives. Recently, biofuels have become the best alternative to address the current energy crisis as clean and high energy fuel replacements. An inexpensive raw material to meet the demands for biofuels are waste derived VFAs which can be successfully utilized to produce a variety of fuels like biobutanol, microbial oils/biodiesel, hydrogen, and biogas [9].
3.2.1 Microbial oil production

Microbial oils have gathered a lot of attention in recent years as they are interesting precursors for oleochemical industry and can be an eco-friendly alternative to the nonrenewable fossil oils as their cultivation period is shorter and have higher biomass and lipid productivities [168]. A bottleneck for the production of microbial oil is the high cost of the substrate, ie sugar based feedstock, which adds up hugely (up to 60%) in the overall production cost [169] as well as the high contamination risk [170]. A solution is to use cheaper renewable substrates as the carbon source for microbial oil production.

VFAs produced via anaerobic digestion (AD) of various wastes like food waste [171], municipal solid waste (MSW) [172], waste activated sludge (WAS) [162], etc. can offer an inexpensive choice for microbial lipid synthesis by oleaginous microorganisms (Figure 3) [173]. Moreover, the fatty acid composition of lipids synthesized from VFAs is similar to that of Jatropha and soybean oil which makes it suitable for the production of biodiesel [169]. Added advantage is their higher theoretical conversion efficiencies as well as shorter metabolic pathways for lipid synthesis compared to sugar based substrates [174].

The oleaginous microorganisms can synthesize and accumulate lipid more than 20% (w/w) dry weight and hence are considered suitable for microbial oil production [175]. The cultural conditions like pH, temperature, carbon-to-nitrogen ratio/N, fermentation period, etc. can be optimized to improve the lipid composition and accumulation [176]. Both the cost of carbon source and microorganism’s performance affect the economic feasibility of microbial oil production. Some well-known oleaginous strains that can synthesize lipids by utilizing the VFA are *Yarrowia lipolytica*, *Cryptococcus curvatus*, and *Cryptococcus albidus* [177]. According to the literature, the high content of VFAs (>10 g/L) inhibits the growth of oleaginous yeasts and impedes the high lipid yields [178]. Although slightly acidic conditions (pH 5.6–7) were adopted for best lipid production from strains with low concentration of VFA (<10 g/L) [169], alkaline conditions can ease the inhibition of high VFAs content. On the other hand, high acetic acid concentrations (70 g/L) and alkaline conditions (pH 8) were shown to favor the cell growth and lipid accumulation of *Yarrowia lipolytica*, resulting in the highest biomass (37.14 g/L) and lipid production of (10.11 g/L) [179]. However, cultures with higher acetic acid content showed decreased biomass and lipid yield due to excessive anion accumulation. Of all other VFAs, the acetic acid is the most suited for lipid synthesis as its conversion pathway to produce

![Figure 3. VFA production and lipid production process integration, adapted from [170,223].](image-url)
acetyl-CoA (an important precursor in lipid biosynthesis) is relatively shorter than others, followed by Butyric and propionic acid. All in all, mixed VFAs have been reported to be more promising for lipid synthesis than individual VFAs [179].

### 3.2.2 Hydrogen

Hydrogen gas is a high value product of anaerobic fermentation which may be used in fuel cells as well as a precursor of several chemicals products [180]. Unlike fossil fuels, H₂ is not available in nature and is conventionally produced by steam reforming of natural gas, water electrolysis and auto thermal processes which are energy intensive and hence not cost effective. The hydrogen production via fermentation of renewable raw materials has benefits over conventional methods as operating conditions are milder than conventional methods making the process more economical and sustainable [181]. However, the bottlenecks of this approach are lower yields and formation rates since bacterial metabolism is slow [182,183]. Biohydrogen can be produced by carrying out both dark and light anaerobic fermentation of biomass and waste [182]. In the first step, dark fermentation is used to convert the hydrolyzed biomass into VFAs, CO₂ and H₂ using acidogenic anaerobes, therefore, H₂ yield is low [48]. More H₂ can be produced utilizing these VFAs via photo-fermentation by phototrophic bacteria (Rhodobacter sp.) [184]. In an study the Rhodobacter sphaeroides was shown to use five different carboxylic acids (malate, propionate, acetate, lactate and butyrate) of which, maximum H₂ production rate (24 mlhydrogen/Lreactor h) was obtained using malate [185].

Another method utilized is electrodialysis which is relatively simpler, faster, and yields more H₂ compared to photofermentation [181]. A low voltage DC current (1–3 V) was passed to the dark fermentation effluents of wheat powder solution containing VFAs to produce H₂ gas. Copper electrode was used because of its high electrical conductivity which facilitates the H₂ production. Highest cumulative H₂ was obtained at pH 2.0, DC voltage 3 and VFAs concentration of 5 g/L [181]. One more effective method is to use microbial electrolysis cell (MEC) also known as bio-
electrochemically assisted microbial reactor [186]. MEC generates the H₂ from organic substrate by applying an electric current. In this regard, H₂ is produced through cathodic reduction of proton released from electrochemically active bacterial (EAB) oxidation of VFAs at the anode [187]. Temperature plays a crucial role in changing the performance of MEC as it affects the activity of microorganisms. The generation of H₂ decreases at the temperature below 25°C and above 40°C, and the optimum temperature of a two chamber MEC fed with acetate was found to be about 30°C [188].

### 3.2.3 Biobutanol

Biobased butanol offers several advantages over bioethanol as a transportation fuel. Biobutanol is less corrosive and less hydrophilic than ethanol hence can be transported in existing pipelines as well as being less sensitive to temperature. Butanol has higher energy density as it contains four carbon atoms compared to two in ethanol, and those extra chemical bonds release more energy while burning [189,190]. Additionally, butanol has close resemblance with gasoline in physico-chemical properties and a low oxygen content [191], so it can blend better with gasoline compared to bioethanol [192]. Apart from being a gasoline additive, biobutanol is also used as a solvent (for paints, resin, etc.), plasticizer, and chemical intermediate for butyl esters or ethers [173].

VFAs produced through fermentative biomass acidification can be biologically reduced to bioalcohols. VFAs like acetic, propionic, and butyric acids are produced together with CO₂ and H₂ during the acidification step of anaerobic digestion [193]. Steinbusch et al. [194] showed that acetic, propionic, and butyric acid can be reduced to the ethanol, propanol, and n-butanol, respectively, by mixed anaerobic cultures with H₂ as electron donor. Of these, n-butanol was produced from butyric acid and its highest measure concentration in batch experiments was 3.66 mM with an efficiency of 47.6%. Maintaining a high hydrogen pressure was crucial to avoid the oxidation of the alcohols produced and to facilitate their production rate [195]. Though a challenge in microbial fermentation of butanol is the butanol toxicity to the same bacteria which causes the lower yield and higher recovery costs. Current research is
focussing on the better product separation, removing inhibitors and process integration to overcome butanol toxicity [190].

A two-step process was suggested by [189], to produce biobutanol from organic waste derived VFA (butyric acid) via non biological pathways. In the first step, VFAs (butyric, iso-butyric, valeric and iso-valeric) are esterified into the VFAmethyl esters (VFAMES) which in the second step gets hydrogenated into their corresponding bioalcohol. The process is less energy intensive as it is purely a chemical process without the need of growing bacteria. The final yield of 1-butanol from butyric acid was 19 wt.% which is comparable to the conventional biological process.

According to a report by Grand View Research, the global bio-butanol market is projected to reach USD 17.78 billion by 2022 [196].

### 3.2.4 Methane

VFAs are formed as important intermediate products in the anaerobic digestion where biogas, the final product rich in methane (65–70 v/v%) [Tchobanoglous, 197], can be used to generate heat and power. The three main VFAs, ie acetate, butyrate, and propionate that are formed as a result of degradation of protein, carbohydrates, and fats during acidogenesis process are said to inhibit CH\(_4\) production significantly, if accumulate in surplus [162]. Of these VFAs, acetic acid can be directly into CH\(_4\) during methanogenesis by acetoclastic methanogens [162] while butyric and propionic acid are first oxidized into acetic acid, H\(_2\), and CO\(_2\) by acetogens and then degraded into methane by methanogenic microorganisms which can only utilize acetate [198]. The interdependent process between the acetogenic bacteria and the methanogens, known as syntrophic interaction [199], is considered to be the rate limiting process step in the formation of biogas in anaerobic digestion [198]. Studies show that the partial pressure of H\(_2\) in reactor determines the conversion of butyric acid and propionic acid to acetate, H\(_2\) and CO\(_2\) with maximum conversion occurring at low partial pressure of H\(_2\) [200]. The propionate oxidation being thermodynamically unfavorable, its conversion appeared to be strongly inhibited in anaerobic digestion [201]. Acetate was found to be the least toxic of all VFAs, followed by butyrate and propionate, effects their conversion rate to CH\(_4\) (Acetate>butyrate>propionate) in batch experiments [202]. Since methanogens are most sensitive to propionate during fermentation, it has been shown to be a major cause of digestive failure [203]. [204], observed no significant inhibition of the activity of methanogenic bacteria even at the highest concentration of acetate and butyrate, ie 2400 and 1800 mg/L, respectively. However, in the presented study the concentration of bacteria decreased from \(6 \times 10^7\) to \(0.6–1 \times 10^7\) /mL as the concentration of propionate increased to 900 mg/L causing a very low CH\(_4\) yield. In the optimization analysis, the maximum accumulative CH\(_4\) yield of 1620 mL was obtained at the concentration of 1600, 1800, and 300 mg/mL for acetate, butyrate, and propionate, respectively [204]. The findings suggest that a low propionate concentration should be maintained in the VFAs solution produced during fermentation to accelerate the methanogenesis if the goal pursued is maximizing methane production.

### 3.3 As a carbon source for biological nutrient removal process

Nutrients, especially nitrogen and phosphorus in the municipal wastewater treatment plant discharge causes eutrophication in surface waters. VFAs are used as easily degradable and cost effective carbon source for biological nutrient removal processes (BNR) at wastewater treatment plants (WWTPs) and can be utilized efficiently for denitrification and bio-P Process (phosphorus removal) [205]. Through proper use of microorganisms, nitrogen and phosphorus can be removed in BNR processes. Nitrogen removal is typically carried out in two steps, ie aerobic nitrification (conversion of ammonia to nitrates and nitrites) followed by anoxic denitrification (conversion of nitrate to nitrogen gas) [9]. It has been reported that the denitrification process is enhanced with the higher amount of VFAs [206]. The process of removing phosphorus by accumulating it with biomass is referred to as enhanced biological phosphorus removal (EBPR) process which consists of consequent anaerobic and aerobic zones. The organic matter is consumed and phosphorus is released under anaerobic conditions which is
followed by the phosphorus uptake in aerobic zone [207]. It has been a common knowledge that efficiency of biological phosphorus removal is directly proportional to the number of phosphorus accumulating organisms (PAO) in the system. In an important study, Mao et al. established that local environmental conditions affect EBPR more than the specific engineered microbial communities [208].

The most favored VFA carbon sources for EBPR process were acetic and propionic acid [209], while acetic acid, propionic acid, and methanol were studied for denitrification [210,211]. VFAs are only present in small amounts in the wastewater which is insufficient for the completion of both, the nitrification and phosphate removal [212]; hence, additional VFA is needed for BNR system [162]. The requirement of C/N was shown to be in the range of 5–10 mg chemical oxygen demand (COD)/mg N for both nitrification and denitrification process [197]. As reported by Grady Jr et al. [213], the removal of 1 mg of phosphorus required an additional 7.5–10.7 mg of COD. Synthetic VFAs can be used as additional carbon source but are expensive so as an economical solution, VFAs can be produced on site through the AD of sludge at WWTPs and later be introduced to the treatment steps in the BNR process [214]. Some WWTPs use ethanol and methanol as carbon source for the denitrification process. If VFAs are added in denitrification step, they will be consumed by denitrification bacteria in place of methanol or ethanol making process more economically favorable for the plant [215–218]. VFAs with lower molecular weight were preferred by denitrifying bacteria so the order of consumption is acetate>propionate>butyrate>valerate. The preferred order could be related to the metabolic pathway in the assimilation of lower molecular weight VFA [219].

The production of enough VFAs on site to sustain the EBPR process is more cost effective than chemical flocculation process for the phosphate removal as concluded by 205. Propionic acid was shown to be more effective than other VFAs for both phosphate and nitrogen removal. Regarding phosphate removal as acetate can sometimes favor the glycogen-accumulating organisms over phosphate accumulating which may lead to the failure of EBPR, propionic acid is preferred over acetic acid [209,220]. It was shown that EBPR operates at optimum with 50:50 or 50:75 mixture of acetic and propionic acid as the removal of P [221]. 222 also found that increasing the ratio of propionic acid to acetic acid significantly increases the P removal efficiency.

4 Other constituent in the anaerobic digestion effluent and their applications

Anaerobic digestion (AD) has rapidly developed in recent years [223,224]. Besides renewable energy, AD plants also produce large amount of liquid anaerobic digestion effluents (ADEs) which may lead to oversupply of ADEs in a short time. The anaerobic effluent still has high COD and is rich in macronutrients (N, P, K, Ca, S, and Mg) and micronutrients (B, Cl, Mn, Fe, Zn, Cu, Mo, and Ni) that exclude the possibility of direct discharge to the environment. Apart from the VFAs content that has its own various application, a lot of studies have been carried out to treat ADE, for example, directly reuse in field as fertilizer [225,226]; cultivate constructed wetland plants and algae, etc. [227,228]; and nutrients recovery [229,230]. Some typical constituents of anaerobic digestion effluent, except for VFAs, are summarized in Table 1.

4.1 Filed application as fertilizer

Plants require 13 mineral nutrient elements for growth, including macronutrients (N, P, K, Ca, Mg, and S) and micronutrients (Fe, Cu, Mn, Zn, B, Mo, and Ni), which are all critical nutrients for plants to complete their life cycle. Conventionally, the anaerobic digestion effluents was subjected to mechanical solid–liquid separated and the solid part could be easily transported to markets or fields for reutilization as fertilizer, either directly or after composting [231]. Many batch experiments and reports show that anaerobic effluent can be used as a fertilizer in fields all over the world [232–234]. The liquid fraction, commonly referred to as the liquid digestate, has also been shown to be a good liquid bio-fertilizer or soil conditioner for crop production due to its high nutrient content [235]. The majority of the
phosphorus is partitioned into the solid fraction while it is estimated that liquid digestate contains 70% to 80% of the total NH$_4^+$-N [236]. The N composition in solid manure (eg poultry broiler) can be as much as five times greater than liquid manure (eg liquid dairy). When digester effluent is field applied as fertilizer, and when incorporated, microorganisms can convert the ammonia to nitrite, which is then rapidly converted to nitrate, the nitrogen form most readily taken up by plants [237]. 226 suggested that the reduction of heavy metal content (Mn, Cu, Sr, Sn, and Ba) along with some of the potential pathogenic bacteria from cow dung made the digestate seems to have more potential than cow dung as fertilizer for soil amendment. The availability of these nutrients in the digestate are known to improve the soil structure and a viable alternative for soil amendment [238]. At the same time, it contributes to the sustainability of anaerobic digestion process. However, this progress has often been limited due to the environmental impact and the consideration of the carrying capacity of nutrients to the surrounding land. Particularly in China, most of the farm lands are not owned by the biogas plant operators but are divided into many small pieces and owned by individual farmers. The land application of these liquid digested slurries is very hard to negotiate between the individual farmers. Furthermore, when compared to traditional chemical fertilizers, transportation of these liquid digestates is uneconomical due to their low fertilizer efficiency and high-water content [239]. Therefore, much of the anaerobic liquid digestate from intensive-scale anaerobic digesters can only be partially used in Chinese farm fields. Besides, the stored digestate will also have some greenhouse gas emissions into the atmosphere which would cause atmosphere pollution [240].

### 4.2 Constructed wetland plants and algae

Studies suggested that wetland plants can well grow up in certain kinds of anaerobic digestion effluent and reduced the pollutant levels. Several genera of wetland plant species such as *Scirpus*, *Typha*, *Phragmites*, *Polygonum*, *Sagittariae*, *Cyperus*, and *Thalia* are competitive and tolerant to eutrophic habitats [235,241]. *Cyperus involucratus Rottb.* and *Thalia geniculate L.* are fast-growing ornamental plants with such capacity. High growth rate and biomass production of emergent plants reflects their potentially high ability to absorb and accumulate nutrients. Therefore, they have been used worldwide in various types of constructed wetlands for treating several types of wastewater [227,242]. Reports showed that satisfactory pollutant removal performance was found in systems planted with these plants. In addition, previous studies have reported that wetland plants provide many benefits for
wastewater treatment including nutrient uptake, microbial growth support, oxygen provision for oxidation processes, and other physico-chemical processes [243,244]. investigated two tropical wetland species growing up in anaerobic digestion effluent, results showed that high removals of biological oxygen demand (BOD) (96–100%), COD (69–73%), PO₄-P (48%), NH₄⁺-N (99%), and inorganic N (64%). The pollutant level in the anaerobic digester effluent was significantly reduced. A similar result was reported as constructed wetlands lowered the concentrations of COD (89%) and turbidity (99%), but inhibition of algal biomass growth was observed due to physico-chemical characteristics of the wastewater [245]. High concentrations of certain nutrients such as ammonium (5–11 mM) can be toxic to the plants whose tolerance levels differ among species [246,247]. Many species have reduced growth rates and biomass, shortened root length, and degraded photo synthetic pigments if ammonium concentrations exceed their tolerance level.

4.3 Nutrients recovery and their applications

Nutrient recovery from digested biodegradable waste as marketable products has become an important task for anaerobic digestion plants to meet both regulatory drivers and market demands [248]. Several organic wastes such as cow manure, pig manure, abattoir waste, municipal waste and agricultural waste can serve as renewable energy sources during anaerobic digestion. A high concentration of ammonia can affect the methanogenesis process and lower the quantity of methane produced during anaerobic digestion. Many kinds of literature have reported a very high ammonia

![Diagram of Nutrient Recovery Process](image)

**Figure 4.** General treatment technology of high nitrogen digestate.
concentration in wastewater ranging from 1,700 mg/L to 14,000 mg/L [249,250], which excess the nitrogen capacity of the land. Inhibitors in AD processes include organics such as chlorophenols, halogenated aliphatics, N-substituted aromatics, or inorganics such as ammonia, sulfide and light metal ions in nature or a combination thereof [149]. Numerous technologies for removing ammonia have been developed and reported such as chemical precipitation, air stripping, ion exchange and adsorption [251,252]. The flowchart depicted in Figure 4 presents the general treatment technology for high nitrogen digestates. Struvite recovery is a mature technology, mostly involving the addition of Mg (MgO/MgCl2) to a solution containing soluble PO4-P (ortho-P) and ammonium, thereby adjusting the pH to 8.3–10 and inducing the precipitation of struvite, MgNH4PO4 · 6H2O [248]. Even though these processes have the ability to remove and recover over 80–90% of the soluble P in the wastewater or effluent flow, yet only 10–40% of the NH4+-N can be captured [253–255] and suit for specific N/P ratio. Extensive literature reported that biochar, stripping and struvite methods can be carried out for ammonium recovery with efficiencies varying between 50%-95% [122,256]. Recent literature consider ammonia stripping process coupled with absorption as an alternative method, in which free ammonia (NH3) reacts with H2SO4 /H3PO4 to form ammonia salt that can be used as a fertilizer [256].

5 Conclusions and Future Prospects

As presented in this review, regardless of the source of provision, the list of applications associated with VFAs as precursor chemicals and materials is extended. It is not beyond expectation that as the societies develop, industries grow and new markets pop up, new applications for VFAs will be defined. The boost in demands of VFAs should be met by petrochemical or biotechnological routes for VFAs (bio)synthesis. Although rather cheap, available at this time in history and main source of VFA production, fossil-resources with their finite amounts and geographical-concentration, fluctuating prices and environmental related issue are unlikely to have a role in future sustainable development of developed and developing countries. However, there is promising prospective in sight as there is a backup plan for production of VFAs that concerns environmentally benign biotechnological approaches using renewable resources for production of VFAs. Production of these bio-based VFAs from anaerobic digestion of organic-rich waste, residual and by-product streams have recently attracted great attention. Although there is a long way for bio-based VFAs to take over the main share of the VFAs market, these green VFAs not only create value from waste but also guarantees sustainable generation and provision of these precious chemical building blocks for generations to come [141].

Nomenclature

| Abbreviation | Description |
|--------------|-------------|
| AD           | Anaerobic Digestion |
| ADEs         | Anaerobic Digestion Effluents |
| BOD          | Biological Oxygen Demand |
| BNR          | Biological Nutrient Removal Processes |
| CAB          | Cellulose Acetate Butyrate |
| CAGR         | Compound Annual Growth Rate |
| COD          | Chemical Oxygen Demand |
| EAB          | Electrochemically Active Bacterial |
| EBPR         | Enhanced Biological Phosphorous Removal |
| EDTA         | Ethylenediaminetetraacetic Acid |
| HB           | HydroxybutyrateHV 3-hydroxyvalerate |
| HH           | 3-hydroxyhexanoate4 |
| HB           | 4-hydroxybutyrate |
| HAc          | Acetic AcidHButyric Acid |
| HCa          | Caprioic Acid |
| HPr          | Propionic AcidHVa Valeric Acid |
| iHBu         | Iso-butyrlic Acid |
| iHVa         | Iso-valoric Acid |
| MEC          | Microbial Electrolysis Cell |
| MMCs         | Mixed Microbial Cultures |
| MSW          | Municipal Solid Waste |
| PET          | Polyethylene Terephthalate |
| PHA          | Polyhydroxyalkanoates |
| TPA          | Terephthalic Acid |
| VFAs         | Volatile Fatty Acids |
| VFAME        | VFAmethyl Ester |
| WAS          | Waste Activated Sludge |
| WWTP         | Wastewater Treatment Plant |
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References

[1] Taherzadeh MJ. Bioengineering to tackle environmental challenges, climate changes and resource recovery. BioEngineering. 2019;10(1):698–699.
[2] Nativ P, Gräber Y, Aviezer Y, et al. A simple and accurate approach for determining the vfa concentration in anaerobic digestion liquors, relying on two titration points and an external inorganic carbon analysis. ChemEngineering. 2021;5:2.
[3] Cavinato C, Da Ros C, Pavan P, et al. Influence of temperature and hydraulic retention on the production of volatile fatty acids during anaerobic fermentation of cow manure and maize silage. Bioresour Technol. 2017;223:59–64.
[4] Gameiro T, Lopes M, Marinho R, et al. Hydrolytic-acidogenic fermentation of organic solid waste for volatile fatty acids production at different solids concentrations and alkalinity addition. Water Air Soil Pollut. 2016;227: DOI:10.1007/s11270-016-3086-6.
[5] Jiang J, Zhang Y, Li K, et al. Volatile fatty acids production from food waste: effects of pH, temperature, and organic loading rate. Bioresour Technol. 2013;143:525–530.
[6] Sukhpun P, Sittijunda S, Reungsang A. Volatile fatty acid production from organic waste with the emphasis on membrane-based recovery. Fermentation. 2021;7:3.
[7] Roberts JD, Caserio MC. Basic principles of organic chemistry (WA Benjamin, Inc.). 1977.
[8] Aydin S, Yesil H, Tugtas AE. Recovery of mixed volatile fatty acids from anaerobically fermented organic wastes by vapor permeation membrane contactors. Bioresour Technol. 2018;250:548–555.
[9] Lee WS, Chua ASM, Yeoh HK, et al. A review of the production and applications of waste-derived volatile fatty acids. Chem Eng J. 2014;235:83–99.
[10] Atasoy M, Owusu-Agyeman I, Plaza E, et al. Bio-based volatile fatty acid production and recovery from waste streams: current status and future challenges. Bioresour Technol. 2018;268:773–786.
[11] Baumann I, Westermann P. Microbial production of short chain fatty acids from lignocellulosic biomass: current processes and market. Biomed Res Int. 2016;2016:1–15.
[12] Bhatia SK, Yang Y-H. Microbial production of volatile fatty acids: current status and future perspectives. Rev Environ Sci Bio/Technol. 2017a;16:327–345.
[13] Sáenz-Galindo A, López-López LI, Fabiola N, et al. Carboxylic Acid: Key Role in Life Sciences (IntechOpen). 2018;35:1789232783. doi:10.5772/intechopen.74654.
[14] Zacharov M-P, Lovitt RB. Recovery of volatile fatty acids (VFA) from complex waste effluents using membranes. Wat Sci Technol. 2013. DOI:10.2166/wst.2013.717.
[15] Jankowska E, Duber A, Chwiałkowska J, et al. Conversion of organic waste into volatile fatty acids–The influence of process operating parameters. Chem Eng J. 2018;345:395–403.
[16] Cheah Y-K, Dosta J, Mata-Álvarez J. Enhancement of volatile fatty acids production from food waste by mature compost addition. Molecules. 2019;24:2986.
[17] Tampio EA, Blasco L, Vainio MM, et al. Volatile fatty acids (VFAs) and methane from food waste and cow slurry: comparison of biogas and VFA fermentation processes. GCB Bioenergy. 2019;11:72–84.
[18] Jomnonkhaow U, Uwineza C, Mahboubi A, et al. Membrane bioreactor-assisted volatile fatty acids production and in situ recovery from cow manure. Bioresour Technol. 2020;321:124456.
[19] Liu H, Han P, Liu H, et al. Full-scale production of VFAs from sewage sludge by anaerobic alkaline fermentation to improve biological nutrients removal in domestic wastewater. Bioresour Technol. 2018;260:105–114.
[20] Xu Q, Liu X, Fu Y, et al. Feasibility of enhancing short-chain fatty acids production from waste activated sludge after free ammonia pretreatment: role and significance of rhamnolipid. Bioresour Technol. 2018;267:141–148.
[21] Yan Y, Feng L, Zhang C, et al. Ultrasonic enhancement of waste activated sludge hydrolysis and volatile fatty acids accumulation at pH 10.0. Water Res. 2010;44:3329–3336.
[22] Yuan H, Chen Y, Zhang H, et al. Improved bioproduction of short-chain fatty acids (SCFAs) from excess sludge under alkaline conditions. Environ Sci Technol. 2006;40:2025–2029.
[23] Zhao J, Wang D, Li X, et al. Free nitrous acid serving as a pretreatment method for alkaline fermentation to enhance short-chain fatty acid production from waste activated sludge. Water Res. 2015;78:111–120.

[24] Zhou M, Yan B, Wong JWC, et al. Enhanced volatile fatty acids production from anaerobic fermentation of food waste: a mini-review focusing on acidogenic metabolic pathways. Bioresour Technol. 2018;248:68–78.

[25] Dwidar M, Park J-Y, Mitchell RJ, et al. The future of butyric acid in industry. ScientificWorldJournal. 2012;12:471417.

[26] Besselink H, Brouwer B, van der Burg B. Validation and regulatory acceptance of bio-based approaches to assure feedstock, water & product quality in a bio-based economy. Ind Crops Prod. 2017;106:138–145.

[27] Wu Q-L, Guo W-Q, Zheng H-S, et al. Enhancement of volatile fatty acid production by co-fermentation of food waste and excess sludge without pH control: the mechanism and microbial community analyses. Bioresour Technol. 2016;216:653–660.

[28] Mostafa NA. Production and recovery of volatile fatty acids from fermentation broth. Energy Convers Manag. 1999;40(14):1543–1553.

[29] Research EM (2020a). Acetic acid market report and forecast 2020-2025. https://www.expertmarketresearch.com/reports/acetic-acid-market

[30] Weissermel K, Arpe H.-J. In:editors. Industrial Organic Chemistry. 4th ed, Vol. (Weinheim: Wiley-VCH). 2003 3527305785. https://doi.org/10.1002/9783527619191.ch2.

[31] Yoneda N, Kusano S, Yasiu M, et al. Recent advances in processes and catalysts for the production of acetic acid. Appl Catal A Gen. 2001;221(1-2):253–265.

[32] Dietrich G, Weiss N, Winter J. Acetothermus paucivorans, gen. nov., sp. nov., a strictly anaerobic, thermophilic bacterium from sewage sludge, fermenting hexoses to acetate, CO2 and H2. Syst Appl Microbiol. 1998;10(2):174–179.

[33] Nayak J, Pal P. Acetic acid production and purification: critical review towards process intensification. Sep Purif Rev. 2016;46: DOI:10.1080/15422119.2016.1185017.

[34] Sim JH, Kamaruddin AH. Optimization of acetic acid production from synthesis gas by chemolithotrophic bacterium—Clostridium aceticium using statistical approach. Bioresour Technol. 2008;99 (8):2724–2735.

[35] Kadere T, Miyamoto T, Kutima PM, et al. Isolation and identification of the genera acetobacter and gluconobacter in coconut toddy (mnazi). Afr J Biotechnol. 2008;7:2963–2971.

[36] Bhatia SK, Yang Y-H. Microbial production of volatile fatty acids: current status and future perspectives. Rev Environ Sci Bio/Technol. 2017b;16(2):327–345.

[37] Ravinder T, Ramesh B, Seenayya G, et al. Fermentative production of acetic acid from various pure and natural cellulosic materials by Clostridium lentocellum SG6. World J Microbiol Biotechnol. 2000;16(6):507–512.

[38] Nayak J, Pal P. Transforming waste cheese—whey into acetic acid through a continuous membrane-integrated hybrid process. Ind Eng Chem Res. 2013;52(8):2977–2984.

[39] Li Y, He D, Niu D, et al. Acetic acid production from food wastes using yeast and acetic acid bacteria micro-aerobic fermentation. Bioprocess Biosyst Eng. 2015;38(5):863–869.

[40] Schwartz RD, Keller FA. Acetic acid production by clostridium thermoaceticum in pH-controlled batch fermentations at acidic pH. Appl Environ Microbiol. 1982;43(6):1385–1392.

[41] Talabardon M, Schwitzguébel JP, Péringer P, et al. Acetic acid production from lactose by an anaerobic thermophilic coculture immobilized in a fibrous-bed bioreactor. Biotechnol Prog. 2000;16(6):1008–1017.

[42] Sengun IY, Karabiyikli S. Importance of acetic acid bacteria in food industry. Food Control. 2011;22 (5):647–656.

[43] Zacharof M-P, Lovitt RW. Complex effluent streams as a potential source of volatile fatty acids. Waste Biomass Valorization. 2013;4(3):557–581.

[44] Gandini A. Polymers from renewable resources: a challenge for the future of macromolecular materials. Macromolecules. 2008;41(24):9491–9504.

[45] Murali N, Srinivas K, Ahiring BK. Biochemical production and separation of carboxylic acids for biorefinery applications. Fermentation. 2017;3(2):22.

[46] Chavez K, Hess D. A Novel method of etching copper oxide using acetic acid. J Electrochem Soc. 2001;148: G640–G643.

[47] Wang HH, Mou J, Ni YH, et al. Phase behavior, interaction and properties of acetic acid lignin-containing polyurethane films coupled with aminopropyltriethoxysilane. Express Polym Lett. 2013;7(5):443–455.

[48] Wang D, Duan Y, Yang Q, et al. Free ammonia enhances dark fermentative hydrogen production from waste activated sludge. Water Res. 2018;133:272–281.

[49] Maxin G, Rulquin H, Glasser F. Response of milk fat concentration and yield to nutrient supply in dairy cows [article]. Animal. 2011;5(8):1299–1310.

[50] Urrutia NL, Harvatine KJ. Acetate dose-dependently stimulates milk fat synthesis in lactating dairy cows [Article]. J Nutr. 2017;147(5):763–769.

[51] March 2020 https://www.researchandmarkets.com/reports/5031436/propionic-acid-market-by-application-and-end-user. Propionic Acid Market by Application and End-User Industry: Global Opportunity Analysis and Industry Forecast, 2019-2026 5031436 (Research And Markets).

[52] Zhang A, Yang S-T. Propionic acid production from glycerol by metabolically engineered Propionibacterium acidipropionici. Process Biochem. 2009;44(12):1346–1351.

[53] Coral J, Karp SG, Porto de Souza Vandenberghle L, et al. Batch fermentation model of propionic acid production by Propionibacterium acidipropionici in different carbon sources. Appl Biochem Biotechnol. 2008;151(2–3):333–341.
[54] Liang Z-X, Li L, Li S, et al. Enhanced propionic acid production from Jerusalem artichoke hydrolysate by immobilized Propionibacterium acidipropionici in a fibrous-bed bioreactor. Bioprocess Biosyst Eng. 2012;35(6):915–921.

[55] Gupta A, Srivastava AK. Continuous propionic acid production from cheese whey using in situ spin filter. Biotechnol Bioeng. 2001;6(1):1–5.

[56] Ramsay JA, Aly Hassan MC, Ramsay BA. Biological conversion of hemicellulose to propionic acid. Enzyme Microb Technol. 1998;22(4):292–295.

[57] Luna-Flores CH, Palfreyman RW, Krömer JO, et al. Improved production of propionic acid using genome shuffling. Biotechnol J. 2017;12(2):1600120.

[58] Hurtaud C, Rulquin H, Vérité R. Effects of level and type of energy source (volatile fatty acids or glucose) on milk yield, composition and coagulating properties in dairy cows. Reprod Nutr Dev. 1998;38(3):315–330.

[59] Lee-Rangel HA, Mendoza GD, González SS. Effect of calcium propionate and sorghum level on lamb performance [Article]. Anim Feed Sci Technol. 2012;177(3–4):237–241.

[60] Liu Q, Wang C, Guo G, et al. Effects of calcium propionate on rumen fermentation, urinary excretion of purine derivatives and feed digestibility in steers [Article]. J Agric Sci. 2009;147(2):201–209.

[61] McNamara JP, Valdez F. Adipose tissue metabolism and production responses to calcium propionate and chromium propionate [Article]. J Dairy Sci. 2005;88(7):2498–2507.

[62] Piettinen H, Huhtanen P. Effects of the ratio of ruminal propionate to butyrate on milk yield and blood metabolites in dairy cows [Article]. J Dairy Sci. 1996;79(5):851–861.

[63] Moloney AP. Growth and carcass composition in sheep offered isoenergetic rations which resulted in different concentrations of ruminal metabolites [Article]. Livestock Production Sci. 1998;56(2):157–164.

[64] Rigout S, Hurtaud C, Lenoscuet S, et al. Lactational effect of propionic acid and duodenal glucose in cows [Article]. J Dairy Sci. 2003;86(1):243–253.

[65] Sanchez PH, Tracey LN, Brown-Silva J, et al. Propionibacterium acidipropioni P1691 and gluco- genic precursors improve rumen fermentation of low-quality forage in beef cattle [Article]. J Anim Sci. 2014;92(4):1738–1746.

[66] Grinsted DA, Barefoot SF, Jensenii G. A heat-stable bacteriocin produced by Propionibacterium jensenii P126. Appl Environ Microbiol. 1992;58(1):215–220.

[67] Ramos OL, Silva SI, Soares JC, et al. Features and performance of edible films, obtained from whey protein isolate formulated with antimicrobial compounds. Food Res Int. 2012;45(1):351–361.

[68] Ali SH, Tarakmah A, Merchant SQ, et al. Synthesis of esters: development of the rate expression for the Dowex 50 WX8-400 catalyzed esterification of propionic acid with 1-propanol. Chem Eng Sci. 2007;62(12):3197–3217.

[69] Ihre H, Hult A, Söderling E. Synthesis, characterization, and 1H NMR self-diffusion studies of dendritic aliphatic polyesters based on 2,2-Bis(hydroxymethyl) propionic acid and 1,1,1-Tris(hydroxypropyl)ethane. J Am Chem Soc. 1996;118(27):6388–6395.

[70] Kim N-U, Lee Y-L. Blocking-artifact detection in frequency domain for frame-rate up-conversion. Pers Ubiquitous Comput. 2018;22(1):173–184.

[71] Consulting ARA (2019). Butyric acid derivatives market surplus US$ 170 Mn by 2026.

[72] Payne M. Propionic and butyric acids. Comprehensive Biotechnol. 1985;3:731–759.

[73] Smith JG, Yokoyama WH, German JB. Butyric acid from the diet: actions at the level of gene expression. Crit Rev Food Sci Nutr. 1998;38(4):259–297.

[74] Zigová J, Štúrđik E. Advances in biotechnological production of butyric acid. J Ind Microbiol Biotechnol. 2000;24(3):153–160.

[75] He G-Q, Kong Q, Chen Q-H, et al. Batch and fed-batch production of butyric acid by clostridium butyricum ZJUCB. J Zhejiang Univ Sci B. 2005;6(11):1076–1080.

[76] Zigova J, SturdiK E, Vandan D, et al. Butyric acid production by clostridium butyricum with integrated extraction and pertraction. Process Biochem. 1999;34(8):835–843.

[77] Jiang L, Wang J, Liang S, et al. Production of butyric acid from glucose and xylose with immobilized cells of clostridium tyrobutyricum in a fibrous-bed bioreactor. Appl Biochem Biotechnol. 2010;160(2):350–359.

[78] Mitchell RJ, Kim J-S, Jeon B-S, et al. Continuous hydrogen and butyric acid fermentation by immobilized clostridium tyrobutyricum ATCC 25755: effects of the glucose concentration and hydraulic retention time. Bioreourc Technol. 2009;100(21):5352–5355. https://www.unboundmedi cine.com/medline/citation/19545998/Continuous_hydrogen_and_butyric_acid_fermentation_by_immobilized_Clostridium_tyrobutyricum_ATCC_25755_effects_of_the_glucose концетрация и hydraulic retention time https://linkinghub.elsevier.com/retrieve/pii/S0960-85240900588-4.

[79] Canganella F, Wiegel J. Continuous cultivation of clostridium thermobutyricum in a rotary fermentor system. J Ind Microbiol Biotechnol. 2000;24(1):7–13.

[80] Huang J, Cai J, Wang J, et al. Efficient production of butyric acid from Jerusalem artichoke by immobilized clostridium tyrobutyricum in a fibrous-bed bioreactor. Bioreourc Technol. 2011;102(4):3923–3926.

[81] Fayolle F, Marchal R, Ballerini D. Effect of controlled substrate feeding on butyric acid production by Clostridium tyrobutyricum. J Ind Microbiol. 1990;6(3):179–183.

[82] Cascone R. Biobutanol--A Replacement for Bioethanol? Chem Eng Prog. 2007;104:4.

[83] Zigová J, SturdiK E, Vandan D, et al. Butyric acid production by clostridium butyricum with integrated...
[84] Michel-Savin D, Marchal R, Vandecastelee JP. Butyrate production in continuous culture of clostridium tyrobutyricum: effect of end-product inhibition. Appl Microbiol Biotechnol. 1990;33(2):127–131.

[85] Claus M, Nunn C, Fritz J, et al. Evidence for a tradeoff between retention time and chewing efficiency in large mammalian herbivores [Article]. Comp Biochem Physiol A Mol Integr Physiol. 2009;154(3):376–382.

[86] Gaebel G, Martens H, Suendermann M, et al. THE EFFECT OF DIET, INTRARUMINAL pH AND OSMOLARITY ON SODIUM, CHLORIDE AND MAGNESIUM ABSORPTION FROM THE TEMPORARILY ISOLATED AND WASHED RETICULO-RUMEN OF SHEEP [Article]. Q J Exp Physiol. 1987;72(2):501–511.

[87] Guilloteau P, Zabielski R, David JC, et al. Sodium-butyrate as a growth promoter in milk replacer formula for young calves [Article]. J Dairy Sci. 2009;92 (3):1038–1049.

[88] Le Gall M, Gallois M, Sève B, et al. Comparative effect of orally administered sodium butyrate before or after weaning on growth and several indices of gastrointestinal biology of piglets [Article]. Br J Nutr. 2009;102 (9):1285–1296.

[89] Butyric acid derivatives market - global industry analysis, size, share, growth, trends, and forecast, 2018-2026, 4851757. (Research And Markets) . April 2019. https://www.researchandmarkets.com/reports/4851757/butyric-acid-derivatives-market-global-industry.

[90] Sander EG, Warner RG, Harrison HN, et al. The stimulatory effect of sodium butyrate and sodium propionate on the development of rumen mucosa in the young calf [Article]. J Dairy Sci. 1959;42(9):1600–1605.

[91] Shen Z, Seyfert HM, Lührke B, et al. An energy-rich diet causes rumen papillae proliferation associated with more igf type 1 receptors and increased plasma igf-1 concentrations in young goats [conference paper]. J Nutr. 2004;134(1):11–17. https://www.scopus.com/inward/record.uri?eid=2-s2.0-9144238707&partnerID=40&ampid=3e50b30ef34619d10b68388a32b6b59

[92] Tamate H, McGilliard AD, Jacobson NL, et al. Effect of various dietsaries on the anatomical development of the stomach in the calf [Article]. J Dairy Sci. 1962;45 (3):408–420.

[93] Vidyarthi VK, Kurar CK. Influence of dietary butyrate on growth rate, efficiency of nutrient utilization and cost of unit gain in Murrah buffalo (Bubalus bubalis) male calves [Article]. Asian-Australas J Anim Sci. 2001;14(4):474–478.

[94] Armstrong DW, Yamazaki H. Natural flavours production: a biotechnological approach. Trends Biotechnol. 1986;4(10):264–268.

[95] Shu C, Cai J, Huang L, et al. Biocatalytic production of ethyl butyrate from butyric acid with immobilized candida rugosa lipase on cotton cloth. J Mol Catal B Enzym. 2011;72(3):139–144.

[96] Cao Y, Li H, Zhang J. Homogeneous synthesis and characterization of cellulose acetate butyrate (CAB) in 1- Allyl-3-Methylimidazolium Chloride (AminCI) ionic liquid. Ind Eng Chem Res. 2011;50(13):7808–7814.

[97] Riemenschneider W. Carboxylic acids, aliphatic. In: Ullmann’s Encyclopedia of Industrial Chemistry. (Wiley). 2000. 978352706732. https://doi.org/10.1002/14356007.a05_235

[98] Entin-Meer M, Rephaeli A, Yang X, et al. Butyric acid prodrugs are histone deacetylase inhibitors that show antineoplastic activity and radiosensitizing capacity in the treatment of malignant gliomas. Mol Cancer Ther. 2005;4(12):1952.

[99] Future MR (February 2021). Iso-butyric acid market: information by application (animal feed, chemical intermediate, food and flavors, pharmaceuticals, perfumes and others), Region — Global Forecast till 2027.

[100] Yadav GD, Lathi PS. Kinetics and mechanism of synthesis of butyl isobutyrate over immobilised lipases. Biochem Eng J. 2003;16(3):245–252.

[101] Sekiguchi Y, Kamagata Y, Nakamura K, et al. Syntrophothermus lipocalidus gen. nov., sp nov., a novel thermophilic, syntrophic, fatty-acid-oxidizing anaerobe which utilizes isobutyrate. Int J Syst Evol Microbiol. 2000;50(2):771–779.

[102] Hamsaveni DR, Prapulla SG, Divakar S. Response surface methodological approach for the synthesis of isobutyl isobutyrate. Process Biochem. 2001;36 (11):1103–1109. 10.1016/S0032-9592(01)00142-X.

[103] Krishna SH, Sattur AP, Karanth NG. Lipase-catalyzed synthesis of isoamyl isobutyrate - optimization using a central composite rotatable design. Process Biochem. 2001;37(1):9–16. http://gateway.isiknowledge.com/gateway/gateway.cgi?GWVersion=2&SrcApp=AegeanSoftware&SrcApp=NetExpress&DestLinkType=FullRecord&DestApp=WOS&KeyUT=000171359000002

[104] Global Valeric Acid Market Outlook (Expert Market Research). 2020 https://www.expertmarketresearch.com/reports/valeric-acid-market.

[105] Zhang M, Wu H, Chen H. Coupling of polyhydroxalkanoate production with volatile fatty acid from food wastes and excess sludge. Process SafEnviron Prot. 2014;92(2):171–178.

[106] Zhang W, Wei Q, Wu S, et al. Batch anaerobic co-digestion of pig manure with dewatered sewage sludge under mesophilic conditions. Appl Energy. 2014;128:175–183.

[107] Styger G, Prior B, Bauer FF. Wine flavor and aroma. J Ind Microbiol Biotechnol. 2011;38(9):1145–1159.

[108] Jackson RS. In: Wine Science: Principles and Applications. 3rd (Elsevier Inc.) ed. 2008. p. 978-0-12-373646-8. doi: https://doi.org/10.1016/B978-0-12-373646-8.X5001-X
[109] Klimavicz JS, Corona CL, Norris EJ, et al. Monoterpenoid isovalerate esters as long-lasting spatial mosquito repellents. In: Norris EJ, Coats JR, and Gross AD, et al, editors. Advances in the Biorational Control of Medical and Veterinary Pests 1289 ACS Symposium Series (American Chemical Society). 2018. p. 205–217. doi:10.1021/bk-2018-1289.ch011

[110] Larios A, Garcia HS, Ollart RM, et al. Synthesis of flavor and fragrance esters using Candida Antarctica lipase. Appl Microbiol Biotechnol. 2004;65(4):373–376.

[111] Lee IY, Nissen SL, Rosazza JP. Conversion of beta-methylbutyric acid to beta-hydroxy-beta-methylbutyric acid by galactomyces reessii. Appl Environ Microbiol. 1997;63(11):4191–4195.

[112] Carr AA, Kosley RW Jr, Van Hjifte L. (2000). Esters of (+)-α-(2,3-dimethoxyphenyl)-1-(4-fluorophenyl)ethyl-4-piperidi nemethanol (United States Patent No. U. S. patent.

[113] Houghton JL, Kuhner PA, Carr AA. Hypertensive African Americans demonstrate increased sensitivity to microcirculatory vasoconstriction induced by ACh. Am J Hypertens. 2000;13(4Part 2):240A. BIOSIS: PREV200000316811.

[114] Suerbaev KA, Gz Z, No A. Synthesis of biological active esters of the isovaleric acid by isobutylene hydroalkoxy-carbonylation. J Pet Environ Biotechnol. 2013;4:1–3.

[115] Rajendiran C, Nagarajan P, Venkateswarlau J. 2018. US: Synthesis of 5-azaacetyldine.

[116] Simon KC, Williams CC, Gentry LR, et al. Effects of meal timing on anabolic hormone status and energy metabolism in neonatal holstein calves. J Dairy Sci. 2010;931:636.

[117] Ensenaier R, Vockley J, Willard JM, et al. A common mutation is associated with a mild, potentially asymptomatic phenotype in patients with isovaleric acidemia diagnosed by newborn screening. Am J Hum Genet. 2004;75(6):1136–1142.

[118] Wasewar KL, Shende DZ. Extraction of caproic acid using tri-n-butyl phosphate in benzene and toluene at 301 K. J Chem Eng Data. 2010;55(9):4121–4125.

[119] Khor WC, Andersen S, Vervaeren H, et al. Electricity-assisted production of caproic acid from grass. Biotechnol Biofuels. 2017;10(1):180.

[120] Adeodato Vieira MG, Da Silva MA, Dos Santos LO, et al. Natural-based plasticizers and biopolymer films: a review. Eur Polym J. 2011;47(3):254–263.

[121] Rotta J, Ozorio RA, Kehrwald AM, et al. Parameters of color, transparency, water solubility, wettability and surface free energy of chitosan/hydroxypropyl methylcellulose (HPMC) films plasticized with sorbitol. Mater Sci Eng C Biomim Supramol Syst. 2009;29(S):619–623.

[122] Huang CB, Alimova Y, Myers TM, et al. Short- and medium-chain fatty acids exhibit antimicrobial activity for oral microorganisms. Arch Oral Biol. 2011;56 (7):650–654.

[123] Van Immerseel F, De Buck J, Boyen F, et al. Medium-chain fatty acids decrease colonization and invasion through hiA suppression shortly after infection of chickens with salmonella enterica serovar enteritidis. Appl Environ Microbiol. 2004;70(6):3582–3587.

[124] Serhan M, Mattar J, Debs L. Concentrated yogurt (Labneh) made of a mixture of goats’ and cows’ milk: physicochemical, microbiological and sensory analysis. Small Ruminant Res. 2016;138:46–52.

[125] Yan S, Wang S, Wei G, et al. Investigation of the main parameters during the fermentation of Chinese luzhou-flavour liquor. J Inst Brewing. 2015;121 (1):145–154.

[126] Zentek J, Buchheit-Renko S, Ferrara F, et al. Nutritional and physiological role of medium-chain triglycerides and medium-chain fatty acids in. Anim Health Res Rev. 2011;12(1):83–93. BIOSIS: PREV201100454528piglets

[127] Refat MS, El-Korashy SA, Kumar DN, et al. FTIR, magnetic, H-1 NMR spectral and thermal studies of some chelates of caproic acid: inhibitory effect on different kinds of bacteria. Spectrochim Acta A Mol Biomol Spectrosc. 2008;70(1):217–233.

[128] Saeed A, Haroon M, Muhammad F, et al. Advances in transition-metal-catalyzed synthesis of 3-substituted isocoumarins. J Organomet Chem. 2017;348–103.

[129] Ohyama Y, Hara S, Masaki S. USE OF CAPROIC ACID TO PREVENT AEROBIC DETERIORATION OF SILAGES AFTER OPENING, WITH SPECIAL REFERENCE TO AMOUNTS AND TIME OF APPLICATION. J Sci Food Agric. 1977;28(4):369–374.

[130] Urban C, Xu J, Straeuber H, et al. Production of drop-in fuels from biomass at high selectivity by combined microbial and electrochemical conversion. Energy Environ Sci. 2017;10(10):2231–2244.

[131] Caproic Acid - Global Market Trajectory & Analytics, 5302114. (Research And Markets). April 2021. https://www.researchandmarkets.com/reports/5302114/caproic-acid-global-market-trajectory-and

[132] Wainaina S, Lukitawesa L, Kumar Awasthi M, et al. Bioengineering of anaerobic digestion for volatile fatty acids, hydrogen or methane production: a critical review. Bioengineered. 2019;10(1):437–458.

[133] Kleerebezem R, van Loosdrecht MC. Mixed culture biotechnology for bioenergy production. Curr Opin Biotechnol. 2007;18(3):207–212.

[134] Lu Y, Slater FR, Mohd-Zaki Z, et al. Impact of operating history on mixed culture fermentation microbial ecology and product mixture. Water Sci Technol. 2011;64(3):760–765.

[135] Dong L, Cao G, Guo X, et al. Efficient biogas production from cattle manure in a plug flow reactor: a large scale long term study. Bioresour Technol. 2019;278:450–455.

[136] Singh AD, Upadhyay A, Shrivastava S, et al. Life-cycle assessment of sewage sludge-based large-scale biogas plant. Bioresour Technol. 2020;309:123373.
[137] Wang B-Y, Zhang N, Li Z-Y, et al. Selective separation of acetate and hexanoic acids across polymer inclusion membrane with ionic liquids as carrier. Int J Mol Sci. 2019;20(16):3915.

[138] Westerholm M, Liu T, Schnürer A. Comparative study of industrial-scale high-solid biogas production from food waste: process operation and microbiology. Bioresour Technol. 2020;304:122981.

[139] Lukitawesa PR, Millati J, Sárvari-Horváth I, R, et al. Factors influencing volatile fatty acids production from food wastewas via anaerobic digestion. Bioengineering. 2020;11(1):29–52.

[140] Magdalena JA, Greses S, González-Fernández C. Impact of organic loading rate in volatile fatty acids production and population dynamics using microalgae biomass as substrate. Sci Rep. 2019;9(1):18374.

[141] Tampio EA, Blasco L, Vainio MM, et al. Volatile fatty acids (VFAs) and methane from food waste and cow slurry: comparison of biogas and VFA fermentation processes. Glob Change Biol Bioenergy. 2019;11(1):72–84.

[142] Tezel U, Tamburak M, Pavlostathi SGA. Anaerobic Biotreatment of Municipal Sewage Sludge. Comprehensive Biotechnology. Vol. 6 (Elsevier). 2011. p. 447–461 9780080885049 doi:10.1016/B978-0-08-088504-9.00329-9.

[143] Zhang Y, Li J, Liu F, et al. Reduction of Gibbs free energy and enhancement of methanogenesis by bicarbonate to promote anaerobic syntrophic butyrate oxidation. Bioresour Technol. 2018;267:209–217.

[144] Anderson AJ, Dawes E. Occurrence, metabolism, metabolic role, and industrial uses of bacterial polyhydroxyalkanoates. Microbiol Rev. 1990;54(4):450.

[145] Arcos-Hernandez M, Montano-Herrera L, Janarthanan OM, et al. Value-added bioplastics from services of wastewater treatment. Water Pract Technol. 2015;10:546.

[146] Raza ZA, Abid S, Banat IM. Polyhydroxyalkanoates: characteristics, production, recent developments and applications. Int Biodeterior Biodegrad. 2018;126:45–56.

[147] Albuquerque MGE, Martino V, Pollet E, et al. Mixed culture polyhydroxyalkanoate (PHA) production from volatile fatty acid (VFA)-rich streams: effect of substrate composition and feeding regime on PHA productivity, composition and properties. J Biotechn. 2011;151(1):66–76.

[148] Kim BS. Production of poly(3-hydroxybutyrate) from inexpensive substrates. Enzyme Microb Technol. 2000;27(10):774–777.

[149] Anjum A, Zuber M, Zia KM, et al. Microbial production of polyhydroxyalkanoates (PHAs) and its copolymers: a review of recent advancements. Int J Biol Macromol. 2016;89:161–174.

[150] Girotto F, Alibardi L, Cosso R. Food waste generation and industrial uses: a review. Waste Manage. 2015;45:32–41.

[151] Kalia V, Raizada N, Sonakya V. Bioplastics. Journal of Scientific & Industrial Research. 2000; 59: 433–445 .

[152] Reis MA, Serafim LS, Lemos PC, et al. Production of polyhydroxyalkanoates by mixed microbial cultures. Bioprocess Biosyst Eng. 2003;25(6):377–385.

[153] Albuquerque MGE, Eiroa M, Torres C, et al. Strategies for the development of a side stream process for polyhydroxyalkanoate (PHA) production from sugar cane molasses. J Biotechnol. 2007;130:411–421.

[154] Dias JML, Lemos PC, Serafim LS, et al. Recent advances in polyhydroxyalkanoate production by mixed aerobic cultures: from the substrate to the final product. Macromol Biosci. 2006;6(11):885–906.

[155] Dionisi D, Majone M, Papa V, et al. Biodegradable polymers from organic acids by using activated sludge enriched by aerobic periodic feeding. Biotechnol Bioeng. 2004;85(6):569–579.

[156] Reis M, Albuquerque M, Villano M, et al. 6.51 - mixed culture processes for polyhydroxyalkanoate production from agro-industrial surplus/wastes as feedstocks Murray, Moo-Young. In:Comprehensive Biotechnology. US: Academic Press; 2011. p. 669–683. ISBN: 978-0-08-088504-9. https://doi.org/10.1016/B978-0-08-088504-9.00464-5.

[157] Chen Z, Huang L, Wen Q, et al. Efficient polyhydroxyalkanoate (PHA) accumulation by a new continuous feeding mode in three-stage mixed microbial culture (MMC) PHA production process. J Biotechnol. 2015;209:68–75.

[158] Chua AS, Takabatake H, Sato H, et al. Production of polyhydroxyalkanoates (PHA) by activated sludge treating municipal wastewater: effect of pH, sludge retention time (SRT), and acetate concentration in influent. Water Res. 2003;37(15):3602–3611.

[159] Jiang Y, Marang L, Tamis J, et al. Waste to resource: converting paper mill wastewater to bioplastic. Water Res. 2012;46(17):5517–5530.

[160] Jiang Y, Hebly M, Kleerebezem R, et al. Metabolic modeling of mixed substrate uptake for polyhydroxyalkanoate (PHA) production. Water Res. 2011;45 (3):1309–1321.

[161] Venkata Mohan S, Venkateswar Reddy M. Optimization of critical factors to enhance polyhydroxyalkanoates (PHA) synthesis by mixed culture using Taguchi design of experimental methodology. Bioresour Technol. 2013;128:409–416.

[162] Luo K, Pang Y, Yang Q, et al. A critical review of volatile fatty acids produced from waste activated sludge: enhanced strategies and its applications. Environ Sci Pollut Res. 2019;26(14):13984–13998.

[163] Frison N, Katsou E, Malamis S, et al. Development of a novel process integrating the treatment of sludge reject water and the production of polyhydroxyalkanoates (PHAs). Environ Sci Technol. 2015;49 (18):10877–10885.

[164] Raheem A, Sikarwar VS, He J, et al. Opportunities and challenges in sustainable treatment and resource reuse of sewage sludge: a review. Chem Eng J. 2018;337:616–641.
[165] Tyagi VK, Lo S-L. Sludge: a waste or renewable source for energy and resources recovery? Renewable Sustainable Energy Rev. 2013;25:708–728.

[166] Tian P-Y, Shang L, Ren H, et al. Biosynthesis of polyhydroxyalkanoates: current research and development. Afr J Biotechnol. 2009;8:709–714.

[167] Pittmann T, Steinmetz H. Polyhydroxyalkanoate production on waste water treatment plants: process scheme, operating conditions and potential analysis for German and European municipal waste water treatment plants. Bioengineering. 2017;4:54.

[168] Cho HU, Park JM. Biodiesel production by various oleaginous microorganisms from organic wastes. Bioresour Technol. 2018;256:502–508.

[169] Fei Q, Chang HN, Shang L, et al. The effect of volatile fatty acids as a sole carbon source on lipid accumulation by cryptococcus albidus for biodiesel production. Bioresour Technol. 2011;102(3):2695–2701.

[170] Llamas M, Magdalena JA, González-Fernández C, et al. Volatile fatty acids as novel building blocks for oil-based chemistry via oleaginous yeast fermentation. Biotechnol Bioeng. 2020;117(1):238–250.

[171] Lim S-J, Kim BJ, Jeong C-M, et al. Anaerobic organic acid production of food waste in once-a-day feeding and drawing-off bioreactor. Bioresour Technol. 2008;99(16):7866–7874.

[172] Sans C, Mata-Alvarez J, Cecchi F, et al. Volatile fatty acids production by mesophilic fermentation of mechanically-sorted urban organic wastes in a plug-flow reactor. Bioresour Technol. 1995;51(1):89–96.

[173] Jin C, Yao M, Liu H, et al. Progress in the production and application of n-butanol as a biofuel. Renew Sust Energ Rev. 2011;15(8):4080–4106.

[174] Gong Z, Zhou W, Shen H, et al. Co-fermentation of acetate and sugars facilitating microbial lipid production on acetate-rich biomass hydrolysates. Bioresour Technol. 2016;207:102–108.

[175] Madani M, Enshaeieh M, Abdoli A. Single cell oil and its application for biodiesel production. Process SafEnviron Prot. 2017;111:747–756.

[176] Beopoulos A, Cescut J, Haddouche R, et al. Yarrowia lipolytica as a model for bio-oil production. Prog Lipid Res. 2009;48(6):375–387.

[177] Chang H, Kim N-J, Kang J, et al. Biomass-derived volatile fatty acid platform for fuels and chemicals. Biotechnol Bioprocess Eng. 2010;15(1):1–10.

[178] Liu J, Huang X, Chen R, et al. Efficient bioconversion of high-content volatile fatty acids into microbially lipids by cryptococcus curvatus ATCC 20509. Bioresour Technol. 2017;239:394–401.

[179] Gao R, Li Z, Zhou X, et al. Enhanced lipid production by yarrowia lipolytica cultured with synthetic and waste-derived high-content volatile fatty acids under alkaline conditions. Biotechnol Biofuels. 2020;13:3.

[180] Singhania RR, Patel AK, Christophe G, et al. Biological upgrading of volatile fatty acids, key intermediates for the valorization of biowaste through dark anaerobic fermentation. Bioresour Technol. 2013;145:166–174.

[181] Tuna E, Kargi F, Argun H. Hydrogen gas production by electrolysis of volatile fatty acid (VFA) containing dark fermentation effluent. Int J Hydrogen Energy. 2009;34(1):262–269.

[182] Karapinar Kapdan I, Kargi F. Bio-hydrogen production from waste materials. Enzyme Microb Technol. 2006;38:569–582.

[183] Levin DB, Pitt L, Love M (2003). Biohydrogen production: prospects and limitations to practical application. Towards a greener world: hydrogen and fuel cells conference and trade show, Canada.

[184] Fedorov A, Tsyganov A, Rao K, et al. Hydrogen photo-production by Rhodobacter sphaerioides immobilised on polyurethane foam. Biotechnol Lett. 1998;20:1007–1009.

[185] Uyar B, Eroglu I, Yücel M, et al. Photofermentative hydrogen production from volatile fatty acids present in dark fermentation effluents. Int J Hydrogen Energy. 2009;34(10):4517–4523.

[186] Kadier A, Kalil MS, Mohamed A, et al. Microbial Electrolysis Cells (MECs) as Innovative Technology for Sustainable Hydrogen Production: fundamentals and Perspective Applications. Hoboken NJ: John Wiley & Sons, Inc; 2017. p. 407–457.

[187] Ahn Y, Im S, Chung J-W. Optimizing the operating temperature for microbial electrolysis cell treating sewage sludge. Int J Hydrogen Energy. 2017;42(45):27784–27791.

[188] Kyazze G, Popov A, Dinsdale R, et al. Influence of catholyte pH and temperature on hydrogen production from acetate using a two chamber concentric tubular microbial electrolysis cell. Int J Hydrogen Energy. 2010;35(15):7716–7722.

[189] Cho S-H, Kim T, Baek K, et al. The use of organic waste-derived volatile fatty acids as raw materials of C4-C5 bioalcohols. J Clean Prod. 2018;201:14–21.

[190] Ebert J. Biobutanol: the next big biofuel? Biomass Mag. 2020. http://biomassmagazine.com/articles/1605/biobutanol-the-next-big-biofuel.

[191] Wu M, Wang M, Liu J, et al. Assessment of potential life-cycle energy and greenhouse gas emission effects from using corn-based butanol as a transportation fuel. Biotechnol Prog. 2008;24(6):1204–1214.

[192] Mohd Yusoff MNA, Mohd Zulkifli NW, Masum BM, et al. Feasibility of bioethanol and biobutanol as transportation fuel in spark-ignition engine: a review. RSC Adv. 2015. DOI:10.1039/C5RA12735A

[193] Tchobanoglous G, Burton FL, Stensel HD, et al. Wastewater engineering: treatment and reuse. US: McGraw-Hill; 2003.

[194] Steinbusch KJJ, Hamelers HVM, Buismans CJN. Alcohol production through volatile fatty acids reduction with hydrogen as electron donor by mixed cultures. Water Res (Oxford). 2008;42(15):4059–4066.

[195] Smith DP, McCarty PL. Reduced product formation following perturbation of ethanol- and propionate-fed
methylene CSTRs. Biotechnol Bioeng. 1989;34 (7):885–895.

[196] Bio-butanol market size to reach $17.78 billion by 2022. (2015). Retrieved 27 Aug from https://www.grandviewresearch.com/press-release/global-bio-butanol-market

[197] Henze M. Capabilities of biological nitrogen removal processes from wastewater. Water Sci Technol. 1991;23 (4–6):669–679.

[198] Sinaga N, Mel M, Pakpahan R, et al. Influence of volatile fatty acid concentration on biogas production in synthropic anaerobic digestion. Journal of Advanced Research in Biofuel and Bioenergy. 2018;1:26–43.

[199] Fetcner-Zwirrello M (2014). Propionic Acid Degradation By Syntrophic Bacteria During Anaerobic Biowaste Digestion [Ph.D. thesis, 10.5445/KSP/100037825

[200] Samsoon PALNS, Dold P, I LRE, M. G. V R. (1988). Pelletization in upflow anaerobic sludge bed reactors. Proceedings of the 5th International Symposium on Anaerobic Digestion, Bologna, Italy.

[201] Gijzen HJ, Zwart KB, Teunissen MJ, et al. Anaerobic digestion of cellulose fraction of domestic refuse by means of rumen microorganisms. Biotechnol Bioeng. 1988;32(6):749–755.

[202] Ren N, Liu M, Wang A, et al. [Organic acids conversion in methanogenic-phase reactor of the two-phase anaerobic process]. Huan Jing Ke Xue. 2003;24(4):89–93.

[203] Stronach SM. Anaerobic Digestion Processes in Industrial Wastewater Treatment. 1st. ed. 1986. ed. Berlin, Germany: Springer Berlin Heidelberg; 1986. DOI:10.1007/978-3-642-71215-9.

[204] Wang Y. Effects of volatile fatty acid concentrations on methane yield and methanogenic bacteria. Biomass Bioenergy. 2009;33(5):848–853. 2033 no. 2005

[205] Gidstedt S (2017). Production of volatile fatty acids by hydrolysing sludge from Sjolunda WWTP [Master’s thesis, http://lup.lub.lu.se/student-papers/record/8921197

[206] Essøy A, Ødegaard H. Nitrogen removal efficiency and capacity in biofilms with biologically hydrolysed sludge as a carbon source. Water Sci Technol. 1994;30(6):63–71.

[207] Sathasivan A. Biological phosphorus removal processes for wastewater treatment Dooge, James. In: Water and wastewater treatment technologies. Oxford (UK): Encyclopedia of Life Support Systems (EOLSS); 2009. p. 1–23.

[208] Mao Y, Graham DW, Tamaki H, et al. Dominant and novel clades of candidatus accumulibacter phosphatis in 18 globally distributed full-scale wastewater treatment plants. Sci Rep. 2015;5:11857.

[209] Shen N, Zhou Y. Enhanced biological phosphorus removal with different carbon sources. Appl Microbiol Biotechnol. 2016;100(11):4735–4745.

[210] Moser-Engeler R, Udert KM, Wild D, et al. Products from primary sludge fermentation and their suitability for nutrient removal. Water Sci Technol. 1998;38 (1):265.

[211] Rahmani H, Rols J, Capdeville B, et al. Nitrate removal by a fixed culture in a submerged granular biofilter. Water Res. 1995;29(7):1745–1753.

[212] Bernat K, Kulikowska D, Godlewski M. Crude glycerol as a carbon source at a low COD/N ratio provides efficient and stable denitrification. Desalin Water Treat. 2016;57(42):19632–19641.

[213] Grady CL Jr, Daigger GT, Love NG, et al. Biological wastewater treatment. Boca Raton, Florida: CRC press; 2011.

[214] Parchami M, Wainaina S, Mahboubi A, et al. MBR-Assisted VFAs production from excess sewage sludge and food waste slurry for sustainable wastewater treatment. Appl Sci (Switzerland). 2020;10:8.

[215] Elefsiniotis P, Li D. The effect of temperature and carbon source on denitrification using volatile fatty acids. Biochem Eng J. 2006;28(2):148–155.

[216] Elefsiniotis P, Wareham DG. Utilization patterns of volatile fatty acids in the denitrification reaction. Enzyme Microb Technol. 2007a;41(1–2):92–97.

[217] Elefsiniotis P, Wareham DG, Smith MO. Use of volatile fatty acids from an acid-phase digester for denitrification. J Biotechnol. 2004;114(3):289–297.

[218] Fass S, Ganaye V, Urbain V, et al. Volatile fatty acids as organic carbon sources in denitrification. Environ Technol (United Kingdom). 1994;15(5):459–467.

[219] Elefsiniotis P, Wareham DG. Utilization patterns of volatile fatty acids in the denitrification reaction. Enzyme Microb Technol. 2007b;41(1):92–97.

[220] Wu C-Y, Peng Y-Z, Li X-L, et al. Effect of carbon source on biological nitrogen and phosphorus removal in an anaerobic-anoxic-oxic (A2 O) process. J Environ Eng. 2010;136(11):1248–1254.

[221] van Loosdrecht M, Oehmen A, Hooijmans C, Brdjanovic, D, Gijzen, H, Yuan, Z, Lopez-Vazquez, C. Modelling the PAO-GAO competition: Effects of carbon source, pH and temperature, et al, editors. 2009. Water research (Oxford).Vol.43, p. 2947–2949. doi:10.1016/j. watres.2009.03.043.

[222] Zhang C, Chen Y, Randall AA, et al. Anaerobic metabolic models for phosphorus- and glycogen-accumulating organisms with mixed acetate and propionic acids as carbon sources. Water Res. 2008;42(14):3745–3756.

[223] Llamas B, Ortega MF, Barthelemy G, et al. Development of an efficient and sustainable energy storage system by hybridization of compressed air and biogas technologies (BIO-CAES). Energy Convers Manag. 2020;210:112695.

[224] Wainaina S, Awasthi MK, Saraiya S, et al. Resource recovery and circular economy from organic solid waste using aerobic and anaerobic digestion technologies. Bioresour Technol. 2020;301:122778.

[225] Liedl BE, Bombardiere J, Chatfield JM. Fertilizer potential of liquid and Solid effluent from thermophilic anaerobic digestion of poultry waste. Water Sci Technol. 2006;53(8):69–79.

[226] Mukhuna M, Roopnarain A, Adeleke R, et al. Comparative assessment of bio-fertiliser quality of cow dung and anaerobic digestion effluent. Cogent Food Agric. 2018;4(1):1435019. 1435019 (1435011 pp.) 1435019 (1435011 pp.). INSPEC: 18693414
[227] Jimenez-Lopez EC, Lopez-Ocana G, Bautista-Margulis RG, et al. Wastewater treatment by constructed wetlands with thalia geniculata and paspalum paniculatum in a tropical system of Mexico. Int J Sustainable Dev Planning. 2017;12(1):42–50. CABl: 20173074032.

[228] Pincam T, Brix H, Jampeetong A. Treatment of anaerobic digester effluent using acorus calamus: effects on plant growth and tissue composition. PLANTS-BASEL. 2018;7(362). DOI:10.3390/plants7020036

[229] Gong X, Li S, Sun X, et al. Maturation of green waste compost as affected by inoculation with the white-rot fungi tramesi versicolor and phanerochaete chrysosporium. Environ Technol. 2017;38(7):872–879.

[230] Zacharof M-P, Mandale SJ, Oatley-Radcliffe D, et al. Nutrient recovery and fractionation of anaerobic digester effluents employing pilot scale membrane technology. JOURNAL OF WATER PROCESS ENGINEERING. 2019;31:100846.

[231] Khoshnevisan B, Duan N, Tsapekos P, et al. A critical review on livestock manure biorefinery technologies: sustainability, challenges, and future perspectives. Renewable Sustainable Energy Rev. 2021;135:110033.

[232] Pivato A, Vanin S, Raga R, et al. Use of digestate from a decentralized on-farm biogas plant as fertilizer in soils: an ecotoxicological study for future indicators in risk and life cycle assessment. Waste Manage (Elmsford). 2016;49:378–389.

[233] Sigurnjak I, Michels E, Crappé S, et al. Does acidification increase the nitrogen fertilizer replacement value of bio-based fertilizers? J Plant Nutr Soil Sci. 2017;180 (6):800–810.

[234] Walsh JJ, Jones DL, Chadwick DR, et al. Repeated application of anaerobic digestate, undigested cattle slurry and inorganic fertilizer N: impacts on pasture yield and quality. Grass Forage Sci. 2018;73(3):758–763.

[235] Pincam T, Brix H, Jampeetong A. Growth performance of tropical wetland species (Cyperus involucratus rotb. and thalia geniculata L.) in anaerobic digester effluent and their water treatment efficiency. Ecol Eng. 2020;143:105667.

[236] Peng W, Zeng Y, Shi Q, et al. Responses of rice yield and the fate of fertilizer nitrogen to soil organic carbon. Plant Soil Environ. 2017;63(9):416–421.

[237] Yasar A, Rasheed R, Tabinda AB, et al. Life cycle assessment of a medium commercial scale biogas plant and nutritional assessment of effluent slurry. Renewable Sustainable Energy Rev. 2017;67:364–371.

[238] Fernandes F, Silinka A, Fuentes-Grunewald C, et al. Valorising nutrient-rich digestate: dilution, settlement and membrane filtration processing for optimisation as a waste-based media for microalgal cultivation. Waste Manage. 2020;118:197–208.

[239] Tsapekos P, Khoshnevisan B, Alvarado-Morales M, et al. Environmental impacts of biogas production from grass: role of co-digestion and pretreatment at harvesting time. Appl Energy. 2019;252:113467.

[240] Nordahl SL, Devkota JP, Amirebrahimi J, et al. Life-Cycle greenhouse gas emissions and human health trade-offs of organic waste management strategies. Environ Sci Technol. 2020;54(15):9200–9209.

[241] Dai S, Li Q, 李庆卫. Removal efficiency of eight plants in two different eutrophic water. J North-East For Univ. 2016;44:80–83. 1000-5382(2016)44:7<80:8ZZW D2>2.0.TX;2-47. CSDC: 5748947.

[242] Zhang C-B, Liu W-L, Pan X-C, et al. Comparison of effects of plant and biofilm bacterial community parameters on removal performances of pollutants in floating Island systems. Ecol Eng. 2014;7:58–63.

[243] Almuktar SAAA, Abed SN, Scholz M. Wetlands for wastewater treatment and subsequent recycling of treated effluent: a review. Environ Sci Pollut Res. 2018;25(24):23595–23623. CABl: 20193370800

[244] Li Y, Zhu G, Ng WJ, et al. A review on removing pharmaceutical contaminants from wastewater by constructed wetlands: design, performance and mechanism. SciTotal Environ. 2014;468:908–932.

[245] Gulzar M, Mahmood K, Zahid R, et al. The effect of particle size on the dispersion and wear protection ability of MoS2 particles in polyalphaolefin and trimethylolpropane ester. Proc Inst Mech Eng, Part J: Eng Tribol. 2018;232(8):987–998.

[246] Gao J, Liu L, Ma N, et al. Effect of ammonia stress on carbon metabolism in tolerant aquatic plant-Myrriophyllum aquaticum. Environ Pollut. 2020;263:114412A.

[247] Jampeetong A, Brix H. Effects of NH4+ concentration on growth, morphology and NH4+ uptake kinetics of Salvinia natans. Ecol Eng. 2009;35(3):695–702.

[248] Vaneeckhaute C, Lebuf V, Michels E, et al. Nutrient recovery from digestate: systematic technology review and product classification. Waste Biomass Valorization. 2017;8(1):21–40.

[249] Anjum R, Grohmann E, Krakat N. Anaerobic digestion of nitrogen rich poultry manure: impact of thermophilic biogas process on metal release and microbial resistances. CHEMOSPHERE. 2017;168:1637–1647.

[250] Bi S, Westerholm M, Qiao W, et al. Metabolic performance of anaerobic digestion of chicken manure under wet, high solid, and dry conditions. Bioresour Technol. 2020;296:122342.

[251] Yin D-M, Westerholm M, Qiao W, et al. An explanation of the methanogenic pathway for methane production in anaerobic digestion of nitrogen-rich materials under mesophilic and thermophilic conditions. Bioresour Technol. 2018;264:42–50.

[252] Zhang M, Lawlor PG, Wu G, et al. Partial nitrification and nutrient removal in intermittently aerated sequencing batch reactors treating separated digestate liquid after anaerobic digestion of pig manure. Bioprocess Biosyst Eng. 2011;34(9):1049–1056.

[253] Hallas JF, Mackowiak CL, Wilkie AC, et al. Struvite phosphorus recovery from aerobically digested municipal wastewater. SUSTAINABILITY. 2019;11:3762.
[254] Muhmood A, Wu S, Lu J, et al. Nutrient recovery from anaerobically digested chicken slurry via struvite: performance optimization and interactions with heavy metals and pathogens. SciTotal Environ. 2018;635:1–9.

[255] Wu Z, Zou S, Zhang B, et al. Forward osmosis promoted in-situ formation of struvite with simultaneous water recovery from digested swine wastewater. Chem Eng J. 2018;342:274–280.

[256] Yin D-M, Taherzadeh MJ, Lin M, et al. Upgrading the anaerobic membrane bioreactor treatment of chicken manure by introducing in-situ ammonia stripping and hyper-thermophilic pretreatment. Bioresour Technol. 2020;310:123470.

[257] Debowski M, Szwaja S, Zielinski M, et al. The Influence of anaerobic digestion effluents (ADEs) used as the nutrient sources for chlorella sp cultivation on fermentative biogas production. Waste Biomass Valorization. 2017;8(4):1153–1161.

[258] Nwoba EG, Mickan BS, Moheimani NR. Chlorella sp. growth under batch and fed-batch conditions with effluent recycling when treating the effluent of food waste anaerobic digestate. J Appl Phycol. 2019;31(6):3545–3556.

[259] Zielinski M, Debowski M, Szwaja S, et al. Anaerobic digestion effluents (ADEs) treatment coupling with chlorella sp microalgae production. Water Environ Res. 2018;90(2):155–163.

[260] Panuccio MR, Papalia T, Attina E, et al. Use of digestate as an alternative to mineral fertilizer: effects on growth and crop quality. Arch Agron Soil Sci. 2019;65(5):700–711.

[261] Tamaki S, Hidaka T, Mizuno T, et al. Anaerobic digestion of oxidation ditch sludge at low temperatures with hyperthermophilic pretreatment. J Water Environ Technol. 2019;17(2):67–75. BIOSIS:PREV201900474446