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Review

Current Status and Prospects of Valorizing Organic Waste via Arrested Anaerobic Digestion: Production and Separation of Volatile Fatty Acids

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Abstract: Volatile fatty acids (VFA) are intermediary degradation products during anaerobic digestion (AD) that are subsequently converted to methanogenic substrates, such as hydrogen (H_2), carbon dioxide (CO_2), and acetic acid (CH_3COOH). The final step of AD is the conversion of these methanogenic substrates into biogas, a mixture of methane (CH_4) and CO_2. In arrested AD (AAD), the methanogenic step is suppressed to inhibit VFA conversion to biogas, making VFA the main product of AAD, with CO_2 and H_2. VFA recovered from the AAD fermentation can be further converted to sustainable biofuels and bioproducts. Although this concept is known, commercialization of the AAD concept has been hindered by low VFA titers and productivity and lack of cost-effective separation methods for recovering VFA. This article reviews the different techniques used to rewire AD to AAD and the current state of the art of VFA production with AAD, emphasizing recent developments made for increasing the production and separation of VFA from complex organic materials. Finally, this paper discusses VFA production by AAD could play a pivotal role in producing sustainable jet fuels from agricultural biomass and wet organic waste materials.

Keywords: arrested anaerobic digestion (AAD); waste valorization; volatile fatty acids (VFA); high-value bio-products; VFA extraction

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1. Introduction

Volatile fatty acids (VFA) are intermediates produced during anaerobic digestion (AD) and have a high market value due to their wide range of applications from food to chemicals, textiles, pharmaceuticals, energy, and materials, including bioplastics [1,2]. VFA are short-chained organic fatty acids comprising C2-C6 carbon atoms, such as acetic acid, propionic acid, butyric acid, valeric acid, and caproic acid [2–4] traditionally produced from fossil fuels. Due to their versatility, they are in high demand, with an estimated global market of 18.5 million tons in the year 2020 and is projected to rise annually by 3% [5]. Meeting the rising demand with fossil fuel-based pathways has deleterious effects on the climate due to the simultaneous production of greenhouse gases (GHGs). On the contrary, organic wastes rich in lignocelluloses such as green and food waste, and agricultural residues such as straw and manure have an untapped potential of being ideal substrates to produce VFA due to their high carbon content. Bio-based approaches such as anaerobic fermentations offer a sustainable alternative to produce VFA than the petrochemical pathways whose carbon footprint is higher and uses fossil fuel-based resources as raw material, depleting and over exploiting the planet's non-renewable energy reserves [2]. VFA can further serve as platform molecules to produce biofuels, biochemicals, and biomaterials through various upgrading and conversion pathways based on catalytic reactions. Currently, the sugar

platform [6–11] is one of the main routes investigated and commercialized for liquid biofuel production through fermentation. Sugar platform involves fermenting pure sugars to ethanol and subsequently to liquid biofuel. Though this pathway has high yield (0.46 g ethanol/g sugar), it is hindered by high costs involved with enzymes, pretreatment, and need for high sugar content biomass [4,12,13]. While the VFA platform is still an emerging technology, it needs further development for higher process yield (g VFA/g substrate), productivity (g VFA/L-day), and cost-effective energy-efficient separation methods to recover VFA from the fermentation broth with residual materials from the raw material input [4,14].

Wet organic waste (WOW) accounts for 33.7% of the 292.4 million tons of municipal solid waste (MSW) produced in the US [15]. A major proportion of this organic waste is landfilled in communities where recycling is not practiced, releasing greenhouse gases into the atmosphere [5,15]. Interest in removing WOW from landfills and diverting it into valuable products such as biogas or VFA has increased significantly in recent years. Other forms of waste disposal methods, such as composting, comes with its limitations as the process is energy-consuming instead of energy-producing. Composting also releases large amounts of CO_2 and the resulting soil amendment products value is variable based on the geographical location. AD is a commercial bioprocess that has been in practice worldwide for the conversion of manure, sewage sludge, food waste, agriculture residues, etc. It is based on a complex consortium of microorganisms working together in a concerted action to degrade organic materials into biogas [16]. The efficiency of AD in degrading waste to biogas depends on the nature of the waste. Waste such as garden waste and lignocellulosic biomass materials often need a pretreatment step to break the barrier made of bonds between lignin and carbohydrate which prevent bioconversion of the materials [17]. These wastes are composed of cellulose, hemicellulose, and lignin and pretreatment degrades all the components while increasing the total reducing sugars. Pretreatment of biomass for AD has been heavily investigated at the laboratory scale [18,19] and implementing these technologies at a commercial scale is now underway.

The advantage of using AAD to treat wastes over AD or composting is that the end-products of the later process are of far higher value than both biogas and soil amendments. Additionally, the retention times to produce VFA using AAD are far lower than traditional AD, lowering the capital cost of the process. As with the AD process, the complex consortia of AAD performing the bioprocess to produce VFA are robust too and can adapt to changes in the input raw materials. The consortia also include microbes producing cellulolytic enzymes eliminating the necessity of high-cost enzyme addition, which often is prohibitive for biorefineries using enzymes. Besides, the mixed culture fermentation of AAD does not need sterility or the addition of expensive growth supplements [14].

AAD, which is also referred to as acidogenic fermentation or arrested methanogenesis, has been tested on various complex wastes such as sewage sludge [20], livestock waste [21], food waste [22], press mud [23], dairy wastewater [24], and corn stover [25,26] and described in several reviews [27–29]. As with any biochemical process, the determining factors for the economics of the process are product yield and productivity. The yield and productivity of AAD are affected by fermentation variables such as pH and hydraulic retention time (HRT) along with the thermodynamic stability of the process, which is also affected by the accumulation of H_2 produced during the process [30]. Other factors such as end-product inhibition also profoundly affect VFA titers and often lead to low yields [29].

One of the major challenges of producing VFA via AAD is the separation and recovery of the products, which can require up to 40% of the process energy costs. The first attempt to commercialize VFA production from WOW was the MixAlco process [31,32]. In this process, the feedstock was treated with lime to increase its digestibility and fed to a mixed culture fermenter rich in acid-forming microorganisms that produce VFA. Calcium carbonate was used to neutralize the acids and to produce their corresponding carboxylate salt. The dilute carboxylate salts (approximately 3%) are concentrated to 19% using an amine solvent that selectively extracts water and are dried using multi-effect evaporators. Finally, the dry salts

are thermally converted to ketones and subsequently hydrogenated to alcohols. Terrabon, the company behind the process, went bankrupt in 2017 due to a lack of funding [33]. Since then, extensive work has been done to improve the separation process to reduce the cost of extracting VFA from the fermentation broth of AAD. This paper presents some of the latest developments and insights into VFA production and separation. The review will finally discuss the role of VFA as platform molecules for producing sustainable aviation fuel (SAF).

2. Arrested Anaerobic Digestion

Arrested anaerobic digestion (AAD) is the rewired form of AD with no methanogenesis step. To curb methanogenesis, the archaea responsible for producing methane should be inhibited by regulating the fermentation variables, such as pH, HRT, organic loading rate (OLR), and redox potential. Besides, inhibitors have further been described for eliminating methanogenesis. As the population of methanogens decreases, methane formation plummets and results in the accumulation of VFA, further inhibiting methanogenesis by lowering the pH. In short, accumulating VFA in the fermentation broth through AAD is achieved using two strategic methods: (1) Inhibiting methanogenic archaea, thereby reducing VFA consumption to produce biogas, (2) Enhancing acidogenesis (acidogenic fermentation) by using high OLR or minimizing the HRT [34]

2.1. Understanding Methanogenesis and Its Inhibition

Methanogenic archaea produce methane from carbon substrates using three different pathways that primarily differ in the enzymes used to generate the intermediate: methyltetrahydro (methano/sarcina) pterin (CH_3-H_4 (M/S) PT) [35,36]. The three pathways are:

- the hydrogenotrophic pathway where CO_2 is reduced to CH_4, with H_2 acting as the electron donor.
- In the aceticlastic pathway, CH_4 is produced from acetate.
- In the methylotropic pathway, methylated compounds are reduced to CH_4.

Biogas in AD is produced from either aceticlastic or hydrogenotrophic methanogenesis pathways [27,37], where the aceticlastic pathway is responsible for converting acetate by genera such as *Methanosarcina* or *Methanosaeta* [38,39] and the hydrogenotrophic pathway includes several other genera, such as *Methanobacterium, Methanobrevibacter, Methanogenium* [40].

Substances for suppressing methanogenesis work by decoupling CoM reductase, a key enzyme in methanogenesis. Many studies have used 2-bromoethanesulfonic acid (BES) as the active inhibitor [3,26,41]. Some studies have found that BES has an inhibitory effect on other groups of bacteria during AD besides methanogenic archaea [41]. Therefore, it is important to only use BES addition for short periods to avoid degradation of the microbial consortia while avoiding adaptation of the methanogens to this compound, as seen after long-term use [42]. Another way to inhibit methanogenesis is to ensure that the fermentation conditions are challenging for methanogens to thrive. Reducing pH during AD fermentation in a continuous stirred tank reactor (CSTR) is a way to favor acidogenesis over methanogenesis and by further reducing the retention time during the operation, it is possible to eliminate the presence of aceticlastic methanogens, which will increase the concentration of acetic acid in the digestate [43]. The rumen of ruminant animals is an example of a natural environment with a short retention time (ca. 20 h) resulting in an extremely low number of aceticlastic methanogens and relatively high production of acetic acid compared to longer-chained VFA [25]. Table 1 reviews recent strategies used in several studies to inhibit methanogenesis.

Table 1. Summary of studies of AAD using different substrates and operating conditions.

Substrate	Inhibition of Methanogenesis	VFA Yield	VFA Type	HRT	Temperature (○C)	Mode	Reference
High-strength cheese whey and brewery wastewater	Acid shock & heat treatment of inoculum	78 g/L	Total	-	40	Batch	[44]
		30 g/L		4	40	Fed-Batch	
Livestock organic waste (Cattle manure–poultry litter)	Low pH-5.5	3.5 g/L	Ac, Pr, Bu	4	35	Fed-batch	[21]
Primary sewage sludge–organic wastes	Low pH-5.5	17.242 g COD/L	Total	7	35	Fed-batch	[20]
Glucose	H_2O_2	1.233 g/L	Total	-	35	Batch	[34]
Wet exploded corn stover	BES	49.31 g/L	Ac, Pr, Bu	6	37	Fed-batch	[26]
Wet exploded corn stover	Rumen culture as inoculum	40.8 g/L	Ac, Pr, Bu	6	37	Fed-batch	[25]
Food waste	Low pH-6	34.05 g/L	Ac, Pr, Bu, Va	-	30	Batch	[45]
Food waste	Low HRT, high OLR	7.5 g/L	Total	6.67	37	Fed-batch	[46]
Cheese production WW	-	0.97 g COD/g SCOD	Total	-	35	Batch	[47]
Sucrose	Heat inactivation of methanogens in inoculum	37 g/L	Ac, Bu	2	35	Continuous	[48]
Citrus waste	Low pH-6, O_2	0.793 g VFA/g VS	Total	-	37.5	Batch	[49]
Food waste–mature compost	Low pH-6, acidogenic reactor effluent as inoculum	20 g COD/L	Total	5	37	Fed-batch	[50]
Organic MSW–food waste	Low pH-6, acidogenic reactor effluent as inoculum	11.73 g /L	Total	3.5	37	Fed-batch	[22]
Food waste	High OLR, pH 10	6.3 g/L	Ac, Pr, Bu	-	28	Batch	[51]
Olive mill WW	Low pH-5, high OLR	27 g/L	Total	2	-	Batch	[52]
Wetland plant litter	High pH-12,	0.127 g/g dry matter	Total	25	25	Batch	[53]
Food waste	Low pH-6, O_2	0.8 g VFA/g VS	Total	-	37	Batch	[54]
Food waste–sewage sludge	High pH -10	8.631 g/ L	Total	-	35	Batch	[55]
Microalgae	High OLR	36.8 g/ L	Total	8	25	Fed-batch	[56]
Palm oil mill effluent	Low HRT	10.5 g/L	Total	5	29	Fed-batch	[57]

Table 1. *Cont.*

Substrate	Inhibition of Methanogenesis	VFA Yield	VFA Type	HRT	Temperature (○C)	Mode	Reference
Waste activated sludge	Bio-surfactants-surfactin, rhamnolipid, saponin	3.3 g COD/L	Total	-	30	Batch	[58]
Waste activated sludge	Low thermal pretreatment, sodium dodecylbenzene sulfonate	0.32 g COD/g VS	Total	-	37	Batch	[59]
Food waste–waste activated sludge	High pH-10, BES	0.343 g COD/g VS	Ac, Pr, Bu, Va	-	35	Batch	[60]
Chicken manure	Thermal shock	0.9 g VFA/g VS	Ac, Pr, Bu	10	37	Fed-batch	[61]

sCOD: soluble chemical oxygen demand. VS: volatile solids. COD: chemical oxygen demand. OLR: organic loading rate. WW: wastewater. Ac: acetic acid, Pr: propionic acid, Bu: butyric acid, Va: valeric acid.

Several compounds, such as long-chain fatty acids [62], 2-Bromoethanesulfonate (BES) [63], ammonia [64], sulfides [65], heavy metals [64], and antibiotics (such as amoxicillin, oxytetracycline, sulfamethoxazole, metronidazole [66], tetracycline [67]), oxygen and their derivatives [68], are known to inhibit methanogenesis. Several other antibiotics such as ampicillin, chloramphenicol and tetracyclines were also investigated [36,69–71] and many other compounds that are inhibitory to methane fermentation are reviewed [36]. However, the most common inhibitor used for inhibiting methanogenesis is BES. BES (2-Bromoethanesulfonic acid) is a structural analog of Coenzyme M, a cofactor responsible for the terminal step of methanogenesis (Figure 1) [72]. Other potential analogs of Coenzyme-M are 2-chloroetthanesulfonate (CES), 2-mercaptoethanesulfonate (MES), and lumazine. These compounds can effectively inhibit the methyl transfer reaction in the final reduction stage of hydrogenotrophic methanogens, thus inhibiting methane formation. BES is widely used and is reported to inhibit methanogenesis effectively. However, in one of the studies using citrus waste, no increase in VFA was seen after inhibiting methanogenesis using BES [49]. BES has been used at various concentrations, and higher concentrations of 10 mM or more stopped CH_4 production completely [25,73].

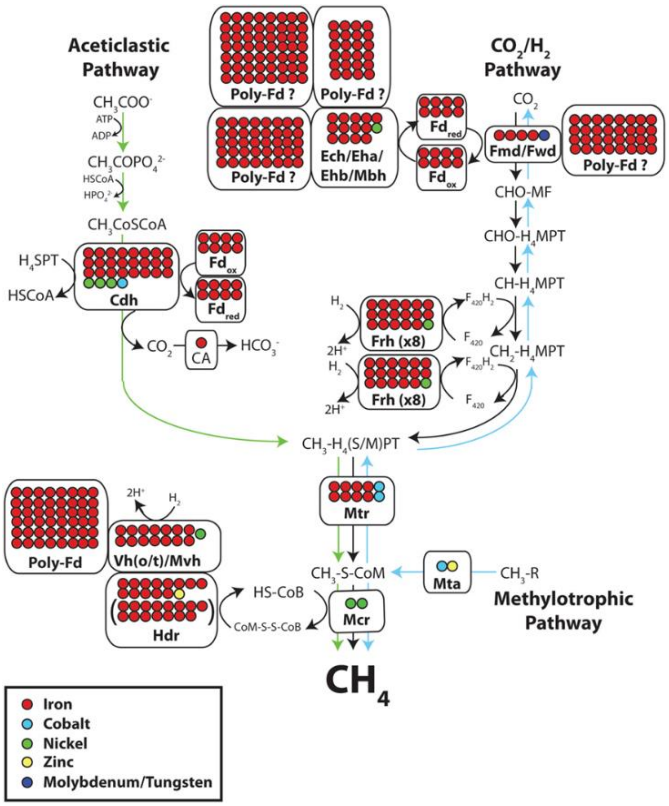

Figure 1. The three different pathways of producing methane, including the metal content of the enzymes in all the three pathways [35]; each trace metal is represented with different colored circles as shown in the legend. The abundance of red circles indicate that Fe is the most abundant metal followed by Ni and Co and traces of other metals as indicated. Reproduced with permission.

2.2. Parameters Affecting Arrested Methanogenesis

Methane production results from a complex microflora possessing several biochemical reactions, which are affected by various parameters, such as substrate availability, inoculum source, pH, organic loading rate, oxidation–reduction potential, pretreatment [59], and hydraulic retention time (HRT). Of all the parameters, pH and HRT are the most important parameters that affect methane production.

2.2.1. pH

pH affects the reaction rate of the different microorganisms present in the anaerobic fermentation process [74] and influences the VFA spectrum found during AAD fermentation. It also affects VFA production by affecting the competition between acetogens and methanogens [75]. Several studies on AAD have used bioreactors operated at pH ranges inhibitory to the methanogens. Methanogens generally grow at neutral pH 7; hence, operating a bioreactor at either low (acidic) or high (alkali) pH will inhibit methanogenesis. However, some methanogenic species have the potential to acclimate to acidic conditions caused by acidogenic fermentation and produce a significant amount of CH_4 even at a low pH range of 4.0–5.3 [76,77], e.g., *Methanosarcina barkeri* [78]. Thus, operating the bioreactor at alkaline conditions (pH 8–10) could be a better alternative to inhibit methanogenesis. However, the volatile solids degradation rate at high pH during AAD was generally low over short fermentation times and constant alkali addition led to an added cost of the bioprocess besides the risk of corrosion of the fermentation equipment [55]. Many studies have reported slightly acidic conditions (pH 5.5–6) to be favorable for high VFA concentrations [79,80] and high VFA yield [81]. However, other studies have reported pH 10 to favor high rates of VFA production [82–86]. This might be due to better buffering capacity at higher pH and higher hydrolysis rates of the raw material used for the fermentation.

Traditionally, AAD is operated at acidic conditions (pH < 6.5) with pH controlled by alkali additions. While acidic conditions positively favor inhibition of methanogenesis, the acid stress on the microbes negatively affects the VFA production as weak acids such as lactic acid and acetic acid will be in the protonated form at low pH. Uncharged acid groups are more lipophilic and can penetrate the bacteria's outer later (lipid bilayer) and release the protons inside the cell and thereby disrupting their functionality [87].

In conclusion, extreme pH (pH higher than 10 or pH lower than 5) can be detrimental to acidogens and a drop in volatile solids reduction and VFA concentration is often noticed [29,43].

2.2.2. HRT

HRT is another critical parameter determining which microbial population can thrive and grow in continuously stirred tank reactors (CSTRs) for AD or AAD. Methanogens have specific growth rates in the range of 0.0167–0.02 h^{-1}, and are slow-growing, compared to the fast-growing acidogens with growth rates around 0.172 h^{-1} [88]. Therefore, at low HRT, the slowest-growing bacteria will be washed out from the CSTR bioreactor. Yarimtepe, Oz and Ince [52] report an HRT of 2 days at a pH range of 5–5.5 to be optimum for producing VFA using pretreated olive mill wastewater. An increase in VFA concentration is noticed with a decrease in HRT, from 2 days to one day, with the highest VFA concentration at an HRT of 8 h using low strength wastewater as substrate [89]. In a recent study with kitchen waste as raw material, the optimal HRT was 10 days with an organic loading rate of 5.0 g VS/ L-d for achieving the highest VFA yield [90]. Due to its high digestibility, food waste produces high VFA yields at a low HRT of 2 days in most studies. However, in the case of co-digestion with garden waste, longer HRTs are preferred for better hydrolysis [91]. HRT is analogous to other parameters such as organic loading rate (OLR) and solid retention rate (SRT), representing the amount of organic mass being fed per unit volume of bioreactor per day [92], since controlling hydraulic rate simultaneously affects OLR and SRT. Overall, the optimal retention time depends on the nature of the substrate and its digestibility, where high concentrations of lignocellulosic materials will demand long retention times without pretreatment of the material.

2.3. New Emerging Technologies

2.3.1. Bioaugmentation

Bioaugmentation is a promising strategy for increasing the VFA titers of AAD reactors [74]. Many reported studies used microbes such as *Escherichia coli* [93], *Moorella thermoacetica* [94], *Acetitomaculum ruminis*, *Acetobacterium woodii (A. woodii)* [26], *Clostridium butyricum* [95], *Clostridium aceticum* [96], *Propionibacterium acidipropionici (P. acidipropionici)* [97] to alter

the microbial diversity during AAD to produce targeted intermediates. As methanogens are inhibited, the syntropic relationship between hydrogenotrophic methanogens and acetogens is disturbed, creating thermodynamic instability within the microbial community, which leads to a decrease in the reduction of volatile solids in the bioreactor [98]. Accordingly, the VFA concentration in a rumen-based bioreactor growing on pretreated corn stover was lowered by 31% after BES addition compared to a bioreactor with active hydrogenotrophic methanogenesis [26]. In a recent study with the same rumen bioreactors, bioaugmentation with homoacetogens restored the balance in the system by substituting the role of hydrogenotrophic methanogens in the AAD reactor. The homoacetogens strains tested were *Acetobacterium woodii* and *Acetomaculum ruminis* resulting in a 70% and 45% increase in the VFA concentration compared to bioreactors operating without an active hydrogen-converting step (Table 2) [26].

Table 2. Effect of bioaugmentation on VFA fermentation using corn stover as substrate [26] (Table adapted with permission).

Bioreactor	Acetic Acid (g/L)	Propionic Acid (g/L)	Butyric Acid (g/L)	Total VFA in Acetic Acid Equivalents (g/L)	Total VFA Yield in Acetic Acid Equivalents (g/g VS)
Control; With Methanogenesis [25]	12.26	10.08	2.42	31.09	1.25 g/gVS
Control; (BES-added) Without Methanogenesis	9.29	5.63	1.23	21.41	0.95 g/gVS
Bioaugmentation with *A. ruminis* after BES addition	16.99	6.88	2.98	32.33	1.34 g/gVS
Bioaugmentation with *A. woodii* after BES addition	30.8	7.91	3.89	49.31	2.19 g/gVS

As most of the AAD reactors operate at short retention times, one concern with applying external cultures for bioaugmenting the AAD bioreactors is the possibility of washout of the microbes after addition to the reactor. Hence, it is crucial to know the specific growth rate of the inoculating microbes and to use HRTs, which can sufficiently support the growth of the targeted strain in the bioreactor. Secondly, the competency between the existing microbial community and the target microbe should be well understood. E.g., bioaugmentation with homoacetogens in the presence of hydrogenotrophic methanogens has shown limited effects on methanogenesis as methanogens generally grow with higher growth rates than homoacetogens with H2 and CO2 as substrates [99,100]. Atasoy and Cetecioglu [95] showed 11 times increase in butyric acid production in a mixed culture fermentation and the total VFA production was 3.5 times higher after bio-augmenting. Overall, it is evident that bioaugmentation has a major potential for improving AAD, which should be studied in the future. Further studies are needed to understand how the targeted microbe or cultures for bioaugmentation can be acclimatized to the bioreactor conditions before it is added to the bioreactors. Additionally, it is important to grow the microbe or culture on the raw material used in the bioreactor. Atasoy and Cetecioglu [97] report that the bacterial community structure did not change after bioaugmentation with *P. acidipropionici* as the microbe easily adapted into the present mixed culture.

2.3.2. Electro-Fermentation

Electro-fermentation technology regulates microbial metabolism using solid electrodes as electron acceptors (anode) or electron donors (cathode) [101]. This technology uses oxidation–reduction potential (ORP) as the regulating parameter, which controls intracellular metabolism [102]. The principle behind this technique is to apply voltage potential across the electrodes to control microbial activity and the product spectrum/pathways. This

technique has been proven to affect methanogenesis [103–105]. One recent study demonstrates the feasibility of using redox potential to arrest methanogenesis electrochemically using solid electrodes. Higher voltage potentials negatively affected methanogenesis [106] and resulted in 68% inhibition of methanogenesis and a 33% increase in acetic acid concentration [106]. This novel approach could regulate the fermentation products by controlling the redox potential in the anaerobic reactors [107]. In another reported study, blast furnace dust (BFD) addition reduced the redox potential and optimized the fermentation by increasing VFA production, resulting in increased biogas production [108]. The micro-electrolysis between iron and carbon (Fe-C) facilitates AD by creating an optimal environment for iron reduction and consequently enhances the organic matter conversion [109]. Fe-C micro-electrolysis also enhanced the interspecies hydrogen transfer [108] and a similar effect was seen when Fe-C micro-electrolysis was coupled with microaerobic fermentation for enhanced VFA production [110].

2.3.3. Re-Wiring Hydrogen Fermentation for VFA

Dark fermentation (DF) is a process to produce bio-hydrogen and is analogous to acidogenesis. During the acidification stage of the AD process, hydrogen is produced as a by-product and hydrogenotrophic methanogens function as hydrogen scavengers ensuring that the hydrogen partial pressure is kept at a low level [26]. During DF, complex substrates such as polysaccharides, proteins, and fats are hydrolyzed by acidogens to monomeric or dimeric sugars, amino acids and long and short-chained fatty acids via hydrolysis processes using a variety of enzymes. After hydrolysis, acetogens take up the hydrolysis products and ferment them through their metabolism into mainly VFA, H_2 and CO_2. One of the drawbacks of DF for the production of hydrogen is the low product yield of hydrogen per unit of substrate [111]. Typically, 4 moles of H_2 (Thauer limit) and 2 moles of acetate are generated per mole of glucose consumed as a by-product by DF. The production of acetate and other organic acids, as well as small amounts of ethanol, restrains the hydrogen yield to maximum 2–3 moles per glucose molecule. Secondly, the concentration of hydrogen will vary with changes in the input material, which makes the process difficult to scale and use commercially for converting wet organic waste [112,113]. Integrating dark fermentation and photo-fermentation was effective with biowaste as feedstock [114,115], but this process is challenging to scale up due to its complexity [116]. In a recent study, a hydrogen yield of 5.6 moles per mole of glucose (beyond the Thauer limit) was found by artificially engineering the microbial consortia and further adapting this culture over a prolonged time [117]. Effective hydrogen production via fermentation might require further research to find efficient hydrogen-producing microbes, which are amendable to genetic engineering to enhance hydrogen production further. Generally, AAD process uses naturally available microbes that are robust and adapted to the input material and admitting genetically engineered microbes into this process might not be beneficial for the economics or allowable for use in all regions of the world [28].

During hydrogen fermentation, the accompanied VFA production is considered prohibitive for the process's outcome. Reducing the by-product accumulation is a strategy to improve hydrogen yield [113]. One similarity between rewiring AD to produce VFA (AAD) compared to hydrogen (DF) is that both the products are intermediate compounds and are precursors for biogas production and that both processes are dependent on the inhibition of methanogens [118] and altering the profiles of VFA during the fermentation will affect the product formation of both processes. However, instead of seeing these two processes separately, VFA produced during DF could be exploited in addition to the H_2. Bioaugmentation with specific microbes such as homoacetogens or H_2-producing microbes could result in high product yields, where H_2 produced could be used as a substrate for the homoacetogens to produce more VFA or could be separated for separate use as a bio-hydrogen product, while recovered CO_2 could be sequentially upgraded into products for hydrogen production [111,119,120].

Hence, rewiring DF to produce more VFA instead of H_2 might be an economical alternative where the co-production of both VFA and H_2 improves the overall economics.

3. Extraction and Purification of VFA

Volatile fatty acids (VFA) in the fermenter require safe extraction that does not disturb the microbial process for practical applications. In addition, continuous extraction of VFA will prevent product inhibition and acid-induced stress on microbes, thus avoiding microbial toxicity and maintaining consistent microbial performance for improved productivity [121,122]. Separation of VFA usually involves more than one stage: (1) Primary extraction stage that removes VFA from the fermentation broth and (2) Secondary purification stage to purify the VFA and concentrate them for potential sale in the market or for upgrading. The current default techniques for VFA purification are traditional distillation, evaporation, and crystallization [123]. However, due to the low dilute acid concentrations in the fermentation broth, evaporating large volume of water is required, making these techniques energy-intensive and expensive [123,124]. Liquid–liquid extraction (LLE) [125] is a separation method based on the affinity of target species (VFA) and requires using a solvent and sometimes a cosolvent [126]. Though LLE has demonstrated high efficiencies in extracting VFA, the process is not environmentally friendly and needs an additional stage to recover the spent solvent, where solvent losses can significantly increase the operational costs of the separation process [127,128]. Other factors such as solvent toxicity, cost, ease of regeneration and selectivity are some of the limitations of this process. In a recent study, hydrophobic deep eutectic solvents (HDES), a new generation of water-immiscible designer solvents, were evaluated for their efficiency in extracting VFA from fermented wastewater. An efficiency of 88% was reported with a four-staged extraction operation with successful regeneration using vacuum evaporation. Hence, these HDES solvents present a greener way of extracting VFA due to their low cost, sustainable manufacturing, and non-toxic nature [122]. Several operations such as electrocoagulation [129], electrodialysis [130,131], adsorption [132–134], extractive distillation [135] and many other membrane-based operations [136] have been explored to extract VFA. While every tested method was feasible for separating the VFA, the process needs to be efficient and economical, including regenerating chemicals and materials used in multiple cycles. Membrane-based separation and adsorption using ion exchange resins are emerging technologies for recovering VFA directly from the fermentation broth [137,138]. In the following, we will review VFA recovery using ion-exchange systems (Table 3) and membrane-based technologies (Table 4).

Table 3. Summary of recent works on VFA recovery using adsorption (ion-exchange).

Materials Used	VFA Recovered	Acid Recovery Efficiency (%)	Regeneration Method	References
Purolite A103S Plus	Ac, Bu	66.16	Not reported	[139]
Amberlyst A21	Total VFA	Up to 80	Not reported	[140]
Amberlite IRA-67	Ac, Bu, La	75	Thermal	[141]
Amberlite IRA-67, Dowex optipore L-493	Ac, Pr	Up to 85	Alkali wash	[132]
Amberlite FPA53	Ac	42.36	Strong alkali wash	[121]
Non-functionalized polystyrene-divinylbenzene-based resin	Total VFA	75.5	N_2 stripping	[133]
Activated Carbon	Ac, Bu	Up to 80	Not reported	[134]
Amberlite IRA-67	La	Not reported	Alkali wash	[142]

Ac: acetic acid, Pr: propionic acid, Bu: butyric acid.

Table 4. Summary of recent works on VFA recovery using membrane-based operations.

Operation Technique	VFA Recovered	Recovery Efficiency	Fouling/ Regeneration	Membrane Details	References
Vapor permeation	Total VFA	Up to 95%	Not reported	Trioctylamine-filled PTFE membrane; area—19.25 cm^2	[138]
Membrane extraction	Total VFA	Not reported	Water rinsing	Silicone membrane; area—24.3 m^2/L_{ferm}	[143]
Membrane extraction coupled with electrodialysis	Total VFA	Up to 98%	Alkali wash	PTFE membrane; membrane configuration—1,3 and 5 membranes stacked. Total active area of 64 cm^2, 192 cm^2 and 320 cm^2 respectively.	[144]
Membrane extraction	Total VFA	Up to 21.5%	Not reported	Silicone membrane; area—125 cm^2	[145]

3.1. Adsorption

Adsorption is a physicochemical method where the solute compound adheres to an added surface. Several studies have shown promising results for mixed VFA extraction using adsorption. Extraction of VFA is typically achieved using ion-exchange resins. VFA in the fermentation broth can be separated using anion exchange resin, where the unprotonated carboxyl group (negative charge) allows ionic bonding with the positively charged functional group [139]. Anion exchange resins are further classified into weak and strong base resins. Weak base anion resins are functionalized with a base group such as pyridine, imidazole and primary, secondary, or tertiary amine.

In contrast, strong base anion resins are predominantly functionalized with quaternary ammonium compounds [123]. A resin screening study studied 11 different anion resins and activated carbon for selective recovery of acetic acid and adsorption kinetics were developed [132] using model VFA solution in water. Resins functionalized by the tertiary amine group can adsorb the VFA as charge-neutral units to maintain neutrality and are usually preferred [133]. Amberlite^{TM} IRA-67, a weak base ion exchange resin, was successfully used to extract lactic acid successively, with no loss in adsorption capacity after resin regeneration. However, a loss in capacity for acetic acid extraction of 4.9% per reuse is observed [142]. Another important aspect of using ion-exchange resin is the opportunity to reduce end-product inhibition of VFA on its formation by continuously keeping the VFA concentration under the inhibitory levels for VFA. A 1.6-fold increase in acetic acid production using continuous in-situ extractive fermentation with the ion exchange resin Amberlite FPA 53 was found during homoacetogenic fermentation of H2 and CO2 with *Acetobacterium woodii* [121]. When studying resin re-generation and re-usability, several studies used VFA dissolved in pure water as model solutions to test the resins, and often no reduction in the adsorption capacity of the resin was noticed in these studies over extended periods [133]. Since fermentation of wet organic waste is very different from these model studies, it might be beneficial to identify the anions in the fermentation broth, which are responsible for resin exhaustion and eliminate these compounds wherever possible to prolong the operational time of the resin and decrease the need for regeneration. Deposition of salts inside the resin pores could further reduce the adsorption capacity of the resin and could be difficult to prevent for complex wastes, but this needs further study [142]

3.2. Membrane-Based Technologies

Several membrane-based technologies exist, such as vapor permeation membrane contactors [138] and membrane contactors for liquid–liquid extraction [125], which can be used to extract VFA. One of the drawbacks of using solvent extraction is the solvent

toxicity to the organisms [3]. It is, therefore, important to avoid direct contact with the fermentation broth to the solvent [29]. However, it is proposed that energy demand can be lowered up to 70% using liquid–liquid extraction with a product recovery of 99% using solvents such as hexyl acetate and nonyl acetate [146]. Using synthetic VFA mixtures, Aydin, Yesil and Tugtas [138] tested air-filled and solvent-filled PTFE membranes for their effectiveness in removing VFA and found the highest efficiency of over 95% with PTFE-trioctylamine during VFA recovery. However, membranes are susceptible to severe fouling by suspended solids in the fermentation broth, which remains a challenge. A solvent-free membrane extraction, using water as an extractant and silicone membrane, has been proposed to solve the problems with fouling, which could solve the problems with existing membrane-based technologies [143]. Several other membrane operations such as nanofiltration, microfiltration, pervaporation, membrane contactors [136] and electrodialysis are still being explored but are hindered by high operational costs and the need for particle removal. VFA extraction from different model anaerobic effluents using various membrane technologies such as reverse osmosis (RO), nanofiltration (NF), forward osmosis and supported liquid membrane technology was evaluated where RO achieved the highest retention while permeance was highest in NF [147]. Green extraction of VFA is now trending research. In one recent study, membrane extraction was coupled with electrodialysis to avoid loss of nutrients in bioreactors while increasing the extraction efficiency of VFA. This study showed a recovery efficiency of up to 98% [144]. Several other studies employing energy-efficient extraction of VFA, such as solar-assisted membrane distillation (MD), pressure-driven operations [148], and electroactive membranes, show a promising result by overcoming the current challenges such as fouling, high energy use, and permeability selectivity [149].

4. Role of VFA in Producing Sustainable Aviation Fuel

With the increasing demand for sustainable aviation fuel (SAF) to reduce anthropogenic emissions and the race towards achieving a net-zero emissions goal by no later than 2050, new technologies that convert organic waste to fuel are needed. Converting VFA to ketones via ketonization opens the door towards producing SAF from VFA. Other possible pathways include converting VFA to their respective alcohols, e.g., converting acetic acid to ethanol, followed by a secondary conversion of ethanol to SAF. However, one of the challenges is converting mixed stream VFA over a pure stream.

Recent progress on catalytic upgrading of VFA to Sustainable Aviation Fuel (SAF) includes pathways designed for mixed VFA upgrading without separating the individual acids upfront [150]. VFA produced during AAD can be upgraded catalytically to SAF by various reaction mechanisms, e.g., coupling. Depending on the chain length, SAF range carbons (C8 +) can directly undergo hydrodeoxygenation to produce SAF. In comparison, the short-chain ketones (<C8) will have to undergo a different coupling stage to produce SAF from a different pathway, i.e., aldol condensation (Figure 2) [150]. Alternatively, lower chain ketones can undergo coupling (via aldol condensation and hydrogenation/alkylation) with other bio-oil products to create fuel rage carbon molecules [151]. While the chemistry of ketonization has been well known and studied over the last several years, conversion of VFA to ketones is hindered by the complexity of the reaction mechanism [152]. E.g., a variety of oxide catalysts were studied for the conversion of acetic acid to acetone at two different temperatures (573 K and 673 K), where acetone yield is high at 97% at 673 K. In contrast, only 9% is converted to acetone at 573 K using the same catalyst (CeO_2) [153,154].

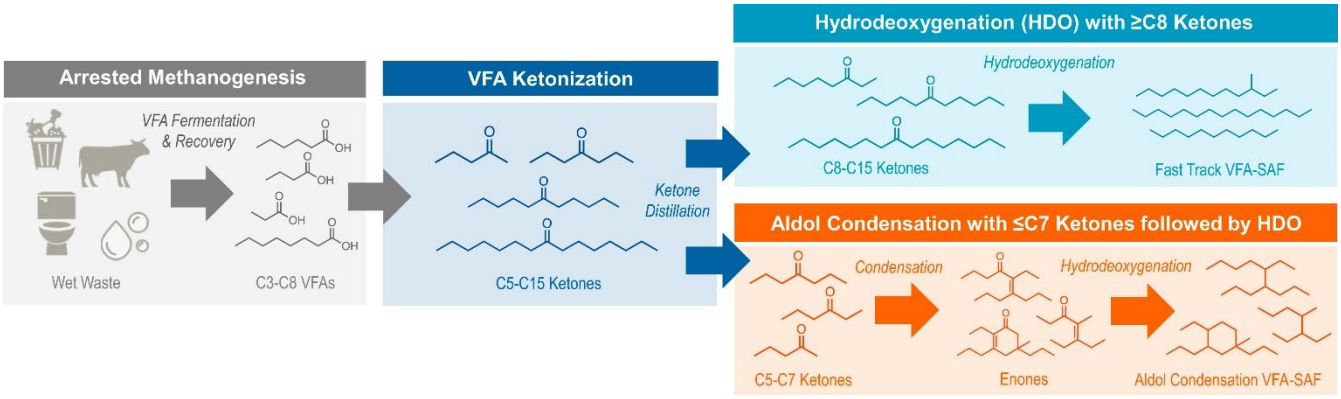

Figure 2. Overall schematic of producing SAF from VFA as platform molecule [150] (reprinted with permission).

During the ketonization of VFA (carboxylic acids), two molecules of acids react to form a ketone, water and carbon dioxide, as shown in Figure 3. When the VFA are symmetric, for e.g., two molecules of acetic acid reacting to form one ketone, the resulting ketone will have the total number of C atoms from acids minus one (in this case it will be acetone). Different ketones are formed when the same reaction occurs in mixed VFA, ranging from 2x times the reactant molecule carbon no. to varying combinations of reactants and intermediate products. In the case of unsymmetrical VFA, a new novel process that uses a metaphotoredox strategy to generate unsymmetrical ketones has been studied, which doesn't require any usage of precursors [155]. Even though this reaction has been known for years, it meets the current industrial and environmental needs for producing SAF [156]. Many recent studies showed promising results with no drop in catalyst activity even after five regeneration [157]. In one study, the ketonization of acetic acid showed a high conversion of 96% with a selectivity of 95% to acetone [158]. All these results show the potential of the ketonization reaction for producing SAF from VFA.

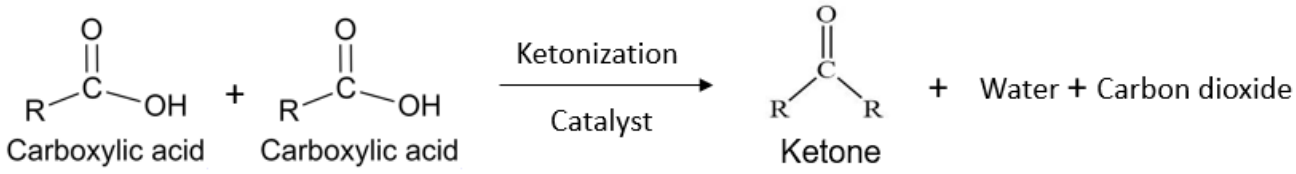

Figure 3. Ketonization of carboxylic acids. Simple reaction chemistry.

5. Conclusions

In summary, VFA makes a versatile end-product of anaerobic fermentation with high value, demand, and applicability. In a circular economy setting, the goal is to reuse waste and valorize it to meet the energy demand and VFA make the ideal intermediate to produce using anaerobic fermentation. However, the current hindrance of this technology for commercialization is represented by the problems with low VFA titers and separations of VFA from the fermentation broth when using wet organic waste materials. As shown in this review, several recent studies have shown promising solutions for overcoming these problems. VFA production might, therefore, have a bright future and be one of the important solutions for producing SAF in the future.

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