Vietnam Journal of Science and Technology ***63*** *(2) (2025) 226-248*

doi.10.15625/2525-2518/19962

A critical review on factors affecting the two-stage anaerobic digestion of biodegradable solid waste

Pham Van Dinh[1, *], Le Tho Bach[1], Pham Van Toi[1], Do Van Manh[2], Tran Thanh Liem[3]

[1]*Faculty of Environmental Engineering, Hanoi University of Civil Engineering, 55 Giai Phong Road, Hai Ba Trung District, Ha Noi, Viet Nam*

[2]*Institute of Science and Technology for Energy and Environment, Vietnam Academy of Science and Technology, 18 Hoang Quoc Viet Road, Cau Giay District, Ha Noi, Viet Nam*

[3]*Deparment of Waste Management, Ministry of Natural Resources and Environment, 10 Ton That Thuyet, Cau Giay District, Ha Noi, Viet Nam*

[*]Emails: *dinhpv@huce.edu.vn*, *dinh88.nuce@gmail.com*,

Received: 25 June 2024; Accepted for publication: 10 April 2025

Abstract. Anaerobic digestion (AD) technology has attracted considerable attention from the scientific community and has become a crucial component of sustainable solid waste management systems. It is the only biotechnological process capable of converting high-moisture biomass waste into energy through a series of biochemical steps, including hydrolysis, acidogenesis, acetate production, and methane generation. Notably, the two-stage anaerobic digestion (TAD) process, which separates methanogenesis and hydrolysis into two distinct reactors, offers significant advantages over conventional methods. The performance of AD systems is influenced by various factors, including growth conditions (such as carbon-to-nitrogen ratio, pH, and temperature), operational parameters (such as retention time and organic loading rate), feedstock pretreatment, and potential inhibitors. While these aspects have been widely studied in single-stage anaerobic digestion systems, research on their impact in TAD systems remains limited. This study aims to provide a comprehensive review of the factors affecting TAD systems. It synthesizes the latest research findings from recent years and discusses optimal operating conditions to enhance TAD performance.

Keywords: Anaerobic digestion, Inhibition, Operating parameter, Two-stage.

Classification numbers: 3.1.1, 3.4.1.

1. INTRODUCTION

Biomass energy is increasingly emerging as a key solution to support sustainable human development. According to the International Energy Agency's net-zero emission scenario, biomass energy's share is expected to rise from 6.6 % in 2020 to 13.1 % by 2030 and 18.7 % by

2050 [1]. Notably, harnessing biomass energy from waste offers a dual benefit: providing a renewable energy source while mitigating environmental pollution caused by waste.

Anaerobic digestion (AD) is the sole biotechnology capable of converting high-moisture biomass waste into energy through a series of metabolic processes, including hydrolysis, acidogenesis, acetate generation, and methanogenesis [2]. These processes can be conducted in a single reactor (single-stage anaerobic digestion - SAD) or in two separate reactors (TAD). Both SAD and TAD systems are influenced by various conditions such as temperature, pH, nutrient availability, and the presence of chemical inhibitors [2, 3]. In recent years, research has increasingly focused on optimizing these conditions to enhance the performance of biogas plants. Numerous review articles have been published to summarize, assess, and update the latest findings. For example, Ajayi-Banji *et al.* [4] examined how operational parameters affect the performance stability of solid-state SAD systems. Zhang *et al.* [5] explored anaerobic digestion of food waste (FW), focusing specifically on single-stage digesters. Mao *et al.* [6] highlighted advancements in anaerobic digestion research, particularly regarding the SAD process. Komilis *et al.* [7] analyzed the impact of operating parameters on methane production from FW in SAD systems. Nsair *et al.* [3] reviewed the operational parameters of biogas plants. While much of this research has centered on SAD systems, studies on TAD systems remain relatively limited. However, TAD systems are gaining attention due to their stability, flexibility, and resilience to fluctuations in waste stream composition [2]. Recent studies, such as those by Dinh *et al.* [2], have explored configurations and operational parameters of AD systems, including TAD systems for BMSW treatment. Srisowmeya *et al.* [8] provided foundational knowledge on TAD systems for FW decomposition, including pre-treatment processes, a comparison of SAD and TAD systems, critical parameters, current challenges, and future directions. Cremonez *et al.* [9] also discussed TAD systems in treating agro-industrial waste, with content similar to that presented by Srisowmeya *et al.* [8]. Despite these contributions, much of the existing literature primarily focuses on SAD systems, leading to a lack of clarity regarding the influence of operating parameters on each reactor within TAD systems. Additionally, several critical topics remain unmentioned, such as the mechanisms by which operational parameters affect these systems, the food-to-microorganism (F/M) ratio, and inhibitory factors specific to each reactor in TAD systems.

The aim of this study is to provide a comprehensive review of the operational parameters of TAD systems, from theoretical foundations to recent experimental research findings. The paper is organized into four sections: Section 1 introduces the current state of research and identifies gaps in the study of TAD systems. Section 2 outlines the theoretical principles of the TAD process. Section 3 delves into the factors influencing TAD performance, including the food-to-microorganism (F/M) ratio, pre-treatment methods, pH and volatile fatty acids (VFAs), temperature, retention time (RT), organic loading rate (OLR), carbon-to-nitrogen (C/N) ratio, and inhibitors. Finally, Section 4 presents the study's conclusions and key takeaways.

2. FUNDAMENTALS OF TWO-STAGE ANAEROBIC DIGESTION

The anaerobic digestion is a sequence of metabolic processes that include hydrolysis, acidogenesis, acetogenesis, and methanogenesis, as shown in Figure 1. Initially, during hydrolysis (also known as solubilization), extracellular enzymes break down high molecular weight compounds such as lipids, carbohydrates, and proteins into soluble organic matter, including fatty acids, sugars, and amino acids [2]. In the subsequent acidogenesis stage, acidogenic microorganisms convert the hydrolysis products into volatile fatty acids (VFAs) [10]. The third step (acetogenesis) converts the majority of VFAs into methane carboxylic acid

(CH_3COOH), hydrogen (H_2), and carbon dioxide (CO_2) via the activity of acetogens [8]. The fourth step (methane generation) is the most important stage in the methane production process thanks to the activity of methanogens. Methane synthesis occurs through two primary mechanisms: hydrogenotrophic and acetoclastic methanogenesis. In the first method, acetotrophic methanogens convert methane carboxylic acid into methane and carbon dioxide. The second way, hydrogenotrophic methanogens synthesize methane from carbon dioxide and hydrogen [2, 8].

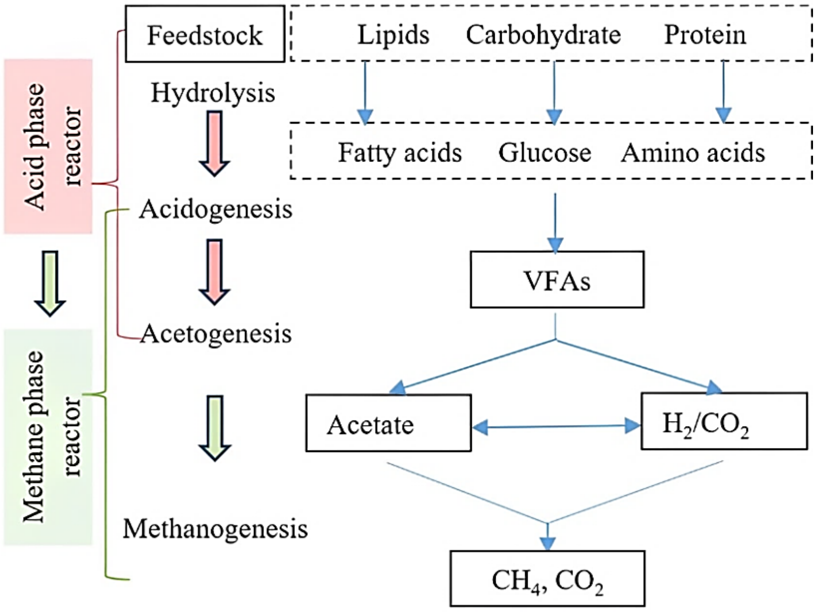

Figure 1. Phase separation in the TAD system. Adapted with modification from [5].

Methanogenesis and hydrolysis/acidogenesis have quite different growth properties. For example, the microorganisms that perform hydrolysis and acidogenic fermentation are fast-growing microorganisms (growth rates ranging from 0.05 to 1.79 h^{-1}) that favor a somewhat acidic environment [11]. Meanwhile, the microorganisms that perform the CH_4 formation step (methanogens) are slow-growing microorganisms (growth rate 0.008 to 0.173 h^{-1}) that prefer a slightly alkali environment [11]. Additionally, the acidogenic bacteria are less susceptible to variations in the concentration and composition of the incoming feed stream than the methanogenic bacteria [12]. These differences could lead to an imbalance between acid production by the acidogens and the acid consumption by the methanogens [12].

Therefore, the idea of a TAD system has been given, wherein the gas-forming and acid-forming operations are executed in different digestion reactors. The configuration and operation of TAD systems are introduced by Dinh *et al.* [2] and shown in Figure 2. The main advantages of TAD systems over SAD systems are their capacity to optimize the different phases, improving the process's performance, stability, and adaptability [2, 13]. The fundamental disadvantage of TAD systems is that their operation and maintenance requirements are higher than those of SAD systems [2]. The recent results of biogas production from experimental research on different TAD systems are shown in Table 1.

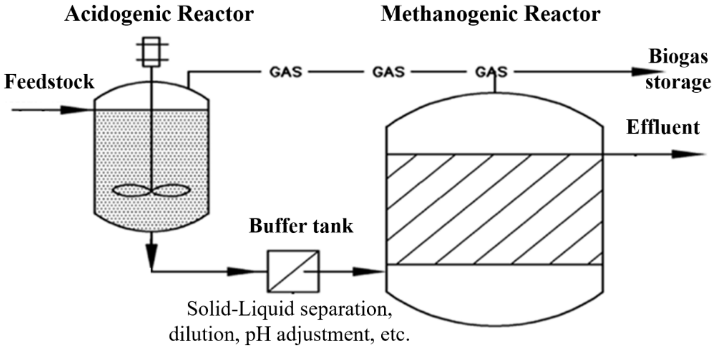

Figure 2. Configuration of a TAD system. Adapted with modification from [2].

Table 1. Recent studies on the application of TAD to deal with biodegradable solid waste

Type of waste	1st Reactor 2nd Reactor	Operation mode	TS (%)	T (°C)	pH	HRT days	OLR (g-VS/L/d)	Biogas yield (ml/g-VS)	Ref.
BMSW	CSTR/ CSTR	Semi-continuous/ Continuous	3.9/ 1.9	37/ 37	5.5-6.0/ -----	5.5/15	9 2.5	710 ml-Biogas/g-VS	[14]
BMSW	CSTR/ UASB	Batch/ Continuous	12/ 4	35-37 35-37	6.5/ 6.5	5.0/ …	16/ 5.1	451 ml-Biogas/g-VS	[13]
BMSW	CSTR/ UASB	Batch/ Continuous	12/ 3.0	35-37 35-37	6.5/ 6.5	5.0/ 3.5	16/ 7.6	405 ml-Biogas/g-VS	[13]
BMSW	CSTR/ CSTR	Semi-continuous/ Continuous	8.2/ 6.7	34.6/ 54.9	--- ---	4.6/ 7.7	16.4 7.4	560 ml-Biogas/g-VS	[15]
Swine waste & biowaste	CSTR/ CSTR	Semi-continuous/ Semi-continuous	3.9/ 3.4	55.0/ 55.9	5.5/ 7.6	3.0/ 22.0	11.2 1.16	402 ml-CH_4/g-VS	[16]
FW & wastewater	CSTR/ CSTR	Continuous/ Continuous	5.7/ 4.8	37/ 37	5.0-5.5/ 7.0-7.5	0.3/ 20.0	106 1.24	728 ml-CH_4/g-VS	[17]
FW	CSTR/ AB	Semi-continuous/ Semi-continuous	11.7/ 10.8	55.0/ 35.0	5.5/ 7.3-7.7	1.3/ 5.0	38.4 6.6	464 ml-CH_4/g-VS	[18]
FW	CSTR/ CSTR	Continuous/ Continuous	3.57/ 3.06	55.0/ 35.0	5.4/ 7.6	3.0/ 12.0	14.2 2.6	440 ml-CH_4/g-VS	[19]
FW	CSTR/ CSTR	Continuous/ Continuous	7.91/ 7.53	55.0/ 35.0	3.6/ 7.3	6.0/ 24.0	12.0 3.1	450 ml-CH_4/g-VS	[19]
Kitchen waste	CSTR/ UASB	Batch/ Continuous	12.9/ 12.5	35-37 35-37	7.0/ 7.0	3.1/ 1.0	16 20 g-COD/L/d	520 ml-CH_4/g-VS	[20]

Notes: AB: anaerobic baffled reactor; COD: chemical oxygen demand; CSTR: continuous stirred tank reactor; FW: Food waste; UASB: Upflow anaerobic sludge blanket reactor; VS: volatile solid.

3. KEY FACTORS

3.1. Food to Microorganism

The ability of the microbiota to consume the substrate is characterized by the rate of food to microorganisms (F/M). Maintaining a balanced F/M ratio is always the most important factor determining the efficiency of bioreactors. The term "food" refers to the organic matter content, which is measured as total organic carbon, COD, or VS. Meanwhile, the amount of microorganisms is generally calculated as mixed liquor volatile suspended solids (MLVSS) in the liquid phase or VS in the solid state. During anaerobic digestion, the growth rate of acidogenic microorganisms is about 10 times higher than that of acetogens and methanogens [11]. So, the F/M ratio must be low enough to maintain metabolic balance in the SAD systems. In fact, for wet SAD, methane formation has been pointed out to be stable at low values of the F/M ratio (< 0.4 g-COD/g-VS/d) [21]. For dry SAD, which is considered to be more robust than wet SAD, the suitable F/M has also been in the low range of 0.13-0.17 g-VS/g-VS/d [2]. Therefore, TAD is expected to achieve higher efficiency.

In the acidogenic reactor of the TAD system, the appropriate F/M ratio varies depending on substrate sources and operating mode. For batch mode operation, Lakeh *et al.* [22] obtained a VFA yield of 0.396 - 0.428 g-COD/g-VS when performing fermentation of BMSW with F/M 0.33 g-COD/g-VSS/d. Also, using feedstock of BMSW, Silva *et al.* [23] investigated the effect of F/M and reported that the maximal VFA production was achieved at F/M of 0.38 - 0.57 g-COD/g-VSS/d. In another test, Sreela-Or *et al.* [24] investigated F/M in the range of 0.35 - 4.38 g-COD/g-VSS/d and reported that the best fermentation was obtained at an F/M ratio of 1.24 g-COD/g-VSS. For continuous mode, thanks to the stability of the microbial system, the fermentation process can be optimized with a high F/M ratio. Nasr *et al.* [25] tested fermentation of starch at different F/M ratios within 0.50 - 2.80 g-COD/g-VS/d. They found that F/M at 1.4 provided the best condition for fermentation with the VFA yield of 0.30 g-VSS/g-starch. Recent studies have shown that with the optimal fermentation activity target, the F/M ratios of the acidogenic reactor should be in the range of 4.0 - 6.0 g-COD/g-VSS/d [21].

Table 2. Optimization of F/M ratio for methane reactor

Original substrate	Optimal F/M (survey range) (g-COD/g-VSS/d)	Operating conditions	Reactor	Ref.
Synthetic wastewater	0.5 - 0.6 (0.07 - 0.6)	28 ^oC; pH 7.0; HRT 1.5d; OLR 3 g-COD/L/d	Granular anaerobic Sequencing batch reactor	[27]
Starch wastewater	1.4 (0.5 - 3.0)	35 ^oC; pH 6.6; HRT 6.7h; OLR 54 g-COD/L/d	UASB	[25]
Grain	1.22 (0.39 - 1.88)	35 ^oC; pH 7.1; HRT 2d; OLR 10 g-COD/L/d	Anaerobic sequencing batch reactor	[31]
Food waste	0.8	37 ^oC; pH 7.55; HRT 0.44 d; OLR 15.8 g-COD/L/d	UASB	[26]
Sugarcane	6.2 ± 2.1	55 ^oC; pH 7.0; HRT 10h; OLR 86 g-COD/L/d	Anaerobic structured-bed reactor	[29]
Sucrose	6.0	25 ^oC; pH 6.5; HRT 2h; OLR 21.4 g-COD/L/d	Upflow fixed-bed anaerobic reactor	[30]
Sucrose	4.2 - 6.9	25 ^oC; pH 7.0; HRT 2h; OLR 24 g-COD/L/d	Anaerobic structured-bed reactor	[28]

The methane reactor in the TAD can reach equilibrium with much higher F/M ratios than those in the SAD. Shin *et al.* [26] reported that the anaerobic granular sludge reactor had a maximum methane yield at an F/M ratio of 0.76 g-COD/g-VSS/d. In this case, 92 % of the soluble substrate was converted to methane, and the remaining portion was probably converted to biomass. Also using granular sludge, Ong *et al.* [27] investigated the effect of F/M in the range of 0.30 - 0.60 g-COD/g-VSS/d in anaerobic SBR under mesophilic conditions and showed that the optimal F/M was at 0.60. Nasr *et al.* [25] experimented with the F/M ratio in the range of 0.50 - 3.00 g-COD/g-VSS/d and found that the optimal OLR of 54 g-COD/L/d was achieved with F/M at 1.40 g-COD/g-VSS/d. For simple substrates such as sucrose, the methane reactor could achieve an F/M ratio of up to 6.00 g-COD/g-VSS/d [28 - 30]. Optimal F/M values for the methane reactor in recent studies are shown in Table 2.

3.2. Pretreatment and solid state

Table 3. Achievements by using the different pre-treatment methods

Method	Conditions	Feedstock	Results	Ref.
Physical Methods				
Mechanical	Grinding: 8 mm to 2.5 mm	FW	Methane production rate increased by 10 - 29 % and methane yield by 9 - 34 %	[41]
Mechanical	Grinding: 0.843 mm to 0.391 mm.	FW & seed sludge	Enhance 40 % solubilization; A particle size of 0.6 mm was the best	[34]
Mechanical	Grinding: 2.14mm to 1.02 mm.	FW	The rate coefficient of the maximum substrate utilization doubled.	[42]
Ultrasound	Ultrasonic at 40 kHz power of 500 W, 35 ^{o}C	Sludge & FW	Increase VS removal efficiency by 47%	[43]
Microwave	800 W (3.5 min) at 80 °C	Sludge	Effective solubilization.	[44]
Thermal	90 ÷120 °C in 50 - 70 min	FW	Methane yield increased by 29 - 40 %.	[45]
Freezing-thaw	Frozen at -80 (6 h) and thawed at 55 °C (30 min)	FW	Increase of 16 ± 4 % COD solubilization.	[46]
Chemical method				
Acid	10 M HCl (18 °C) for 2 days	FW	Biogas production decreased by 66 %	[46]
Acid & base	NaOH and HCl	Straw	Acid pre-treatment enhances biogas yield by 43.9 % compared to alkaline pre-treatment	[47]
Biological method				
Microaeration	Composting	BMSW	Specific microbial growth rate increased by 160 - 205 %	[48]
Microaeration	Aeration, 35°C	FW & Brown water	Cumulative biogas yield increased by 21 %	[39]
Combined method				
Thermo-acid	HCl (18 °C) for 2 d and 120 °C for 0.5 h	FW	Increase 32 % COD solubilization and 40 % biogas production	[46]
Thermo-acid	1.12 % HCl (94 min) or 1.17 % HCl (86 min) at 100 °C	KW	Solubilization increased by 120 %	[49]
Biological-physicochemical	*Bacillus* 9 wt%, ultrasonic for 10 min and 500 mg/L citric acid	Oily waste water	Biogas yield increased by 280 %	[50]

In the digestion of BMSW, hydrolysis is mentioned as the rate-limiting step [32]. Hence, to accelerate the anaerobic process, many studies have studied how to drive the first step faster by breaking the complex structures of organic matter. This process is called pre-treatment. High cost of energy and material consumption is always a big restriction of pre-treatment methods. Pre-treatment methods will be applied depending on the raw material and can be categorized into three main basics: physical, chemical, and biological pre-treatments.

Physical pre-treatment methods aim to enhance the surface area of the organic matter to provide better contact between substrate and microorganisms [33]. these methods are very diverse, such as mechanical, ultrasound, microwave, thermal, and de-pressure. Among those, the mechanical method is widely used to reduce substrate particle sizes [5]. In the SAD systems, the particle size after pre-treatment is too small (< 0.6 mm), leading to accelerated VFA generation, which can cause the system to become unbalanced [5, 34]. However, in the TAD system, the smaller the particle size of the feedstock, the better the solubility, and the shorter the RT required in the fermentation reactor, which is overall good for the system. The thermal method has also received many concerns. The optimal treatment range for sewage sludge is reported to be 160 - 180 °C for 30 - 60 minutes [35]. Other recommended physical methods are shown in Table 3.

Chemical pre-treatment methods are used to destroy the complex structures (etc., cell walls or membranes) of the organic matter [36]. For this purpose, both strong acids and alkalis can be used [37]. However, strong acids may lead to creating inhibitory production for AD, such as furaldehyde ($C_5H_4O_2$) and hydroxylmethyl furfural ($C_6H_6O_3$), hence, strong acidic pretreatment is therefore typically avoided [6]. The use of an alkali pre-treatment would be preferred, with the following order of efficiency: NaOH > KOH > $Mg(OH)_2$ and $Ca(OH)_2$ [38]. Sometimes, oxidative reagents were used, such as hydrogen peroxide, ozone, fenton, peroxymonosulfate, and dimethyl dioxirane [6].

Biological pre-treatment methods are often not widespread. These methods add specific enzymes such as peptidase, carbohydrolase, and lipase to the digestion reactors under anaerobic or aerobic conditions [33]. Among them, aerobic pre-treatment is preferred. Macro- or micro-aeration can enhance the hydrolytic process effect of complex organic matter by improving hydrolytic enzymes [39]. Miah *et al*. [40] improved 210 % biogas production (at 65 ^{o}C) by increasing protease excreted by *Geobacillus* (under aerobic condition). However, this method often takes more time than others.

Besides pretreatment, the substrate's solid state also has a significant impact on the hydrolysis process. The high viscosity of the mixes due to an excessive solid content can result in inadequate mixing or the mixing process requiring too much energy [32, 51, 52]. Additionally, an increase in solid content (from 5 to 40 %) raises the concentration of inhibitors and insoluble solids, which inhibits the rate of hydrolytic conversion [52]. Longer RT than usual (10 - 15 d) is required when the feedstock has a high solid content (TS > 15 %) [32]. Therefore, when utilizing a mixed reactor, a TS of 15 - 20 % in the feedstock is commonly thought to be the top limit for hydrolysis.

3.3. Temperature

Temperature is one of the most basic environmental parameters that first determines the activity of microorganisms in general and anaerobic microorganisms in particular. The influence of temperature on AD is a combination of temperature effects on enzyme activity, bacterial growth, ionization equilibria, and substrate solubility [35]. Commonly, anaerobic microorganisms can grow in a wide range of temperatures, including psychrophilic (< 25 ^oC), mesophilic (25 - 40 ^oC), and thermophilic (> 45 ^oC) [53, 54]. The impact of temperature on microbial activity in each temperature range can be described in Figure 3.

In the acidogenic reactor, the effects of temperature are quite complex and can be regarded as two forces acting simultaneously but in opposite directions. Higher temperatures increase the rate of enzyme activities. However, the enzymes are also denatured by prolonged exposure to elevated temperatures. Therefore, enzyme activity peaks are formed for each thermal region, as illustrated in Figure 3 [55]. At high temperatures, substrate solubility also increased. Furthermore, the thermophilic regimes have increased pathogen destruction in comparison to mesophilic conditions [2]. As a result, thermophilic temperature seems to be preferable to mesophilic temperature [56]. However, according to Kozuchowska *et al.* [57] and Sánchez *et al.* [58], mesophilic conditions brought a more stable operation than thermophilic temperature. In addition, acidification enzyme activities at mesophilic temperatures were reported to be significantly higher than at thermophilic temperatures [59]. For these reasons, mesophilic hydrolysis/acidogenesis is more popular and attractive than the thermophilic process [2].

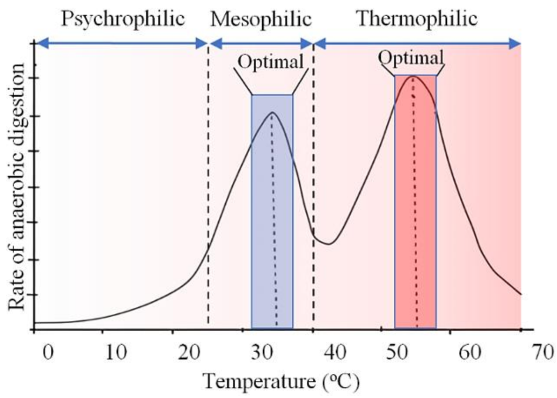

Figure 3. Effect of temperature on AD. Data was synthesized from [2, 12], and [54].

In the methanogenic reactor, an increasing temperature has several benefits, including enhanced biological and reaction rates, along with higher biogas production [53, 58, 60-62]. Thus, applying thermophilic conditions results in higher OLR. However, it should be noted that applying higher temperatures would increase free ammonia, which is inhibitory to anaerobes [63]. It's also reported that the temperature in the reactors should be prevented from oscillating as small as possible, that is, < 1 °C/day under thermophilic conditions and 2 - 3 °C/day under mesophilic conditions [64]. Moreover, the thermophilic process requires more energy for heating than the mesophilic process [65]. Therefore, it is necessary to consider the issue of energy balance.

3.4. pH and VFAs

Four steps of AD are acceptable in the pH range of 6.5 - 7.5 [32]. However, there are different optimal pH values for each of the steps. Hydrolysis could occur with a pH within 4 - 11 [66], but a pH value of 6.0 - 8.0 is often considered as an optimal range for this step [2]. For acidogenesis, a pH from 5.5 to 6.5 is the optimal range for VFA production [2, 6, 67, 68]. The acetogenic process was inhibited by pH < 3.8 [69]. A slightly acidic condition (pH of 6.0 to 6.5) is better for acetogen working, and they are less sensitive to fluctuation by pH of the incoming substrate [70], [32]. In the methanogenic process**,** methane-forming bacteria are extremely sensitive to pH value. The methanogenesis can perform in a pH range of 6.5-8.2, but the optimal value ranges from 7.0 to 7.2 [2, 6]. If the pH value is below 6.0, methane-forming bacteria can be strongly inhibited [32]. Gerardi [64] reported that methanogenesis could not occur under conditions of pH < 6.2. Mao *et al.* [6] agreed with Nayono [71] that a neutral pH value is the best condition for methanogenesis. The optimal pH values for different AD stages are shown in Figure 4.

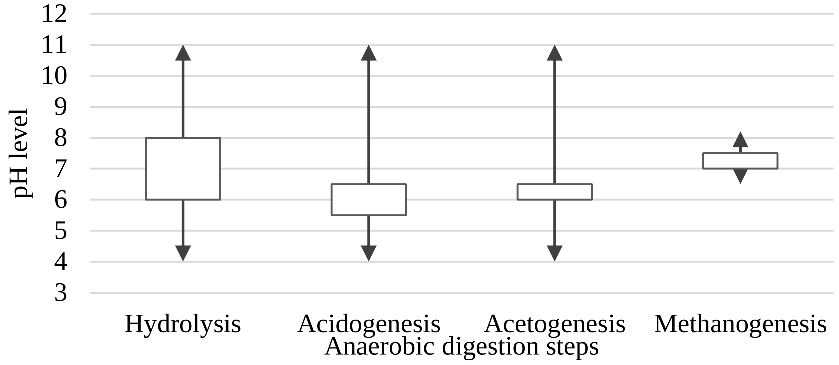

Figure 4. Optimal range of pH conditions for steps in AD. Data was synthesized from [2, 6, 66].

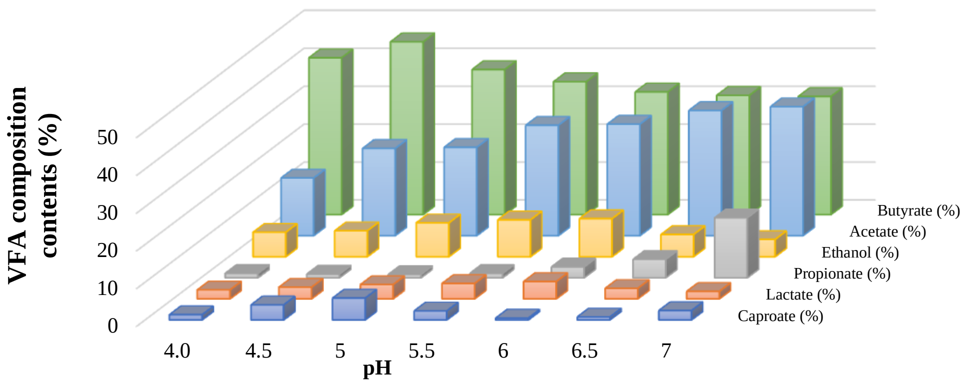

Figure 5. Influence of pH on VFA composition. Adapted with modification from [75]

The main products of acidogenesis are volatile fatty acids (VFAs), which are primarily butyric, acetic, propionic, and valeric acids [72 - 74]. The VFA composition varies depending on the substrate type. For glucose substrates, the dominant products are acetic and butyric acids [75]. For the MSW substrate, the main VFA components are acetic, propionic, and butyric acids [13]. The VFA component also changes according to pH conditions. At a low pH, the VFAs are mainly butyric and acetic acids, while propionic, butyric, and acetic acids are dominant when the pH is at neutral and slightly alkaline conditions (Figure 5) [75, 76]. The presence of acetic acid at a high rate proves that the acetogenesis process is taking place in the acid fermentation reactor. The higher ratio of acetic acid shows that the acetogenesis process is nearly complete, and it helps the gasification process in the methane tank to proceed faster. Thus, in terms of target VFA composition, mildly basic environments are better than acidic conditions.

The methanogenic process involves the consumption of VFAs, so there will be an increase in the pH of the incoming substrate flow. In addition, acidification is followed by acetogenesis, which converts $N\text{-}NH_2$ to NH_4^+, which is a buffer [13]. Thus, to achieve optimal pH conditions in the methane reactor, the incoming substrate should have pH < 7.0 [13]. The specific value will depend on the substrate characteristics. Although the TAD system is optimal for individual reactors, it disrupts the H+ ion balance between the one side that produces H+ and the other side that consumes H+. To overcome this problem, the effluent stream can be circulated back to the acid fermentation tank or intermediate tank before the methane reactor. In this case, if the pH in the acid reactor is still < 5.5, an alkaline chemical should be added to the reactor [71].

3.5. Retention time and organic loading rate

Hydraulic retention time (HRT) refers to the time substrate remains in the reactor, while solid retention time (SRT) refers to the time microorganisms are maintained in the reactor. HRT can be described by the equation HRT = V/Q, where V (L) is the reactor volume and Q (L/d) is the influent flow rate. The minimal HRT is determined by the growth rate of the slowest-growing anaerobes of the essential anaerobic microorganisms community [71]. The OLR is defined by the equation: $\mathrm{OLR} = \mathrm{C}/\mathrm{HRT}$, where C is the VS concentration of the substrate (g-VS/L) [77]. If the organic concentration of the feedstock is a constant, the relationship between OLR and HRT is inverse, and the shorter the HRT, the higher the value of OLR will be achieved [71]. When the OLR exceeds a threshold value, the accumulation of VFAs occurs, leading to pH drops. This inhibits methanogens and stops biogas production [32, 65]. Therefore, an early indication of overloading of OLR is decreasing biogas production and reducing pH value.

According to Pavan *et al.* [15], it would be safe for the hydrolysis/acidogenesis of source-sorted BMSW (TS 8.2 %) when HRT is in the range of 2 d to 3 d at the mesophilic temperature. At the same previous temperature, Paudel *et al.* [17] stated that one day of HRT was the best condition for the fermentation of FW (TS 5.7 %). For agro-industrial wastewater, Dareioti *et al.* [78] found the greatest acidogenesis efficiency even at a lower HRT (0.75 d). Overall, the HRTs of 1 d to 3 d are preferred when treating high solids waste in mesophilic environments. If the reactor is operated in batch mode, RT should be kept in the range of 7 - 12 d [2]. It is possible to enhance reactor capacity, consume less water, and use less energy by keeping the high-solid state of the feedstock. However, if the solid concentration is too high, the mixtures may become highly viscous, requiring too much energy to mix [32, 78]. Furthermore, an increase in solid content (between 5 % and 40 %) causes inhibitor and insoluble solid concentrations to rise, which in turn decreases the rate of hydrolytic conversion [52]. Additionally, when the feedstock has a high solid content (TS > 15 %), a longer RT (10 - 15 d) is required than usual [32].

In the methane reactor, to optimize biogas production under mesophilic conditions, an SRT of 20 days or more is required, whereas under thermophilic temperatures, the SRT should be between 7 and 15 days. HRT is typically shorter than SRT and can be influenced by factors such as temperature, OLR, and the characteristics of hydrolytic products. The HRT can range from just a few hours to over 20 days [2]. For sludge treatment, Turovskiy *et al.* [79] recommended an HRT of about 10 days under mesophilic conditions. Regarding food waste (FW), Paudel *et al.* [17] found that the methanogenic reactor performed optimally for biogas production under mesophilic conditions with an HRT of 20 days and an OLR of 1.24 g-VS/L/d. Recent studies have achieved significantly higher OLRs. For instance, Nagao *et al.* [80] reported a high VS removal of 92.5 % and a methane yield of 432 mL/g-VS at an OLR of 12.9 g-VS/L/d. Similarly, Paudel *et al.* [17] reached the highest biogas yield of 700 mL/g-VS removed at an OLR of 5.7 g-VS/L/d. For high-solid reactors, Rincón *et al.* [81] showed that the optimal HRT for processing solid waste from olive mills was 17 days with an OLR of 9.2 g-COD/L/d. Li *et al.* [14] observed that an OLR of up to 3.8 g-VS/L/d and an HRT of 15 days resulted in a biogas yield of 540 mL/g-VS from the digestion of BMSW under mesophilic conditions. Under thermophilic conditions, Pavan *et al.* [15] discovered that the highest biogas yield for BMSW was obtained with an OLR of 5.7 g-VS/L/d and an HRT of 12.5 days. Moreover, they suggested that the HRT for BMSW treatment under thermophilic conditions should be between 8 and 9 days.

3.6. Carbon to nitrogen

The C/N ratio is a relative measure of the balancing nutrient present in the feedstock [32]. If the C/N ratio is excessively high, the substrate will lack nitrogen, which is necessary for the microbial mass building up. On the contrary, when the C/N ratio is too low, substrate decomposition will potentially release a lot of free ammonia, which negatively affects bacterial activity [77]. Therefore, a stable long-term operation and effectiveness of AD require an appropriate balance between C and N. The recommended range for the C/N ratio in anaerobic digestion was between 20 and 30, with 25 being the optimal ratio [6, 82, 83]. However, recent studies have shown that the AD runs better at low C/N ratios (15 - 20); see Table 4.

Table 4. Optimizing C/N in AD of biodegradable waste

C/N	Materials	Reference
15.8	Food waste and cattle manure	[84]
17.0	Waste activated sludge and grass	[85]
19.6	Green waste and food waste	[86]
20.0	Green waste and food waste	[87]
20.0	Swine manure and straw	[88]
27.2	Dairy, cattle manure, and wheat straw	[89]
29.6	Rice straw and sludge	[90]

Table 5. Co-digestion of different organic substrates for AD

Feedstock	Results of co-digestion	Ref.
Cornstalk and pig manure	Improve biogas production	[95]
Food waste and waste activated sludge	Useful to improve methane production	[96]
Waste activated sludge and grass	Enhance methane production	[85]
Rice straw and sludge	Improve the bio-gasification from AD	[90]
Cow slurry, olive pomace, and apple pulp	Stable biogas production	[97]
Microalgae and sewage sludge	Increase the efficiency of methane product	[98]
Cattle manure and cardoon silage	Improve methane yield	[99]
Food waste and brown water	Improve methane yield	[100]
Food waste and yard waste	Improve methane yield	[101]
Food waste and cattle manure	Improve biogas production	[102]
Cattle manure and wheat straw	Enhance methane production	[89]
Distiller’s grains & food waste	Enhance methane production	[103]

Remarkably, single organic waste often cannot reach the optimal range of C/N ratio. For example, the carbon-to-nitrogen ratio of vegetables is 10-50 [91] and the ratio of FW is often < 15 [92-94]. Furthermore, an imbalance of nutrients in the anaerobic digestion of a single substrate may occur: while certain macronutrients (K, Na, etc.) are excessive, other trace elements (Zn, Fe, Mo, etc.) are insufficient [5, 92]. For this reason, multiple substrate types should be mixed in the digestion process (co-digestion) [2]. Co-digestion of substrates such as

FW, cattle manure, wastewater, sewage sludge, and green waste has been widely carried out, as shown in Table 5.

3.7. Inhibitions

Inhibiting compounds either already appear in the feedstock or are produced during the digestion process [37]. Inhibitors in an anaerobic reactor may cause acute or chronic toxicity. Acute toxicity is caused by the rapid exposure of un-acclimated microorganisms to a relatively high concentration of toxic waste. Chronic toxicity is caused by the gradual and relatively long exposure of an un-acclimated microorganism to a poisonous waste [64].

3.7.1. Ammonia

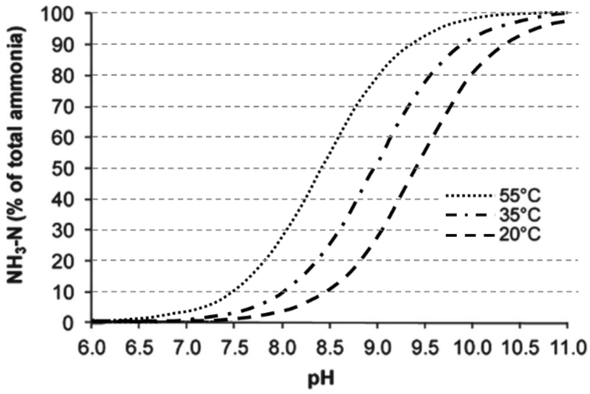

Figure 6. Effects of pH and temperature on free-NH_3 formation. Adapted with modification from [106].

Table 6. Inhibition of AD by ammonia concentrations

Operation	Results	Ref.
OLR 2.0 g-VS/L/d; T 35 °C; pH 8.0	The concentration of FAN above 0.6 g/L was the main factor influencing system stability.	[109]
TS 6.5 %, pH 7÷8.5, mesophilic and thermophilic	FAN of 215 and 486 mg/L causing biogas generation was inhibited 50 % under mesophilic and thermophilic conditions, respectively.	[110]
Review paper	The ammonia concentration of 1.7÷14 g/L resulted in decreasing 50 % of methane yield.	[107]
T 51 °C, pH 8, OLR 9.4 g-VS/L/d	FAN concentration of 1.45 g/L caused methane gas yield to decrease 50 %.	[111]
COD 4 g/L, T 55 °C, HRT 7 d	TAN from 8 to 13 g/L caused 100 % inhibition. TAN concentrations below 1.5 g/L improved methanogenic activities.	[112]
T 25 °C, pH 7.0	TAN of 3.6 g/l caused the level of *Methanosarcina* (one kind of methane-forming bacteria) to decrease from 3.8 % to 1.2 %	[113]
T 54÷60 °C, C/N 8÷35.	In high TS conditions, TAN of 1.2 g/L caused inhibition. FAN was less inhibitory in a low-solids digester than in a high TS digester.	[108]
TS 18.4 %; T 37 °C and 55 °C;	50 % inhibition at 37 °C and 55 °C by 3.0 - 3.7 g-ammonia/L for digestion of glucose.	[114]

TAN: Total ammonia nitrogen; T: Temperature.

Ammonia is mostly found as ammonium (NH_4^+) and free ammonia (FAN), which are produced during the AD process of nitrogen-rich organic feedstock [5, 104]. The concentration of FAN is primarily determined by temperature, pH, and the total ammonia concentration [105, 106]. This relation can be described in Figure 6.

Zhang *et al.* [5] reviewed many previous papers and reported that ammonia could be the buffer to enhance the AD because ammonia can neutralize the VFAs generated during the digestion process; see equations (1), (2), and (3). However, at high concentrations, free ammonia has been suggested to be one of the main inhibitors. Because free ammonia can diffuse to the cell membrane, it leads to a loss of proton balance and potassium deficiency [107, 108]. Table 6 shows the remarkable results of recent studies about the inhibition of AD by ammonia.

$$C_xH_yCOOH \leftrightarrow C_xH_yCOO^- + H^+ \quad (1)$$

$$NH_3.H_2O \leftrightarrow NH_4^+ + OH^- \quad (2)$$

$$C_xH_yCOOH + NH_3.H_2O \leftrightarrow C_xH_yCOO^- + NH_4^+ + H_2O \quad (3)$$

where C_xH_yCOOH represent the VFAs.

3.7.2. Soluble sulfide

Sulfur is commonly present in substrates and is converted to sulfide during anaerobic digestion (AD) [115]. Sulfide can exist in either a soluble form (HS-) or an insoluble form [64]. Soluble sulfide is particularly toxic because it can easily penetrate cell membranes, leading to protein denaturation and disrupting metabolic processes [37, 64]. Chen *et al.* [107] highlighted numerous studies that demonstrated the toxic effects of soluble sulfide on various microbial groups within anaerobic digesters. At a neutral pH, soluble sulfide concentrations as low as 200 mg/L can be harmful [64]. According to Peu *et al.* [115], maintaining a minimum carbon-to-sulfur ratio of approximately 40 in the substrate can reduce the formation of soluble sulfide in biogas to below 2 % (v/v). To mitigate sulfide toxicity in anaerobic digesters, adding iron is an effective strategy [64].

3.7.3. Heavy and light metals

Although many heavy metals (Ni, Co, and Mo) at trace levels are necessary for the growth activity or function of microorganisms. Exceeding trace concentrations, they may cause inhibition or toxicity for microorganisms [64, 116]; this may lead to anaerobic digester failure [64, 107]. Because at high concentrations, heavy metals could cause the interruption of the microorganism function and structure [107]. A distinctive property of heavy metals is that they cannot be biodegraded and can accumulate to fatal concentrations for the microorganism [5, 107]. Li *et al.* [116] pointed out the toxicity of heavy metals in AD in the following order: (least toxic) Pb < Cd < Cr < Zn ~ Ni << Cu (most toxic). Like heavy metals, light metals (Ca, Mg, K, Na) are also necessary for microbial growth and affect specific growth rates like any other nutrient. At low concentrations (100 - 400 mg/l), they are necessary and enhance anaerobic bacterial activity [64]. At high concentrations, they exhibit significant toxicity [64, 107]. In addition to serving as nutrients for microbial development, the majority of metals are necessary cofactors for enzymes that are part of the acetoclastic methanogenesis pathway. Additionally, it has been demonstrated that these metals are necessary for the acetotrophic process of methanogenesis, which involves hydrogenotrophic methanogenesis when acetate is converted to carbon dioxide and hydrogen [117]. Table 7 shows the reported stimulant and inhibition concentrations of some metals.

Table 7. Critical concentrations for inhibitors, summarized from [79], [6], and [117]

Substance	Stimulant concentration (mg/L)	Inhibition concentration (mg/L)	Substance	Stimulant concentration (mg/L)	Inhibition concentration (mg/L)
Al^{3+}		1000÷2500	Mg^{2+}	720	1000 ÷ 3000
As	0.7		Mn	0.027	
Ca^{2+}	100 ÷1035	2500 ÷ 8000	Mo	0.05	
Cd	1.6	36 ÷ 3400	Na+	100 ÷ 350	3500 ÷ 8000
Co	0.03÷19	35 ÷ 950	Ni^{2+}	0.03 ÷ 27	35 ÷ 1600
Cr^{6+}		3 soluble (200 ÷ 250 total)	Pb	0.2	67.2 ÷ 8000
Cr^{3+}		2 soluble (180 - 420 total)	S	-	200
Cu^{2+}	0.03÷2.4	12.5 ÷ 350	Se	0.04	
Fe	1000÷5000		W	0.04	
K+	400	2500 ÷ 28934	Zn^{2+}	0.03÷2.00	75÷1500

3.7.4. Organic compounds

Organic compounds can inhibit AD because the accumulation of non-polar organics in bacterial membranes disrupts the cell membrane [107]. Organic compounds have been reported to be poisonous to AD, including halogenated substances, alkyl benzenes, carboxylic acids, amides, phenol and alkyl phenols, ethers, ketones, aldehydes, nitrophenols, alcohols, alkanes, nitriles, amines, acrylates, and pyridine and its derivatives [107].

4. CONCLUSIONS AND RECOMMENDATIONS

The separation of hydrolysis/acidogenesis and methanogenesis in different reactors allows the TAD system to operate optimally at each, helping the system achieve a high F/M ratio and OLR load. The system can be well balanced and have a flexible operation (the two reactors do not necessarily have to operate at the same load, temperature, retention time, and pH conditions).

The efficiency of the fermentation in the hydrolytic/acidogenic reactor is firstly influenced by the pretreatment process. Among the pretreatment methods being tested, the grinding method is showing high efficiency, simplicity, and feasibility for feedstock of BMSW. In this reactor, the F/M ratio can reach 4 g-COD/g-VSS/d. pH should be between 6.0 and 6.5. The C/N nutrient ratio does not greatly affect the operation of the reactor. Retention time depends on the type of substrate. For BMSW, it should be about 3 - 5 days. The temperature should be operated in warm mode (35 - 37 ^{o}C).

In the methane reactor, the pH in the reaction tank should be maintained in the range of 7.0 - 7.2. The F/M ratio can be up to 3 g-COD/g-VS/d with an optimal range of 0.6 - 1.4 g-COD/g-VS/d. This reactor begins to be inhibited when FAN > 0.2 g/L and can fail when FAN increases to 1.45 g/L. In mesophilic conditions, the reactor is well operated with OLR in the range of 4-8 g-VS/L/d, meanwhile, the OLR can be up to 13 g-VS/L/d in thermophilic conditions.

Acknowledgments: This study is funded by the Vietnamese Ministry of Education and Training under grant number B2023-XDA-07.

Credit authorship contribution statement. Pham Van Dinh: Conceptualization, Methodology, Data Collection, Writing -Original Draft, Data Analysis, Review, Editing, and Revising. Leu Tho Bach: Review and Editing. Pham Van Toi: Data Collection and Manuscript Writing. Do Van Manh: Data Collection and Editing. Tran Thanh Liem: Review and Editing.

Declaration of competing interest. The authors declare that there is no conflict of interest regarding the publication of this manuscript. In addition, the ethical issues, including plagiarism, informed consent, misconduct, data fabrication and/or falsification, and redundancy have been completely observed.

REFERENCES

1. Gül T., Cozzi L., and Havlik P. - What does net-zero emissions by 2050 mean for bioenergy and land use, IEA, 2021. https://www.iea.org/articles/what-does-net-zero-emissions-by-2050-mean-for-bioenergy-and-land-use.
2. Dinh P. V., Takeshi F., Bach L. T., Toan P. P. S., and Giang H. M. - A review of anaerobic digestion systems for biodegradable waste: Configurations, operating parameters, and current trends, Environ. Eng. Res. **25** (2020) 1-17. https://doi.org/10.4491/eer.2018.334
3. Nsair A., Onen Cinar S., Alassali A., Abu Qdais H., and Kuchta K. - Operational parameters of biogas plants: A review and evaluation study, Energies **13** (2020) 3761. https://doi.org/10.3390/en13153761
4. Ajayi-Banji A., and Rahman S. - A review of process parameters influence in solid-state anaerobic digestion: Focus on performance stability thresholds, Renew. Sust. Energ. Rev. **167** (2022) 112756. https://doi.org/10.1016/j.rser.2022.112756
5. Zhang C., Su H., Baeyens J., and Tan T. - Reviewing the anaerobic digestion of food waste for biogas production, Renew. Sust. Energ. Rev. **38** (2014) 383-392. http://dx.doi.org/ 10.1016/j.rser.2014.05.038
6. Mao C., Feng Y., Wang X., and Ren G. - Review on research achievements of biogas from anaerobic digestion, Renew. Sust. Energ. Rev. **45** (2015) 540-555. https://doi.org/ 10.1016/j.rser.2015.02.032
7. Komilis D., Barrena R., Grando R. L., Vogiatzi V., Sánchez A., and Font X. - A state of the art literature review on anaerobic digestion of food waste: influential operating parameters on methane yield, Rev. Environ. Sci. Biotechnol. **16** (2017) 347-360. https://doi.org/ 10.1007/s11157-017-9428-z
8. Srisowmeya G., Chakravarthy M., and Devi G. N. - Critical considerations in two-stage anaerobic digestion of food waste - A review, Renew. Sust. Energ. Rev. **119** (2020) 109587. https://doi.org/10.1016/j.rser.2019.109587
9. Cremonez P. A., Teleken J. G., Meier T. R. W., and Alves H. J. - Two-Stage anaerobic digestion in agroindustrial waste treatment: A review, J. Environ. Manage. **281** (2021) 111854. https://doi.org/10.1016/j.jenvman.2020.111854
10. Chozhavendhan S., Karthigadevi G., Bharathiraja B., Kumar R. P., Abo L. D., Prabhu S. V., . . . Jayakumar M. - Current and prognostic overview on the strategic exploitation of anaerobic digestion and digestate: A review, Environ. Res. **216** (2023) 114526. https://doi.org/10.1016/j.envres.2022.114526
11. Xu S. Y., Karthikeyan O. P., Selvam A., and Wong J. W. - Effect of inoculum to substrate ratio on the hydrolysis and acidification of food waste in leach bed reactor, Bioresour. Technol. **126** (2012) 425-430. https://doi.org/10.1016/j.biortech.2011.12.059

12. USEPA - Biosolids Technology Fact Sheet: Multi-stage Anaerobic Digestion. National Service Center for Environmental Publications, 2006. https://www.epa.gov/sites/production/files/2017-04/documents/multi_stage_anaerobic_digestion.pdf.
13. Dinh P. V., and Fujiwara T. - Application of an Integrated Granular and Suspended Sludge Methane Reactor for a Two-Stage Anaerobic Digestion System to Deal with Biodegradable Municipal Solid Waste, Fermentation **9** (2023) 720. https://doi.org/10.3390/fermentation9080720
14. Li W., Guo J., Cheng H., Wang W., and Dong R. - Two-phase anaerobic digestion of municipal solid wastes enhanced by hydrothermal pretreatment: Viability, performance and microbial community evaluation, Appl. Energy **189** (2017) 613-622. https://doi.org/10.1016/j.apenergy.2016.12.101
15. Pavan P., Battistoni P., Cecchi F., and Mata-Alvarez J. - Two-phase anaerobic digestion of source sorted OFMSW (organic fraction of municipal solid waste): performance and kinetic study, Water Sci. Technol. **41** (2000) 111-118. http://wst.iwaponline.com/content/41/3/111.article-info
16. Schievano A., Tenca A., Scaglia B., Merlino G., Rizzi A., Daffonchio D., *et al.*. - Two-stage vs single-stage thermophilic anaerobic digestion: comparison of energy production and biodegradation efficiencies, Environ. Sci. Technol. **46** (2012) 8502-8510. https://doi.org/10.1021/es301376n
17. Paudel S., Kang Y., Yoo Y. S., and Seo G. T. - Effect of volumetric organic loading rate (OLR) on H2 and CH4 production by two-stage anaerobic co-digestion of food waste and brown water, Waste Manage, Oxford, 2016, pp. 484-493. http://dx.doi.org/10.1016/j.wasman.2016.12.013
18. Chu C. F., Li Y. Y., Xu K. Q., Ebie Y., Inamori Y., and Kong H. N. - A pH- and temperature-phased two-stage process for hydrogen and methane production from food waste, Int. J. Hydrogen Energy **33** (2008) 4739-4746. http://dx.doi.org/10.1016/j.ijhydene.2008.06.060
19. Wu L. J., Kobayashi T., Li Y. Y., and Xu K. Q. - Comparison of single-stage and temperature-phased two-stage anaerobic digestion of oily food waste, Energy Convers. Manage. **106** (2015) 1174-1182. http://dx.doi.org/10.1016/j.enconman.2015.10.059
20. Zhang B., Zhang L., Zhang S., Shi H., and Cai W. - The influence of pH on hydrolysis and acidogenesis of kitchen wastes in two-phase anaerobic digestion, Environ. Technol. **26** (2005) 329-340. https://doi.org/10.1080/09593332608618563
21. Fuess L. T., Eng F., Bovio-Winkler P., Etchebehere C., Zaiat M., and Nascimento C. A. O. D. - Methanogenic consortia from thermophilic molasses-fed structured-bed reactors: microbial characterization and responses to varying food-to-microorganism ratios, Brazilian J. Chem. Eng. (2022) 1-21. https://doi.org/10.1007/s43153-022-00291-x
22. Lakeh A. B., Azizi A., Koupaie E. H., Bekmuradov V., Hafez H., and Elbeshbishy E. - A comprehensive study for characteristics, acidogenic fermentation, and anaerobic digestion of source separated organics, J. Clean. Prod. **228** (2019) 73-85. https://doi.org/10.1016/j.jclepro.2019.04.223
23. Silva F., Serafim L., Nadais H., Arroja L., and Capela I. - Acidogenic fermentation towards valorisation of organic waste streams into volatile fatty acids, Chem. Biochem. Eng. Q. **27** (2013) 467-476.

24. Sreela-Or C., Imai T., Plangklang P., and Reungsang A. - Optimization of key factors affecting hydrogen production from food waste by anaerobic mixed cultures, Int. J. Hydrogen Energy. **36** (2011) 14120-14133. https://doi.org/10.1016/j.ijhydene.2011.04.136

25. Nasr M., Tawfik A., Ookawara S., and Suzuki M. - Biological hydrogen production from starch wastewater using a novel up-flow anaerobic staged reactor, BioResources **8** (2013) 4951-4968. http://doi.org/10.15376/biores.8.4.4951-4968

26. Shin H.-S., Han S., Song Y., and Lee C. - Performance of UASB reactor treating leachate from acidogenic fermenter in the two-phase anaerobic digestion of food waste, Water Res. **35** (2001) 3441-3447. https://doi.org/10.1016/S0043-1354(01)00041-0

27. Ong S., Hu J., Ng W., and Lu Z. - Granulation enhancement in anaerobic sequencing batch reactor operation, J. Environ. Eng. **128** (2002) 387-390. https://doi.org/10.1061/(ASCE) 0733-9372(2002)128:4(387)

28. Blanco V. M. C., Fuess L. T., and Zaiat M. - Calcium dosing for the simultaneous control of biomass retention and the enhancement of fermentative biohydrogen production in an innovative fixed-film bioreactor, Int. J. Hydrogen Energy. **42** (2017) 12181-12196. https://doi.org/10.1016/j.ijhydene.2017.02.180

29. Fuess L. T., Fuentes L., Bovio-Winkler P., Eng F., Etchebehere C., Zaiat M., and do Nascimento C. A. O. - Full details on continuous biohydrogen production from sugarcane molasses are unraveled: Performance optimization, self-regulation, metabolic correlations and quanti-qualitative biomass characterization, Chem. Eng. J. **414** (2021) 128934. https://doi.org/10.1016/j.cej.2021.128934

30. del Pilar Anzola-Rojas M., da Fonseca S. G., da Silva C. C., de Oliveira V. M., and Zaiat M. - The use of the carbon/nitrogen ratio and specific organic loading rate as tools for improving biohydrogen production in fixed-bed reactors, Biotechnology Reports **5** (2015) 46-54. https://doi.org/10.1016/j.btre.2014.10.010

31. Cassidy D., Hirl P., and Belia E. - Methane production from the soluble fraction of distillers' dried grains with solubles in anaerobic sequencing batch reactors, Water Environ. Res. **80** (2008) 570-575. https://doi.org/10.2175/106143007X221517

32. Ostrem K. - Greening waste: Anaerobic digestion for treating the organic fraction of municipal solid wastes, Columbia University, 2004.

33. Ariunbaatar J., Panico A., Esposito G., Pirozzi F., and Lens P. N. - Pretreatment methods to enhance anaerobic digestion of organic solid waste, Appl. Energy **123** (2014) 143-156. https://doi.org/10.1016/j.apenergy.2014.02.035

34. Izumi K., Okishio Y.-k., Nagao N., Niwa C., Yamamoto S., and Toda T. - Effects of particle size on anaerobic digestion of food waste, 2010. https://doi.org/10.1016/ j.ibiod.2010.06.013

35. Krishna D., and Kalamdhad A. S. - Pre-treatment and anaerobic digestion of food waste for high rate methane production–A review, J. Environ. Chem. Eng. **2** (2014) 1821-1830. https://doi.org/10.1016/j.jece.2014.07.024

36. Chiu S. L., and Lo I. M. - Reviewing the anaerobic digestion and co-digestion process of food waste from the perspectives on biogas production performance and environmental impacts, Environ. Sci. Pollut. Res. **23** (2016) 24435-24450. http://dx.doi.org/10.1007/ s11356-016-7159-2

37. Appels L., Baeyens J., Degrève J., and Dewil R. - Principles and potential of the anaerobic digestion of waste-activated sludge, Prog. Energy Combust. Sci. **34** (2008) 755-781. https://doi.org/10.1016/j.pecs.2008.06.002

38. Kim J., Park C., Kim T. H., Lee M., Kim S., Kim S.-W., and Lee J. - Effects of various pretreatments for enhanced anaerobic digestion with waste activated sludge, J. Biosci. Bioeng. **95** (2003) 271-275. http://dx.doi.org/10.1016/S1389-1723(03)80028-2

39. Lim J. W., and Wang J. Y. - Enhanced hydrolysis and methane yield by applying microaeration pretreatment to the anaerobic co-digestion of brown water and food waste, Waste Manage. **33** (2013) 813-819. https://doi.org/10.1016/j.wasman.2012.11.013

40. Miah M. S., Tada C., and Sawayama S. - Enhancement of biogas production from sewage sludge with the addition of Geobacillus sp. strain AT1 culture, Japanese Journal of Water Treatment Biology **40** (2004) 97-104. https://doi.org/10.2521/jswtb.40.97

41. Agyeman F. O., and Tao W. - Anaerobic co-digestion of food waste and dairy manure: Effects of food waste particle size and organic loading rate, J. Environ. Manage **133** (2014) 268-274. https://doi.org/10.1016/j.jenvman.2013.12.016

42. Kim I., Kim D., and Hyun S. - Effect of particle size and sodium ion concentration on anaerobic thermophilic food waste digestion, Water Sci. Technol. **41** (2000) 67-73. https://doi.org/10.2166/wst.2000.0057

43. Zhang Z. L., Zhang L., Zhou Y. L., Chen J. C., Liang Y. M., and Wei L. - Pilot-scale operation of enhanced anaerobic digestion of nutrient-deficient municipal sludge by ultrasonic pretreatment and co-digestion of kitchen garbage, J. Environ. Chem. Eng. **1** (2013a) 73-78. http://dx.doi.org/10.1016/j.jece.2013.03.008

44. Appels L., Houtmeyers S., Degrève J., Van Impe J., and Dewil R. - Influence of microwave pre-treatment on sludge solubilization and pilot scale semi-continuous anaerobic digestion, Bioresour. Technol. **128** (2013) 598-603. http://dx.doi.org/10.1016/j.biortech.2012.11.007

45. Li Y., and Jin Y. - Effects of thermal pretreatment on acidification phase during two-phase batch anaerobic digestion of kitchen waste, Renewable Energy **77** (2015) 550-557. https://doi.org/10.1016/j.renene.2014.12.056

46. Ma J., Duong T. H., Smits M., Verstraete W., and Carballa M. - Enhanced biomethanation of kitchen waste by different pre-treatments. Bioresour. Technol., **102** (2011) 592-599. http://dx.doi.org/10.1016/j.biortech.2010.07.122

47. Wang D., Ai P., Yu L., Tan Z., and Zhang Y. - Comparing the hydrolysis and biogas production performance of alkali and acid pretreatments of rice straw using two-stage anaerobic fermentation, Biosyst. Eng. **132** (2015) 47-55. https://doi.org/10.1016/j.biosystemseng.2015.02.007

48. Güelfo L. F., Álvarez-Gallego C., Márquez D. S., and García L. R. - The effect of different pretreatments on biomethanation kinetics of industrial Organic Fraction of Municipal Solid Wastes (OFMSW), Chem. Eng. J. **171** (2011) 411-417. https://doi.org/10.1016/j.cej.2011.03.095

49. Vavouraki A. I., Angelis E. M., and Kornaros M. - Optimization of thermo-chemical hydrolysis of kitchen wastes, Waste Manage. **33** (2013) 740-745. http://dx.doi.org/10.1016/j.wasman.2012.07.012

50. Peng L., Bao M., Wang Q., Wang F., and Su H. - The anaerobic digestion of biologically and physicochemically pretreated oily wastewater, Bioresour. Technol. **151** (2014) 236-243. http://dx.doi.org/10.1016/j.biortech.2013.10.056

51. Rosgaard L., Andric P., Dam-Johansen K., Pedersen S., and Meyer A. S. - Effects of substrate loading on enzymatic hydrolysis and viscosity of pretreated barley straw, Appl. Biochem. Biotechnol. **143** (2007) 27-40. https://doi.org/10.1007/s12010-007-0028-1

52. Kristensen J. B., Felby C., and Jørgensen H. - Yield-determining factors in high-solids enzymatic hydrolysis of lignocellulose, Biotechnol. Biofuels **2** (2009) 1-10. https://doi.org/10.1186/1754-6834-2-11

53. El-Mashad H. M., Zeeman G., van Loon W. K. P., Bot G. P. A., and Lettinga G. - Effect of temperature and temperature fluctuation on thermophilic anaerobic digestion of cattle manure, Bioresour. Technol. **95** (2004) 191-201. http://dx.doi.org/10.1016/j.biortech.2003.07.013

54. Mata-Alvarez J. - Biomethanization of the organic fraction of municipal solid wastes. Fundamentals of the anaerobic digestion process, IWA publishing, London, UK, 2003.

55. Robinson P. K. - Enzymes: principles and biotechnological applications, Essays Biochem. **59** (2015) 1. https://doi.org/10.1042/bse0590001

56. Nie E., He P., Zhang H., Hao L., Shao L., and Lü F. - How does temperature regulate anaerobic digestion? Renew, Sust. Energ. Rev. **150** (2021) 111453. https://doi.org/10.1016/j.rser.2021.111453

57. Kozuchowska J., and Evison L. M. - VFA production in pre-acidification systems without pH control, Environ. Technol. **16** (1995) 667-675. https://doi.org/10.1080/09593331608616306

58. Sánchez E., Borja R., Weiland P., Travieso L., and Martín A. - Effect of substrate concentration and temperature on the anaerobic digestion of piggery waste in a tropical climate, Process Biochem. **37** (2001) 483-489. http://dx.doi.org/10.1016/S0032-9592(01)00240-0

59. Zhuo G., Yan Y., Tan X., Dai X., and Zhou Q. - Ultrasonic-pretreated waste activated sludge hydrolysis and volatile fatty acid accumulation under alkaline conditions: effect of temperature, J. Biotech. **159** (2012) 27-31.

60. El-Mashad H. M., van Loon W. K. P., and Zeeman G. - A Model of Solar Energy Utilisation in the Anaerobic Digestion of Cattle Manure, Biosyst. Eng. **84** (2003) 231-238. http://dx.doi.org/10.1016/S1537-5110(02)00245-3

61. Kim J. K., Oh B. R., Chun Y. N., and Kim S. W. - Effects of temperature and hydraulic retention time on anaerobic digestion of food waste, J. Biosci. Bioeng. **102** (2006) 328-332. http://dx.doi.org/10.1263/jbb.102.328

62. Kim M., Ahn Y.-H., and Speece R. E. - Comparative process stability and efficiency of anaerobic digestion; mesophilic vs. thermophilic, Water Res. **36** (2002) 4369-4385. http://dx.doi.org/10.1016/S0043-1354(02)00147-1

63. Gallert C., Bauer S., and Winter J. - Effect of ammonia on the anaerobic degradation of protein by a mesophilic and thermophilic biowaste population, Appl. Microbiol. Biotechnol. **50** (1998) 495-501. https://doi.org/10.1007/s002530051326

64. Gerardi M. H. - The microbiology of anaerobic digesters. Wiley-Interscience, New Jersey, USA, 2003.

65. Zaher U., Cheong D. Y., Wu B., and Chen S. - Producing energy and fertilizer from organic municipal solid waste. Department of Biological Systems Engineering, Washington State University, 2007.

66. Zhang P., Chen Y., and Zhou Q. - Waste activated sludge hydrolysis and short-chain fatty acids accumulation under mesophilic and thermophilic conditions: effect of pH, Water Res. **43** (2009) 3735-3742. https://doi.org/10.1016/j.watres.2009.05.036

67. Jiang J., Zhang Y., Li K., Wang Q., Gong C., and Li M. - Volatile fatty acids production from food waste: Effects of pH, temperature, and organic loading rate, Bioresour. Technol. **143** (2013) 525-530. http://dx.doi.org/10.1016/j.biortech.2013.06.025

68. Lindner J., Zielonka S., Oechsner H., and Lemmer A. - Effect of different pH-values on process parameters in two-phase anaerobic digestion of high-solid substrates, Environ. Technol. **36** (2015) 198-207. https://doi.org/10.1080/09593330.2014.941944

69. Moestedt J., Nordell E., Hallin S., and Schnürer A. - Two-stage anaerobic digestion for reduced hydrogen sulphide production, J. Chem. Technol. Biotechnol. **91** (2016) 1055-1062. https://doi.org/10.1002/jctb.4682

70. Yu H., Q, and Fang H. H. P. - Acidogenesis of dairy wastewater at various pH levels, Water Sci. Technol. **45** (2002) 201-206.

71. Nayono S. E. - Anaerobic digestion of organic solid waste for energy production, Karlsruhe Institute of Technology, 2010.

72. Buyukkamaci N., and Filibeli A. - Volatile fatty acid formation in an anaerobic hybrid reactor, Process Biochem. **39** (2004) 1491-1494. http://dx.doi.org/10.1016/S0032-9592(03)00295-4

73. Cysneiros D., Banks C. J., Heaven S., and Karatzas K. A. G. - The effect of pH control and ‘hydraulic flush’ on hydrolysis and Volatile Fatty Acids (VFA) production and profile in anaerobic leach bed reactors digesting a high solids content substrate, Bioresour. Technol. **123** (2012) 263-271. http://dx.doi.org/10.1016/j.biortech.2012.06.060

74. Pham T. N., Nam W. J., Jeon Y. J., and Yoon H. H. - Volatile fatty acids production from marine macroalgae by anaerobic fermentation, Bioresour. Technol. **124** (2012) 500-503. http://dx.doi.org/10.1016/j.biortech.2012.08.081

75. Fang H. H., and Liu H. - Effect of pH on hydrogen production from glucose by a mixed culture, Bioresour. Technol. **82** (2002) 87-93. https://doi.org/10.1016/j.biortech.2003.07.013

76. Horiuchi J. I., Shimizu T., Kanno T., and Kobayashi M. - Dynamic behavior in response to pH shift during anaerobic acidogenesis with a chemostat culture, Biotechnol. Tech. **13** (1999) 155-157. https://doi.org/10.1023/A:1008947712198

77. Hartmann H., and Ahring B. K. - Strategies for the anaerobic digestion of the organic fraction of municipal solid waste: an overview, Water Sci. Technol. **53** (2006) 7-22. https://doi.org/10.2166/wst.2006.231

78. Dareioti M. A., and Kornaros M. - Effect of hydraulic retention time (HRT) on the anaerobic co-digestion of agro-industrial wastes in a two-stage CSTR system, Bioresour. Technol. **167** (2014) 407-415. https://doi.org/10.1016/j.biortech.2014.06.045

79. Turovskiy I. S., and Mathai P. - Wastewater sludge processing. Wiley-Interscience, New Jersey, USA, 2006.

80. Nagao N., Tajima N., Kawai M., Niwa C., Kurosawa N., Matsuyama T., *et al.* - Maximum organic loading rate for the single-stage wet anaerobic digestion of food waste, Bioresour. Technol. **118** (2012) 210-218. http://dx.doi.org/10.1016/j.biortech.2012.05.045

81. Rincón B., Borja R., González J. M., Portillo M. C., and Sáiz-Jiménez C. - Influence of organic loading rate and hydraulic retention time on the performance, stability and microbial communities of one-stage anaerobic digestion of two-phase olive mill solid residue, Biochem. Eng. J. **40** (2008) 253-261. http://dx.doi.org/10.1016/j.bej.2007.12.019

82. Puyuelo B., Ponsá S., Gea T., and Sánchez A. - Determining C/N ratios for typical organic wastes using biodegradable fractions, Chemosphere **85** (2011) 653-659. http://dx.doi.org/10.1016/j.chemosphere.2011.07.014

83. Li Y., Park S. Y., and Zhu J. - Solid-state anaerobic digestion for methane production from organic waste, Renew. Sust. Energ. Rev. **15** (2011) 821-826. http://dx.doi.org/10.1016/j.rser.2010.07.042

84. Zhang C., Xiao G., Peng L., Su H., and Tan T. - The anaerobic co-digestion of food waste and cattle manure, Bioresour. Technol. **129** (2013c) 170-176. http://dx.doi.org/10.1016/j.biortech.2012.10.138

85. Dai X., Li X., Zhang D., Chen Y., and Dai L. - Simultaneous enhancement of methane production and methane content in biogas from waste activated sludge and perennial ryegrass anaerobic co-digestion: The effects of pH and C/N ratio, Bioresour. Technol. **216** (2016) 323-330. http://dx.doi.org/10.1016/j.biortech.2016.05.100

86. Kumar M., Ou Y. L., and Lin J. G. - Co-composting of green waste and food waste at low C/N ratio, Waste Manage. **30** (2010) 602-609. http://dx.doi.org/10.1016/j.wasman.2009.11.023

87. Zhong W., Chi L., Luo Y., Zhang Z., Zhang Z., and Wu W. M. - Enhanced methane production from Taihu Lake blue algae by anaerobic co-digestion with corn straw in continuous feed digesters, Bioresour. Technol. **134** (2013b) 264-270. http://dx.doi.org/10.1016/j.biortech.2013.02.060

88. Wu X., Yao W., Zhu J., and Miller C. - Biogas and CH4 productivity by co-digesting swine manure with three crop residues as an external carbon source, Bioresour. Technol. **101** (2010) 4042-4047. http://dx.doi.org/10.1016/j.biortech.2010.01.052

89. Wang X., Yang G., Feng Y., Ren G., and Han X. - Optimizing feeding composition and carbon–nitrogen ratios for improved methane yield during anaerobic co-digestion of dairy, chicken manure and wheat straw, Bioresour. Technol. **120** (2012) 78-83. http://dx.doi.org/10.1016/j.biortech.2012.06.058

90. Yan Z., Song Z., Li D., Yuan Y., Liu X., and Zheng T. - The effects of initial substrate concentration, C/N ratio, and temperature on solid-state anaerobic digestion from composting rice straw, Bioresour. Technol. **177** (2015) 266-273. http://dx.doi.org/10.1016/j.biortech.2014.11.089

91. Asquer C., Pistis A., and Scano E. A. - Characterization of fruit and vegetable waste as a single substrate for the anaerobic digestion, Environ. Eng. Manag. J. **12** (2013) 89-92. http://omicron.ch.tuiasi.ro/EEMJ/pdfs/vol12/no11suppl/24_Asquer_13.pdf

92. Zhang L., Lee Y. W., and Jahng D. - Anaerobic co-digestion of food waste and piggery wastewater: focusing on the role of trace elements, Bioresour. Technol. **102** (2011) 5048-5059. https://doi.org/10.1016/j.biortech.2011.01.082

93. Zhang R., El-Mashad H. M., Hartman K., Wang F., Liu G., Choate C., and Gamble P. - Characterization of food waste as feedstock for anaerobic digestion, Bioresour. Technol. **98** (2007) 929-935. https://doi.org/10.1016/j.biortech.2006.02.039

94. Han S. K., and Shin H. S. - Biohydrogen production by anaerobic fermentation of food waste, Int. J. Hydrogen Energy. **29** (2004) 569-577. http://dx.doi.org/10.1016/j.ijhydene.2003.09.001

95. Wang M., Zhang X., Zhou J., Yuan Y., Dai Y., Li D., *et al.* - The dynamic changes and interactional networks of prokaryotic community between co-digestion and mono-digestions of corn stalk and pig manure, Bioresour. Technol. **225** (2017) 23-33. http://dx.doi.org/10.1016/j.biortech.2016.11.008

96. Alqaralleh R. M., Kennedy K., Delatolla R., and Sartaj M. - Thermophilic and hyper-thermophilic co-digestion of waste activated sludge and fat, oil and grease: Evaluating and modeling methane production, J. Environ. Manage. **183** (Part 3**)** (2016) 551-561. http://dx.doi.org/10.1016/j.jenvman.2016.09.003

97. Riggio V., Comino E., and Rosso M. - Energy production from anaerobic co-digestion processing of cow slurry, olive pomace and apple pulp, Renewable Energy **83** (2015) 1043-1049. http://dx.doi.org/10.1016/j.renene.2015.05.056

98. Olsson J., Feng X. M., Ascue J., Gentili F. G., Shabiimam M. A., Nehrenheim E., and Thorin E. - Co-digestion of cultivated microalgae and sewage sludge from municipal waste water treatment, Bioresour. Technol. **171** (2014) 203-210. http://dx.doi.org/10.1016/j.biortech.2014.08.069

99. Kalamaras S. D., and Kotsopoulos T. A. - Anaerobic co-digestion of cattle manure and alternative crops for the substitution of maize in South Europe. Bioresour. Technol., **172** (2014) 68-75. http://dx.doi.org/10.1016/j.biortech.2014.09.005

100. Rajagopal R., Lim J. W., Mao Y., Chen C. L., and Wang J. Y. - Anaerobic co-digestion of source segregated brown water (feces-without-urine) and food waste: For Singapore context, Sci. Total Environ. **443** (2013) 877-886. http://dx.doi.org/10.1016/j.scitotenv.2012.11.016

101. Brown D., and Li Y. - Solid state anaerobic co-digestion of yard waste and food waste for biogas production, Bioresour. Technol. **127** (2013) 275-280. http://dx.doi.org/10.1016/j.biortech.2012.09.081

102. Marañón E., Castrillón L., Quiroga G., Fernández-Nava Y., Gómez L., and García M. M. - Co-digestion of cattle manure with food waste and sludge to increase biogas production, Waste Manage. **32** (2012) 1821-1825. http://dx.doi.org/10.1016/j.wasman.2012.05.033

103. Wang L.-H., Wang Q., Cai W., and Sun X. - Influence of mixing proportion on the solid-state anaerobic co-digestion of distiller's grains and food waste, Biosyst. Eng. **112** (2012) 130-137. http://dx.doi.org/10.1016/j.biosystemseng.2012.03.006

104. Yenigün O., and Demirel B. - Ammonia inhibition in anaerobic digestion: A review, Process Biochem. **48** (2013) 901-911. http://dx.doi.org/10.1016/j.procbio.2013.04.012

105. Hansen K. H., Angelidaki I., and Ahring B. K. - Anaerobic digestion of swine manure: inhibition by ammonia, Water Res. **32** (1998) 5-12. https://doi.org/10.1016/S0043-1354(97)00201-7

106. Fernandes T. V., Keesman K. J., Zeeman G., and van Lier J. B. - Effect of ammonia on the anaerobic hydrolysis of cellulose and tributyrin, Biomass Bioenergy **47** (2012) 316-323. http://dx.doi.org/10.1016/j.biombioe.2012.09.029

107. Chen Y., Cheng J. J., and Creamer K. S. - Inhibition of anaerobic digestion process: A review, Bioresour. Technol. **99** (2008) 4044-4064. http://dx.doi.org/10.1016/j.biortech.2007.01.057

108. Kayhanian M. - Ammonia inhibition in high-solids biogasification: an overview and practical solutions, Environ. Technol. **20** (1999) 355-365. https://doi.org/10.1080/09593332008616828

109. Duan N., Dong B., Wu B., and Dai X. - High-solid anaerobic digestion of sewage sludge under mesophilic conditions: Feasibility study, Bioresour. Technol. **104** (2012) 150-156. http://dx.doi.org/10.1016/j.biortech.2011.10.090

110. El Hadj T. B., Astals S., Gali A., Mace S., and Mata-Alvarez J. - Ammonia influence in anaerobic digestion of OFMSW. Water Sci. Technol., **59** (2009) 1153-1158. https://doi.org/10.2166/wst.2009.100

111. Nakakubo R., Møller H. B., Nielsen A. M., and Matsuda J. - Ammonia inhibition of methanogenesis and identification of process indicators during anaerobic digestion, Environ. Eng. Sci. **25** (2008) 1487-1496. https://doi.org/10.1089/ees.2007.0282

112. Sung S., and Liu T. - Ammonia inhibition on thermophilic anaerobic digestion, Chemosphere **53** (2003) 43-52. https://doi.org/10.1016/S0045-6535(03)00434-X

113. Angenent L. T., Sung S., and Raskin L. - Methanogenic population dynamics during startup of a full-scale anaerobic sequencing batch reactor treating swine waste, Water Res. **36** (2002) 4648-4654. https://doi.org/10.1016/S0043-1354(02)00199-9

114. Gallert C., and Winter J. - Mesophilic and thermophilic anaerobic digestion of source-sorted organic wastes: effect of ammonia on glucose degradation and methane production. Appl. Microbiol. Biotechnol., **48** (1997) 405-410. https://doi.org/10.1007/s002530051071

115. Peu P., Picard S., Diara A., Girault R., Béline F., Bridoux G., and Dabert P. - Prediction of hydrogen sulphide production during anaerobic digestion of organic substrates, Bioresour. Technol. **121** (2012) 419-424. http://dx.doi.org/10.1016/j.biortech.2012.06.112

116. Li C., and Fang H. H. - Inhibition of heavy metals on fermentative hydrogen production by granular sludge, Chemosphere **67** (2007) 668-673. https://doi.org/10.1016/j.chemosphere.2006.11.005

117. Romero-Güiza M., Vila J., Mata-Alvarez J., Chimenos J., and Astals S. - The role of additives on anaerobic digestion: a review, Renew. Sust. Energ. Rev. **58** (2016) 1486-1499. https://doi.org/10.1016/j.rser.2015.12.094