Do furanic and phenolic compounds of lignocellulosic and algae biomass hydrolyzate inhibit anaerobic mixed cultures? A comprehensive review

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Introduction

Fossil fuels coming from coal, natural gas and petroleum represent about 80% of the primary energy resources consumed in the world, leading not only to their rapid depletion but also to many environmental damages, including global warming (Nigam and Singh, 2010; Saidur et al., 2011). Recently, the development of renewable energy sources has become a worldwide issue. Particularly, the production of second generation biofuels (i.e. bioethanol, biohydrogen and methane) through conversion of lignocellulosic substrates (i.e. agricultural residues, energy crops cultivated in no-arable lands and softwoods) has taken high consideration due to their composition rich in carbohydrates, their abundance, their renewability and they do not enter in competition with food feedstock (Hendriks and Zeeman, 2009; Mata-Alvarez et al., 2000; Monlau et al., 2013a; Mosier et al., 2005). Even though, most of the research has focused so far on terrestrial biomass, the utilisation of marine biomass such as micro and macro algae to produce so called "third" generation biofuels has gained a tremendous attention worldwide (Chen et al., 2013; John et al., 2011; Jung et al., 2013; Prajapati et al., 2013; Rojan et al., 2011; Ruiz et al., 2013; Sialve et al., 2009).

Among renewable biofuels, biohydrogen and methane produced respectively by dark fermentation and anaerobic digestion (AD) when operated with mixed cultures, represent promising routes for the valorisation of lignocellulosic and algal biomass (Fig. 1). Anaerobic digestion is a process consisting in four physiological steps: hydrolysis, acidogenesis, acetogenesis and methanogenesis. During AD, the biomass is transformed into biogas, a mixture of methane (CH_4) and carbon dioxide (CO_2). The process can also be stopped at the acidogenic phase, so-called dark fermentation, where VFAs (Volatile Fatty Acids) and a biogas composed of a mixture of H_2 and CO_2 are produced concomitantly. To avoid the methanogenic step, the operational parameters in the reactor are fixed to inhibit methanogens, such as low pH, short hydraulic retention time and heat-shock pre-treatment of the inoculum (Guo et al., 2010; Hawkes et al., 2007; Nath and Das, 2004).

One major challenge in using lignocellulosic biomass is their native recalcitrant structure due to their natural physicochemical barriers, which inherently provide tensile strength and protection against pests and pathogens, but also confers a resistance to hydrolysis for further conversion by anaerobic fermentative bacteria (Monlau et al., 2012a; Vancov et al., 2012). Carbohydrate compounds (i.e. cellulose and

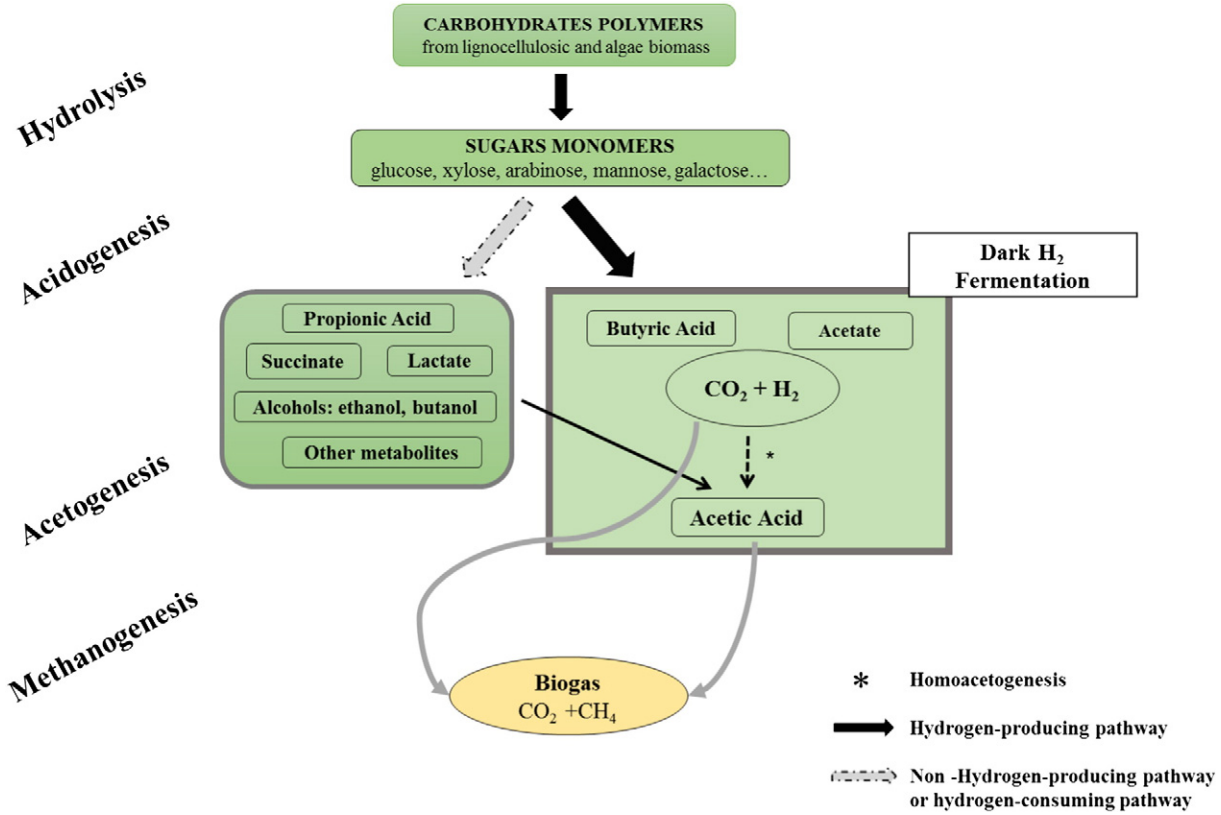

Fig. 1. Scheme of carbohydrate polymers degradation through dark fermentation and anaerobic digestion bioprocesses operated with mixed cultures (adapted from Monlau et al., 2013a).

hemicelluloses) entrapped in the lignocellulosic matrix are associated in a complex and structured form presenting natural physico-chemical barrier properties that limit their hydrolysis and degradation during the fermentative processes (Monlau et al., 2012a; Taherzadeh and Karimi, 2008). The lignin composition and content as well as the degree of polymerisation and crystallinity of cellulose, the structure of hemicelluloses, the pectin content, the accessible surface area and pore volume have been identified as the main parameters influencing the biodegradability (Monlau et al., 2012a, 2013a; Taherzadeh and Karimi, 2008). Similarly, most of the algae species present a rigid cell wall conferring a resistance to bacterial attack and limiting their degradation during the anaerobic process (Gonzalez-Fernandez et al., 2012a; Ras et al., 2010). To overcome these natural barriers, several types of pretreatment technologies commonly used for bioethanol production have been transferred with the purpose of increasing the biohydrogen and methane production from lignocellulosic residues and, more recently, from algal biomass too (Gonzalez-Fernández et al., 2011; Monlau et al., 2013a; Sambusiti et al., 2013a). Among them, thermal and thermo-chemical pretreatments, which help mainly on solubilisation of carbohydrate polymers into soluble sugars (i.e. glucose, xylose, arabinose and galactose), have gained into considerable consideration, during the past five years (Gonzalez-Fernandez et al., 2012a; Hendriks and Zeeman, 2009; Monlau et al., 2012b; Panagiotopoulos et al., 2009; Park et al., 2013; Sambusiti et al., 2013a). Even if such pretreatments are often efficient in increasing the accessibility of biodegradable compounds to microorganisms by weakening the physicochemical barriers of the lignocellulosic biomass, they release also soluble sugar-derived by-products such as furfural, 5-HMF (hydroxylmethyl furfural), or lignin-derived by-products such as vanillin, syringaldehyde and other phenolic compounds (Du et al., 2010; Fox and Noike, 2004; Monlau et al., 2012b; Sambusiti et al., 2013a). Recently, the release of furanic compounds in hydrolysates after thermal or thermo-chemical pretreatments of algal biomass was reported (Jung et al., 2011a,b; Park et al., 2011a, 2013). Their concentration and nature in the hydrolysate depend on several factors such as mainly the biomass origin, the kind of pre-treatment and, the operating conditions, i.e. contact time, pH, pressure, temperature, concentrations and solid loading (Mussatto and Roberto, 2004). The negative impact of such by-products was first reported by Mashevitskaya and Plevako (1938) who found that HMF interfered with the growth of the microorganism *Monilia murmanica*. Since, the presence of by-products has been reported as inhibitory of the ethanol fermentation (Delgenes et al., 1996; Palmqvist and Hahn-Hägerdal, 2000), xylitol (Kelly et al., 2008), butanol production (Ezeji et al., 2007), enzymatic hydrolysis (Kim et al., 2010; Ximenes et al., 2010), biohydrogen production using pure cultures (Cao et al., 2009; Tai et al., 2010; Ho et al., 2010) and, more recently, in mixed cultures (Quémeneur et al., 2012). Overall, the inhibitory effect depends greatly of the type of microorganism and metabolism. In fact, Delgenes et al. (1996) studied the effect of six lignocellulosic degradation products (vanillin, furaldehyde, hydroxymethylfuraldehyde, hydroxybenzaldehyde and syringaldehyde) added separately on batch ethanol production using glucose-fermenting *Saccharomyces cerevisiae* yeast and *Zymomonas mobilis* bacteria and two xylose-fermenting yeasts *Pichia stipitis* and *Candida shehatae*. The glucose-fermenting yeast *S. cerevisiae* and xylose-fermenting yeasts *C. shehatae* and *P. stipitis* were very sensitive to the presence of inhibitors and were almost completely inhibited by furfural, HMF, syringaldehyde and vanillin concentrations at 2–5 g L^{-1}, whereas *Z. mobilis* was found more resistant at such concentrations (Delgenes et al., 1996).

Due to their strong inhibitory effects on productivity and end-products formation, these by-products may constitute a limiting factor in the feasibility of using lignocellulosic materials for biotechnological conversion (Cao et al., 2009). To avoid the negative effect of such by-products on ethanol production, Almeida et al. (2009) proposed several processes for hydrolyzate detoxification, including evaporation, adsorption on active charcoal, adsorption on ion exchangers, solvent extraction, alkaline treatment or enzymatic treatment. However, detoxification methods increase significantly the overall costs due not only to capital and chemical costs, but also to the loss of sugars from primary material (Almeida et al., 2009). In an economic analysis of bioethanol production from willow hydrolyzate, Von Sivers et al. (1994) evaluated that the detoxification step contributed to 22% of the total cost production. Therefore, it is important to develop cheap and efficient methods for detoxification or to avoid the detoxification steps. For this purpose, it was envisaged to operate the anaerobic fermentative processes with mixed cultures, which seem to be more tolerant than ethanol-fermentative micro-organisms to these by-products. That represents a promising and sustainable alternative to produce energy from lignocellulosic and algal biomass hydrolysates without using any detoxification methods (Hendriks and Zeeman, 2009; Kaparaju et al., 2009; Monlau et al., 2012b). Torry-Smith et al. (2003) reported the implementation of an Upflow Anaerobic Sludge Blanket (UASB) reactor as purification step of bioethanol effluents to detoxify the process water for further reuse and, hence, for reducing the overall production cost of the process. By using such technology, and besides the production of methane issued from the conversion of the residual COD, the inhibitory bioethanol by-products were also mainly consumed during the anaerobic process.

So far, several papers reviewed the effects of such by-products on ethanol production (Klinke et al., 2004; Palmqvist and Hahn-Hägerdal, 2000; Taherzadeh and Karimi, 2007). However, to our knowledge, no paper summarised the effect of such by-products on anaerobic fermentative bioprocesses, operated with mixed cultures. The aim of this paper is to analyse and discuss the literature data on the effect of such by-products on biohydrogen and methane production operated with mixed cultures. First, the biochemical compositions of lignocellulosic and algal biomass are detailed and a brief description of the anaerobic fermentative processes (i.e. dark fermentation, anaerobic digestion) is made. Then, the nature of the by-products released in hydrolysates and the main factors influencing their release are reported and discussed. Finally, the impact of such by-products on both biohydrogen and methane production using mixed cultures is summarised.

Chemical composition of lignocellulosic and algal biomass

Lignocellulosic biomass

Lignocellulosic substrates are mainly composed of three types of polymers: cellulose, hemicelluloses and lignin along with smaller amounts of ash, pectins, proteins and soluble sugars (Hendriks and Zeeman, 2009; Jorgensen et al., 2007). The composition of the three main fractions (cellulose, hemicelluloses and lignin) varies according to the type, variety, part and maturity of the plant (Mosier et al., 2005; Sambusiti et al., 2013b; Vanholme et al., 2010). Table 1 presents the compositions of the main biomass components, i.e. cellulose, hemicelluloses and lignin, encountered in the most common sources of lignocellulosic biomass. Hardwoods were not considered here due to their common conversion to energy by thermo-chemical processes, which differs from fuels produced biologically.

The cellulose, as main structural constituent in plant cell walls, is a linear polysaccharide polymer of D-glucose subunits made of cellobiose units linked by β-(1 → 4) glycosidic bonds (Fengel, 1992; Fengel and Wegener, 1984). Cellulose in biomass is majorly in a form of well-organised crystalline structure and only in a small percentage as unorganised amorphous structure (Taherzadeh and Karimi, 2008). Cellulose is known to be more susceptible to microbial degradation in its amorphous form (Monlau et al., 2013a).

Hemicelluloses are composed of five-carbon (C_5) and six-carbon (C_6) sugars. The dominant sugars in hemicelluloses are mannose (C_6 sugar) in softwoods and xylose (C_5 sugar) in hardwoods and agriculture

Table 1
Chemical composition (i.e. cellulose, hemicelluloses and lignin) of various lignocellulosic substrates expressed in terms of % DM (Dry Matter) (adapted and modified from Ruiz et al., 2013).

Substrates	Cellulose (%)	Hemicelluloses (%)	Lignin (%)	References
Grass/graminae				
Wheat straw	33–40	20–34	13–18	Ruiz et al. (2013); Talebnia et al. (2010)
Sunflower stalk	34–42	19–21	12–30	Akpinar et al. (2009); Diaz et al. (2011); Monlau et al. (2012b); Ruiz et al. (2013)
Barley straw	36	12–29	8–15	Park and Kim (2012); Persson et al. (2009); Sun and Tomkinson (2005)
Rice straw	35–37	16–22	12–15	Hsu et al. (2010); Yadav et al. (2011)
Maize stems	36–38	10–30	3.5–10.5	Monlau et al. (2012a); Sun and Tomkinson (2005)
Corn stover	37–39	23–31	14–18	Lee (1997); Saha et al. (2013); Sills and Gossett (2012); Theerarattananoon et al. (2012)
Switch grass	17–36	20–28	18–26	Gnansounou and Dauriat (2010); Sills and Gossett (2012)
Sweet sorghum	27–38	15–20	10–20	Li et al. (2010) Monlau et al. (2012a)
Forage sorghum	32–36	20–23	18–26	Li et al. (2010); Manzanares et al. (2012)
Miscantus	38–43	24–37	19–25	Brosse et al. (2009); Kurakake et al. (2001); Velasquez et al. (2003)
Switchgrass	33–41.2	26–31	17–19	Hu et al. (2011); Keshwani and Cheng (2009)
Softwood				
Larix leptolepis	43	24	29	Park and Kim (2012)
Eucalyptus	34–44	18–19	19–30	Gnansounou and Dauriat (2010); Park and Kim (2012); Romani et al. (2010)
Softwood stems	40–50	25–35	25–35	Sun and Cheng (2002)
Pinus radiata	45	22.5	27	Araque et al. (2008)
Spruce	44	21	29	Shafiei et al. (2010)
Cellulose waste				
Newspapers	60.3	16.4	12.4	Lee et al. (2010)
Paper sludges	60.8	14.2	8.4	Peng and Chen (2011)

residues (Emmel et al., 2003; Sun and Cheng, 2002). Hemicelluloses also contain small amounts of acetyl groups (Monlau et al., 2013a).

Finally, lignin is the third most abundant polymer in nature, after cellulose and hemicelluloses. Lignin is a main constituent of cell walls, providing to the plant its structural rigidity, impermeability and resistance against microbial attack and oxidative stress (Monlau et al., 2013a; Taherzadeh and Karimi, 2008). Three phenyl propionic alcohols exist as monomers of lignin: (i) coniferyl or guaiacyl alcohol (G), (ii) coumaryl or 4, hydroxycinnamyl alcohol (H) and (iii) sinapyl or syringyl alcohol (S). The nature and the quantity of lignin monomers (H, G and S) vary according to the plant species, its maturity and their spatial localisation within the cells (Barakat et al., 2012; Yoshizawa et al., 1993). Lignin from softwoods (gymnosperms) contains mainly guaiacyl units, those from hardwoods (angiosperms) mainly guaiacyl and syringyl units, whereas the lignin from herbaceous plants (non-woody or graminae) contains all the three units (H, G, S) in significant amounts but at different ratios, G and S units being the main ones (Billa and Monties, 1995; Boerjan et al., 2003; Lapierre et al., 1986; Vanholme et al., 2010).

Algal biomass

Algal biomass has been recently investigated as a possible and complementary alternative to lignocellulosic substrates to produce biofuels, due to several advantages, such as (1) a higher productivity yields, (2) they do not require arable lands for growth and therefore do not outcompete food resources, and (3) they can grow in a variety of environments including fresh water, salt water and municipal wastewaters (Chisti, 2007; Sialve et al., 2009; N. Wei et al., 2013). Commonly, algae are grouped in two main categories, i.e. micro and macro algae, based on their morphology and size (John et al., 2011). Microalgae are microscopic photosynthetic organisms and mainly unicellular. In contrast, macroalgae are composed of multiple cells and organised in structure resembling to roots, stems and leaves of higher plants (Chisti, 2008; John et al., 2011). Macroalgae are classified into three categories i.e. red, green and brown, according to the thallus color derived from the presence of natural pigments and different types of chlorophylls (Jung et al., 2011b; Park et al., 2011a; Sze, 1993). During their growth, algae can accumulate carbohydrates, lipids and proteins over a short time period (John et al., 2011). The proportion of the different components depends mainly to the environmental culture conditions such as irradiance, pH, temperature and nitrogen depletion (Chen et al., 2013). Table 2 shows the composition in terms of lipids, proteins and carbohydrates encountered in the most common sources of marine algae. Generally, macroalgae are characterised by lower contents of proteins and lipids but higher carbohydrates content compared to microalgae. Since carbohydrates are the precursors of furanic derivatives (i.e. furfural, 5-HMF) a special focus on their nature in both macroalgae and microalgae is made here below.

The carbohydrate composition in macroalgae depends mainly on their category: brown, red or green. The main carbohydrates in green algae correspond to mannan, ulvan, starch and cellulose (Jung et al., 2011b). In contrast, the main carbohydrates in brown algae are alginates, laminarin and mannitol, while red algae are mainly composed of cellulose, agarose, agaropectin and carrageenan (Andrade et al., 2004; Park et al., 2011a, 2013; Whyte and Englar, 1981). Interestingly, some macroalgae strains such as *Saccharina japonica*, *Laminaria japonica* and *Gelidium amansii*, were reported to have carbohydrates content up to 50%, as shown in Table 2.

As shown also in Table 2, some microalgae strains present naturally high carbohydrate contents. Carbohydrates generally accumulate in plastids as reserve materials (i.e. starch), or are the main constituent of cell wall (Chen et al., 2013). Cell walls of microalgae consist of an inner cell wall layer and an outer cell wall layer and their composition varies from one species to another (Chen et al., 2013). The outer cell wall is generally composed of polysaccharides such as pectin, agar and alginate whereas the inner cell wall layer is mainly composed of cellulose (Yamada and Sakaguchi, 1982).

Anaerobic fermentative processes

In this section, a brief description of the dark fermentation and anaerobic digestion processes operated with mixed cultures is presented. In Fig. 1, a conceptual scheme of the different steps occurring in dark fermentation and anaerobic digestion are represented. Here, only carbohydrate conversion was considered as such polymers are also precursors of furanic derivatives compounds from lignocellulosic and algal biomass.

Dark fermentation

Biohydrogen can be produced by dark fermentation that constitutes an intermediate part of the full anaerobic digestion process, involving H_2-producing fermentative bacteria and where the last methanogenic step does not occur. To avoid methanogenesis, pure cultures can also be used, but mostly mixed culture consortia are preferred since they are less expensive, easier to operate because of the absence of sterile

Table 2
Chemical composition (i.e. lipids, proteins and carbohydrates) of various macro and micro algae expressed in terms of % DM.

Subsubstrates	Lipids (%)	Proteins (%)	Carbohydrates (%)	References
Macroalgae				
Green algae				
Codium fragile	1.8	10.9	32.3	Jung et al. (2011b)
Enteromorpha linza	1.8	31.6	37.4	Jang et al. (2012)
Ulva Lactuca	6.2	20.6	54.3	Kim et al. (2011)
Red algae				
Gelidium amansii	0–3.1	15.6–16.3	61–67.3	Jung et al. (2011b); Park et al. (2011a)
Porphyra tenera	4.4	38.7	35.9	Jung et al. (2011b)
Gracilaria verrucosa	3.2	15.6	33.5	Jung et al. (2011b)
Brown algae				
Laminaria Japonica	1.8–2.4	9.4–14.8	51.9–59.7	Jung et al. (2011b); Kim et al. (2011)
Hizikia fusiforme	0.4–1.5	5.9–13.9	28.6–59	Jang et al. (2012); Jung et al. (2011b)
Saccharina japonica	0.5	19.9	44.5	Jang et al. (2012)
Sargassum fulvellum	1.6	10.6	66	Jang et al. (2012)
Ecklonia stolonifera	2.4	13.6	48.6	Jung et al. (2011b)
Unduria pinnatifida	1.8–2.0	15.9–18.3	40.1–52	Jang et al. (2012); Jung et al. (2011b)
Sargassum fulvelum	1.4	13	39.6	Kim et al. (2011)
Microalgae				
Scenedesmus obliqus	12–14	50–56	10–17	Becker (1994)
Scenedesmus dimorphus	16–40	8–18	21–52	Becker (1994)
Chlorella vulgaris	14–22	51–58	12–17	Becker (1994)
Porphyridium cruentum	9–14	28–39	40–57	Becker (2007)
Spirogyra sp.	11–21	6–20	33–64	Becker (1994)
Prymnesium parvum	22–38	28–45	25–33	Becker (1994)
Porphyridium cruentum	9–14	28–39	40–57	Becker (1994)
Anabaena cylindrica	4–7	43–56	25–30	Becker (1994)
Spirulina Platensis	16	42	11	Sydney et al. (2010)
Euglena gracilis	14–20	39–61	14–18	Becker (2007)
Dunaliela tertiolecta	11	29	13	Sydney et al. (2010)
Dunaliela salina	6–9	12–57	32–55	Becker (2007); Feinberg (1984)
Chlamydomonas	23	17	59	Feinberg (1984)
Cyclotella cryptica	18	13	67	Feinberg (1984)

conditions and convert a broader source of substrates (Guo et al., 2010; Ntaikou et al., 2010). Fermentative H_2-producing mixed cultures are easily sampled from natural environments, such as soils and anaerobic sludge (Ntaikou et al., 2010). One major disadvantage of using mixed cultures is the presence of no-hydrogen-producing microorganisms such as methanogens, homoacetogens, sulfate-reducing bacteria (SRB) and lactic acid bacteria (LAB). Furthermore, metabolism of these fermentative bacteria are involved in either a direct consumption of hydrogen or generate by-products such as propionate, ethanol and lactate that are produced through a zero-H_2 producing pathway (Guo et al., 2010; Ntaikou et al., 2010).

Among these no-hydrogen producing species, methanogens are considered as the main hydrogen-consuming microorganisms and can be deactivated in methanogenic inoculum by using several pretreatments such as heat shock, pH shock or addition of chemical inhibitors (i.e. bromoethanesulfonate, acetylene, inorganic acids and chloroform) (S. Chang et al., 2011; Guo et al., 2010; Sarkar et al., 2013). Such inoculum pretreatments utilise the capacity of some acidogenic H_2-producing bacteria, ie. *Clostridium* sp. to sporulate at high temperatures and germinate when the environmental conditions become favourable again while the non-spore-forming microorganisms i.e. methanogenic archae are eradicated (Argun et al., 2008; Fang et al., 2006; Lay et al., 2003).

There are two common pathways in the production of biohydrogen by dark fermentation: one producing acetate and the second butyrate, as shown in Fig. 1. Theoretically, 4 mol of hydrogen can be produced from glucose through the acetate pathway and 2 mol through the butyrate pathway (Antonopoulou et al., 2006). When using mixed cultures, metabolic pathways are more variable in regards to the composition and structure of the microbial community, the type and concentration of substrates and the operating conditions. Hawkes et al. (2007) suggested an average theoretical pathway for mixed cultures leading to 2.5 mol H_2 mol^{-1} hexose and a ratio of butyrate/acetate of 3:2. However, recent studies showed that acetate accumulation and consequently butyrate/acetate ratio do not correlate with biohydrogen production and only the amount of easily accessible sugars can predict the amount of biohydrogen that can be produced (Guo et al., 2014; Monlau et al., 2012a).

Anaerobic digestion

Anaerobic digestion corresponds to a full microbiological degradation process under anaerobic conditions leading to stabilisation of organic matter and the formation of a biogas composed mainly of CH_4 (55–75%) and CO_2 (25–45%). Commonly, mixed consortia used for anaerobic digestion include a large range of inoculum, such as municipal anaerobic digested sludge, rumen liquor from cattle, digestate from agricultural anaerobic digestion plant and organic fraction from municipal solid wastes.

Microbial ecology in anaerobic digestion is complex and involves several microbial groups at each step of the process. Anaerobic digestion is generally divided into four main steps, so-called hydrolysis, acidogenesis, acetogenesis and methanogenesis (Fig. 1). During the hydrolysis step, organic polymers, such as carbohydrates, are hydrolysed into simple sugars monomers. Hydrolytic bacteria, known as primary fermenting bacteria, are facultative anaerobes and hydrolyse the substrate with extracellular enzymes. A wide range of enzymes, i.e. cellulases, hemicellulases, proteases, amylases and lipases, can be produced at this stage (Taherzadeh and Karimi, 2008). When microorganisms produce suitable enzymes, hydrolysis is a relatively fast step. In contrast, if the substrate is not fully accessible to enzymes, as in the case of lignocellulosic substrates, hydrolysis becomes the rate-limiting step (Taherzadeh and Karimi, 2008). During acidogenesis, primary fermentative bacteria convert hydrolysis products to a biogas composed of CO_2 and H_2 and to microbial metabolites including volatile fatty acids, i.e. acetate, propionate, butyrate and valerate, other acids, such as lactate, succinate and alcohols, i.e. ethanol, butanol, acetone. Acidogenic bacteria are

able to metabolise organic compounds at very low pH around 4. Methanogenic microorganisms cannot use directly all products from the acidogenic step. Except for acetate, H_2 and CO_2, they have to be further transformed, during a so-called acetogenic phase, to acetate, hydrogen and carbon dioxide by secondary fermenting bacteria, also called Obligate Hydrogen-Producing Bacteria (OHPB). However, thermodynamics of these reactions are unfavourable and these microorganisms can only live in syntrophy with end-product users, i.e. methanogens. Indeed, the methanogenic step corresponds to the final conversion of acetate, carbon dioxide (CO_2) and hydrogen (H_2) into a biogas which is composed mainly of CH_4, and CO_2. Methanogenic microorganisms involved are obligate anaerobic archaea and two groups of methanogens are mainly distinguished, the hydrogenotrophic and acetoclastic methanogens, which transform the mixture CO_2/H_2 and acetate into methane, respectively. Hydrogenotrophic microorganisms convert H_2 and CO_2 produced by fermentative bacteria into CH_4, keeping a low hydrogen partial pressure and thus supporting the growth of acetogenic bacteria. The relative abundance of hydrogenotrophs and acetotrophs are variable according to environmental factors (i.e. acetate, ammonia, hydrogen and hydrogen sulphide concentrations) and operating conditions (i.e. Hydraulic Retention Time, pH, type of substrate and source of inoculum) (Demirel and Scherer, 2008) as well as solid contents (Abbassi-Guendouz et al., 2013). During start-up of anaerobic digesters, it was reported that hydrogenotrophic methanogens (i.e. *Methanoculleus*, *Methanobacterium*) are first dominant with a subsequent decrease of the H_2 concentration and, after stabilisation of the process, a shift to acetoclastic methanogens (i.e. *Methanosarcina*, *Methanosaeta*) occurs (Demirel and Scherer, 2008; Illmer et al., 2014).

Furthermore, high levels of ammonia favour the dominance of hydrogenotrophic methanogens in mesophilic anaerobic digestors (Kampmann et al., 2012; Krakat et al., 2010). Approximately 65–70% of the methane produced in anaerobic digesters comes from acetate, when acetotrophic methanogens are dominant, otherwise, in absence of acetoclastic methanogens such as *Methanosaeta* sp., acetate oxidation to H_2 and CO_2 is the main dominant pathway (Karakashev et al., 2006).

By-products from algae and lignocellulosic biomass hydrolyzate

Nature of by-products

To overcome natural physico-chemical barriers of lignocellulosic and algae biomass, a pretreatment step is generally applied prior to anaerobic fermentation (Gonzalez-Fernandez et al., 2012b, 2013; Jung et al., 2011a, b; Ruiz et al., 2013). Generally, pretreatment methods are divided into three main categories: physical, thermo-chemical and biological processes as well as a combination of these (Mosier et al., 2005). Among them, thermal and thermo-chemical pretreatments have been widely investigated to overcome the physico-chemical barriers of lignocellulosic biomass and algae to enhance biofuel production (Gonzalez-Fernandez et al., 2012b; Monlau et al., 2013a; Ruiz et al., 2013; Sambusiti et al., 2013a; Taherzadeh and Karimi, 2008). Besides solubilisation of carbohydrate polymers into soluble sugars (mainly glucose, xylose and arabinose), such pretreatments also lead to the generation of derived lignocellulosic by-products as shown in Fig. 2 (Jönsson et al., 2013; Mussatto and Roberto, 2004; Palmqvist and Hahn-Hägerdal, 2000). These by-products are generally divided into three groups: furans, weak acids and phenolic compounds.

Furanic compounds such as furfural and 5-HMF originate from the dehydration of pentose and hexose simple sugars, respectively. A recent study reviewed the different routes of furfural and HMF formation from simple sugars. At least four routes for the formation of HMF from glucose and three routes for furfural formation from xylose were identified (Rasmussen et al., 2014).

Phenolic compounds, such as vanillin and syringaldehyde, are generated from the degradation of syringyl (S) and guaïacyl (G) units of lignin polymers, respectively (Barakat et al., 2012). Recent findings showed that biomass monomeric sugars can further react to form pseudo-lignin compounds when exposed to severe pretreatments conditions (Sannigrahi et al., 2011). This phenomenon results in an increase of the acid insoluble Klason lignin content. Hu et al. (2012) observed also the generation of pseudo-lignin compounds during dilute-acid pretreatment of hybrid poplar. They suggested that 3,8-dihydroxy-2-methylchromone and 1,2,4-benzenetriol derived from furfural and 5-HMF, respectively, were the key intermediates of pseudo-lignin formation during polymerisation and/or condensation reactions.

Lignocellulosic hydrolyzates contain also weak acids mainly acetate, formic acid and levulinic acid (Jönsson et al., 2013). Palmqvist and Hahn-Hägerdal (2000) reported that furfural and 5-HMF can be indeed degraded into weak acids (i.e. formic acid and levulinic acid) under very strong pretreatment conditions (i.e. high acidity and/or high temperature). Acetate is generated after hydrolysis of hemicellulose acetyl groups during thermal and thermo-chemical pretreatments (Panagiotopoulos et al., 2011).

Factors influencing the release of by-products

The presence of derived lignocellulosic by-products was reported previously after various types of pretreatment of lignocellulosic materials, such as microwaves (Jackowiak et al., 2010), steam explosion (Badshah et al., 2012; Cantarella et al., 2004; Di Girolamo et al., 2013), liquid hot water (Kaparaju et al., 2009; Monlau et al., 2012b; Sambusiti et al., 2013a), subcritical water (Fox et al., 2003), wet oxidation (Du et al., 2010; Fox and Noike, 2004; Klinke et al., 2002) or thermo-chemical pretreatments (Du et al., 2010; Fox et al., 2003; Larsson et al., 1999; Monlau et al., 2012b). In Table 3, the effects of various thermal and thermo-chemical pretreatments on the release of the most commonly found by-products (i.e. furfural, 5-HMF, phenol, acetate and formic acid) in lignocellulosic hydrolyzates are summarised. The composition in by-products (Table 3) depends mainly on the type of biomass as well as on the nature and severity of the pretreatment (Mussatto and Roberto, 2004; Panagiotopoulos et al., 2011). The by-products listed here are not exhaustive since, in a recent study, Du et al. (2010) reported 40 potential inhibitory by-products generated during various thermal and thermo-chemical pretreatments of different lignocellulosic biomass. Furfural and 5-HMF are mostly formed at low pH (i.e. thermal and thermo-acid pre-treatment) and generally negligible at high pH (i.e. thermo-alkaline pre-treatment) (Du et al., 2010; Monlau et al., 2012b). In contrast, at high pH, phenolic compounds are preponderant because such pre-treatment has mainly an effect on lignin degradation (Monlau et al., 2012b; Naseeruddin et al., 2013; Taherzadeh and Karimi, 2008).

Recently, Panagiotopoulos et al. (2011) found that the ratio $\sum$ (soluble sugars)/$\sum$ (inhibitors) can be used as a good tool for assessing the suitability of a hydrolyzate to be further fermented (Table 3). As the ratio $\sum$ (soluble sugars)/$\sum$ (inhibitors) depends not only on the nature of the biomass but also on pretreatment severity (temperature, residence time and chemical concentration), a severity factor (R_0) and a combined severity factor (CS) were proposed to compare thermal and thermo-chemical pretreatments, respectively (Panagiotopoulos et al., 2011; Pedersen and Meyer, 2010). Severity factor Ro is used to compare results of thermal pretreatments carried out at different temperature and time conditions (Overend and Chornet, 1987; Ruiz et al., 2013). The R_0 severity factor is generally expressed using a Log function as shown in Eq. (1).

$$\text{Log } R_0 = \text{Log}[t \ \exp[(T-100)]/14.75] \quad (1)$$

where t corresponds to reaction time (min), T is the temperature (°C), 100 is the temperature of reference and 14.75 is an empirical parameter related with activation energy, assuming pseudo first order kinetics. The results are usually represented as a function of log (R_0).

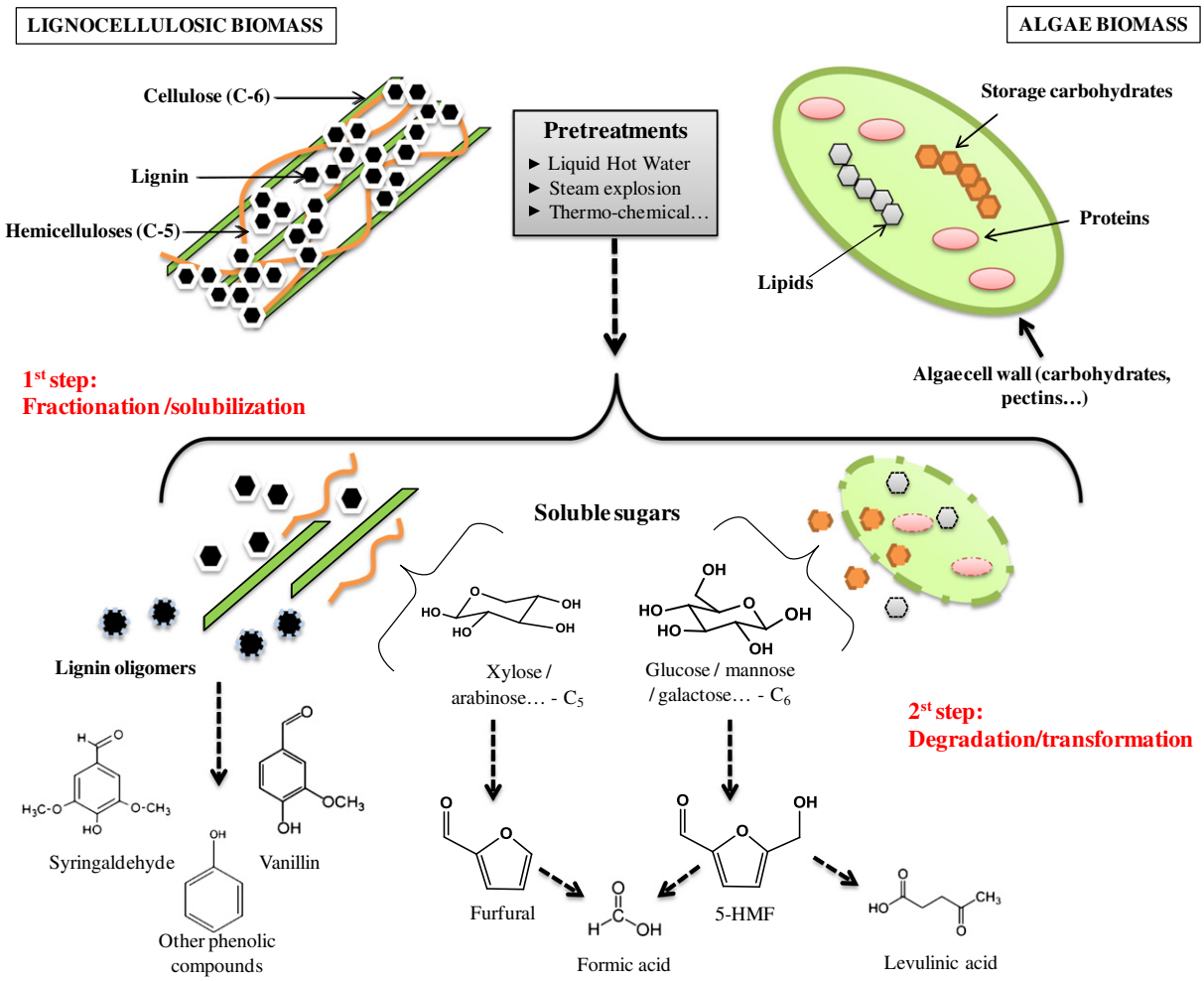

Fig. 2. Global scheme of by-products generation (i.e. aliphatic acids, furanic derivatives and phenolic compounds) after thermal and thermo-chemical pretreatments of lignocellulosic and algal biomass.

A combined severity (CS) factor taking into account the pH value of the liquor after dilute-acid pretreatment was proposed to consider additional effect of the acid catalyst (Abatzoglou et al., 1992; Di Girolamo et al., 2013; Larsson et al., 1999; Panagiotopoulos et al., 2011; Park et al., 2013). The combined severity factor is defined in Eq. (2)

$$CS = \log(R_0) - pH \quad (2)$$

However, such equations did not consider the effect of pH variation, which increases during thermo-alkaline pretreatment. For this reason a combined severity (CS_2) factor was proposed (Pedersen and Meyer, 2010). The severity of the pretreatment procedure at basic pH values can here be easily compared by using Eq. (3) (Pedersen and Meyer, 2010)

$$CS_2 = \log(R_0) + |pH - 7| \quad (3)$$

Recently, the use of thermal and thermo-chemical pretreatments on algal biomass (i.e. microalgae, macroalgae) or lipid extracted algae residues were reported and an increase of anaerobic fermentation performances was shown (Jung et al., 2011a,b; Gonzalez-Fernandez et al., 2012b, 2013; Keymer et al., 2013; Ruiz et al., 2013). The lack of lignin in algal biomass makes simpler the use of pre-treatments and the conditions required for the solubilisation of carbohydrate polymers are less drastic than those used with lignocellulosic residues (Ruiz et al., 2013). Nonetheless, generation of furan derivatives (i.e. furfural and 5-HMF) was reported in algae biomass hydrolyzates likely by degradation of the carbohydrate polymers such as cellulose, starch, agar and alginate compounds (Fig. 2 and Table 3) (Chen et al., 2013; Jung et al., 2011a,b; Park et al., 2011a; Yun et al., 2013). Jung et al. (2011b) reported furfural contents ranging from 1.79 g L^{-1} to 4.84 g L^{-1} after thermal pre-treatment of the brown macroalgae *L. japonica* at 170 °C during 5 and 40 min respectively. Jung et al. (2011a) reported 5-HMF concentrations ranging from 2 g L^{-1} to 8 g L^{-1} after thermo dilute-acid pre-treatment of *S. japonica*. Consistently, Yun et al. (2013) reported 5-HMF generation between 0.2 g L^{-1} and 4.3 g L^{-1} after dilute acid pre-treatment of the microalgae *C. vulgaris*.

Effect of by-products on biological anaerobic process using mixed cultures

Furanic and phenolic compounds were reported to inhibit enzymatic hydrolysis of various fermentative bacteria in pure-culture bioprocesses operated for ethanol, biohydrogen, xylitol, butanol and lipid production (Cao et al., 2009; Delgenes et al., 1996; Ezeji et al., 2007; Ho et al., 2010; Kelly et al., 2008; Ximenes et al., 2010). The effect of weak acid mainly acetate derived from acetyl groups of hemicelluloses, which was already reported to have a negative effect on ethanol fermentation, will not be discussed here. Indeed, acetate is a metabolic intermediate of anaerobic digestion and higher concentration of acetate than generally reported in lignocellulosic hydrolyzates can be easily tolerated by anaerobic consortia. Concerning biohydrogen production through dark fermentation, until now no work reported the effect of initial acetate addition on dark fermentation process operated with mixed cultures. Nevertheless,

Table 3
Composition of various hydrolyzates issued from algae and lignocellulosic biomass in terms of soluble carbohydrates and by-products generation.

Pretreatments	Substrates	Pre-treatment conditions	Soluble sugars and by-products concentration (g L^{-1})								∑ soluble sugars/∑ furans[b]	∑ soluble sugars/∑ furans + phenols	References
			Hexose sugars	Pentose sugars	Soluble sugars[a]	Furfural	5-HMF	Phenols	Acetate	Formate			
Thermal	Corn stover	Hot water, 200 °C, 10 min; biomass/liquid:1:20; log Ro = 3.94	3.7	8.8	12.5	1	0.2	–	5.3	–	10.4	–	Bondesson et al. (2013)
	Eucalyptus	Hot water, 200 °C, 20 min, biomass/liquid: 1/10 w/v; log Ro = 4.24	2.33	8.36	10.69	3.29	0.44	–	2.21	–	2.9	–	W.Q. Wei et al. (2013)
	Mapple chips	Hot water, 200 °C, 20 min; 23% (w/w TS); log Ro = 4.24	0.6	9.2	9.8	4.1		1.3	13.1		2.4	1.8	Kim et al. (2011)
	Wheat straw	Steam explosion, 220 °C, 2.5 min, biomass/liquid: 1:5; log Ro = 3.93	4.4	25	29.4	0.89	0.26	–	7.5	–	25.5	–	Alvira et al. (2011)
	Wheat straw	Hot water, 80 °C, 6 min follow by 180 °C, 15 min follow by 190 °C, 3 min	2.9	12.6	15.5	0.25	0.14	0.14	–	–	39.7	29.2	Kaparaju et al. (2009)
	Laminaria Japonica macroalga	Hot water, 170 °C, 5 min; biomass/liquid:1:12; log Ro = 2.76	2.22	1.76	3.98	1.79	–	–	–	–	–	–	Jung et al. (2011b)
	Laminaria Japonica macroalga	Hot water, 170 °C, 30 min; biomass/liquid:1:12; log Ro = 3.53	3.39	2.55	5.94	3.88	–	–	–	–	–	–	Jung et al. (2011b)
Thermo-acidic	Cassava residues	170 °C, 30 min; 4% (w/w) H_2SO_4; biomass/liquid:1:10 (w/v)	5.1	9.4	14.5	2.05		–	5.1	–	7.1	–	Zhang et al. (2012)
	Rice husk	121 °C, 180 min, 4% v/v H_2SO4, biomass/liquid:1:10 (w/v)	1.83	8.61	10.44	0.94		0.15	1.96	–	11.1	9.6	Cao et al. (2009)
	Rice straw	160 °C, 25 min; 1% H_2SO_4; biomass/liquid:1:10 (w/v), CS = 2.5	5.95	11.7	17.65	2.5	0.3	–	1.9	–	6.3	–	Hsu et al. (2010)
	Rice straw	160 °C, 5 min; 1% H_2SO_4; biomass/liquid:1:10 (w/v), CS = 1.8	4.01	14.4	18.41	0.1	0.9	–	1.3	–	18.41	–	Hsu et al. (2010)
	Saccharum biomass	Oxalic acid 3.21% w/w, 158 °C, 16 min, biomass/liquid 1:4 w/w, log Ro = 2.93	2.6	32.1	34.7	0.68	0.1	6.58	3.6	–	44.5	4.7	Scordia et al. (2010)
	Saccharum biomass	Oxalic acid 3.21% w/w, 182 °C, 34 min, biomass/liquid 1:4 w/w, log Ro = 3.93	2.8	16.3	19.1	6.08	0.78	7.21	7.7	–	2.8	1.4	Scordia et al. (2010)
	Spruce	150 °C, 20 min, 2,4% w/w H_2SO4, CS = 1.8	21.1	5.7	26.8	0.5	0.5		4.8	0.7	26.8	–	Larsson et al. (1999)
	Spruce	240 °C, 5 min, 2,4% w/w H_2SO4, CS = 4.5	12.1	1.1	13.2	1.2	1.26		4.8	215	5.36	–	Larsson et al. (1999)
	C. vulgaris microalga	HCl, 3% v/w, 60 min, biomass/liquid 1:10 w/w.	–	–	–	–	4.3	–	–	–	–	–	Yun et al. (2013)
	Gelidium amansii macroalga	180 °C, 15 min; 0.5% H_2SO_4 (w/w); biomass/liquid: 10 (w/v), CS = 2.7				13.32			1.33	0.33			Park et al. (2013)
Thermo-alkaline	P. Juliflora stem	NaOH 0.1 M, 30 °C, 18 h, biomass/liquid 1:10 w/v	–	–	3.16	0.135		3.94	–	–	23.4	0.8	Naseeruddin et al. (2013)
	P. Juliflora stem	KOH 0.3 M, 30 °C, 18 h, biomass/liquid 1:10 w/v	–	–	7.43	0.842		3.32	–	–	8.8	1.8	Naseeruddin et al. (2013)
	P. Juliflora stem	Ammonia 3% w/v, 30 °C, 18 h, biomass/liquid 1:10 w/v	–	–	2.44	1.559		5.12	–	–	1.6	0.3	Naseeruddin et al. (2013)
	Rice husk	Alkaline peroxide-soaking, 1% H_2O_2 w/v, 1.6% Overnight at 25 °C	7.97	1.12	9.09	0.08	0.032	5.23	2.2	0.82	81.1	1.7	Banerjee et al. (2011)

[a] Soluble sugars are the sum of hexose and pentose sugars.
[b] Furanic compounds are the sum of furfural and 5-HMF.

Table 4
Summary of the impact of by-products released during thermal and thermo-chemical pretreatments on dark fermentative biohydrogen production using mixed cultures as inoculum.

Inoculum, fermentation process	Substrate	By-products concentrations in fermentative processes	Results	References
Heat pretreated sludge, batch, 37 °C, pH = 5.5, 50 d I conc.: 250 mg COD L^{-1}	None	Furfural: 1 g L^{-1} 5-HMF: 1 g L^{-1} Phenol: 1 g L^{-1} Vanillin: 1 g L^{-1} Syringaldehyde: 1 g L^{-1}	Y_{H2} = 0 and no biogas production	Quémeneur et al. (2012)
Heat pretreated sludge, batch, 37 °C, pH = 5.5, 50 d I conc.: 250 mg COD L^{-1}	Xylose: 5 g L^{-1}	None Furfural: 1 g L^{-1} 5-HMF: 1 g L^{-1} Phenol: 1 g L^{-1} Vanillin: 1 g L^{-1} Syrinhgaldehyde:1 g L^{-1}	Y_{H2} = 1.67 mol/$mol_{xylo\ cons}$ λ = 3.2 d Y_{H2} = 0.51 mol/$mol_{xyl\ cons}$ λ = 19 d Y_{H2} = 0.40 mol/$mol_{xyl\ cons}$ λ = 10 d Y_{H2} = 1.28 mol/$mol_{xyl\ cons}$ λ = 23 d Y_{H2} = 1.30 mol/$mol_{xyl\ cons}$ λ = 16.5 d Y_{H2} = 1.39 mol/$mol_{xyl\ cons}$ λ = 8.1 d	
Heat pretreated sludge, batch, 35 °C, pH = 5.5, I conc.: 8.8 to 9.45 g VS L^{-1}	Galactose:10 g_{COD} L^{-1}	5-HMF: 0, 0.5, 1 g L^{-1} 5-HMF: 1.2 g L^{-1} 5-HMF: 1.5 and 2 g L^{-1}	Y_{H2}: 1.3–1.6 mol $_{H2}$/mol_{sugar} and 100% sugar utilisation Y_{H2}: 0.6 mol $_{H2}$/mol_{sugar} and 100% sugar utilisation Y_{H2} = 0 but 100% sugar utilisation	Park et al. (2011a)
	Gelidium amansii pretreated (H_2SO_4, 150 °C) 24.5 gTS L^{-1}	5-HMF: 2.4 g L^{-1} 5-HMF:0.02–0.05 g L^{-1}	Y_{H2} = 0 mol H_2/mol sugars added Y_{H2} = 0.9–1.07 mol H_2/mol sugars added	
Mixed anaerobic granular sludge, batch, 37 °C, pH = 5.5, I conc.: 2 g VSS L^{-1}	Glucose: 5 g L^{-1}	Furfural: 0.5 g L^{-1}, 5-HMF: 0.5 g L^{-1}, without linoleic acid pretreatment of inoculum Furfural: 0.5 g L^{-1}, 5-HMF: 0.5 g L^{-1}, with linoleic acid pretreatment of inoculum Furfural: 1 g L^{-1}, HMF: 1 g L^{-1}, with linoleic acid pretreatment of inoculum	Y_{H2} from 0.67 to 1.46 mol H_2/mol glucose Y_{H2} from 1.5 to 1.7 mol H_2/mol glucose Y_{H2} from 0.91 to 1.28 mol H_2/mol glucose	Veeravalli et al. (2013)
Heat pretreated sludge, batch, 37 °C, pH = 5.5, 27 d I conc.: 250 mg VS L^{-1}	Sunflower stalks, pretreated (HCl, 170 °C)	Furfural: 1.15 g L^{-1} 5-HMF: 0.13 g L^{-1} total phenols 0.02 g L^{-1}	Y_{H2} = 0 within 10 d	Monlau et al. (2013b)
	Glucose: 5 g L^{-1}	No addition	Y_{H2} = 2.04 mol/mol $_{glc\ cons}$	
	Glucose: 5 g L^{-1} +3.75% sunflower stalks hydrolysate (dilute acid pre-treatment, 170 °C, 1 h, 4 g HCl/100 gTS)	Furfural: 0.043 g L^{-1} 5-HMF: 0.005 g L^{-1} Total phenols 0.001 g L^{-1}	Y_{H2} = 1.89 mol/mol $_{glc\ cons}$	
	Glucose: 5 g L^{-1} +7.5% sunflower stalks hydrolysate	Furfural: 0.086 g L^{-1} 5-HMF: 0.009 g L^{-1} Total phenols 0.002 g L^{-1}	Y_{H2} = 0.44 mol/mol $_{glc\ cons}$	
	Glucose: 5 g L^{-1} +15% sunflower stalks hydrolysate	Furfural: 0.172 g L^{-1} 5-HMF: 0.019 g L^{-1} Total phenols 0.003 g L^{-1}	Y_{H2} = 0 metabolic shift towards ethanol 1.6 mol_{EtOH}/mol $_{glc\ cons}$	
	Glucose: 5 g L^{-1} +35% sunflower stalks hydrolysate	Furfural: 0.402 g L^{-1} 5-HMF: 0.044 g L^{-1} Total phenols 0.007 g L^{-1}	Y_{H2} = 0 metabolic shift towards ethanol 1.9 mol_{EtOH}/mol $_{glc\ cons}$	

Enriched hydrogenogenic culture from lab CSTR, adapted to hydrolysate Batch, 70 °C	Wheat straw hydrolysate (hydrothermal pre-treatment) Sugars: 0.8–3.9 g L^{-1}	Sugars: 0.8 g L^{-1} Furfural: 0.013 g L^{-1} 5-HMF: 0.007 g L^{-1} Total phenols: 0.007 g L^{-1}	Y_{H2} = 318 mL/$g_{sugar\ added}$ λ = 12 h Furfural remaining: 0.3 mg/L 5-HMF remaining: 0.0 mg/L	Kongjan et al. (2009)
		Sugars: 3.1 g L^{-1} Furfural: 0.050 g L^{-1} 5-HMF: 0.028 g L^{-1} total phenols 0.028 g L^{-1}	Y_{H2} = 187 mL/$g_{sugar\ added}$ λ = 10 h Furfural remaining: 2 mg/L 5-HMF remaining: 0.6 mg/L	
		Sugars: 3.9 g L^{-1}Furfural: 0.056 g L^{-1} 5-HMF: 0.035 g L^{-1} total phenols 0.035 g L^{-1}	Y_{H2} = 148 mL/$g_{sugar\ added}$ λ = 39 h Furfural remaining: 7 mg/L 5-HMF remaining: 0.8 mg/L	
Enriched-adapted culture, CSTR 70 °C, HRT = 3 d		Furfural: 0.05 g L^{-1} 5-HMF: 0.028 g L^{-1}	Y_{H2} = 178 mL/$g_{sugar\ added}$ Furfural and 5-HMF were undetectable in the CSTR outlet	
Heat pretreated sludg, batch, 35 °C, pH = 5.5, I conc.: 1.14 gVS L^{-1}	*Laminaria japonica* pretreated (HCl+thermal) 20 g COD L^{-1}	5-HMF: 2–8 g L^{-1} in pretreated sample, concentration not available in fermentative process	Inverse relationship between 5-HMF concentration and H_2 yield (from 150 mLH_2/gTS to almost 0)	Jung et al. (2011b)
Heat pretreated sludge, batch, 35 °C, pH = 5.5, I conc.: 1.14 gVS L^{-1}	*Laminaria japonica* pretreated (thermal at 170 °C, 5–40 min) 20 g COD L^{-1}	Furfural: 1.8–4.8 g L^{-1} in pretreated sample, concentration not available in fermentative process	Increased of hydrogen production from range time varying from 5 min to 20 min. From 20 min to 40 min, no hydrogen potentials increase and augmentation in the lag phase.	Jung et al. (2011b)
Heat pretreated sludge, batch, 45 °C, pH = 6.5	Rice straw hydrolysate (various acids, 150 °C)	Not measured Removed by lime and activated carbon	Y_{H2} = 0 within 10 d Y_{H2} = 5 to 10 mmol/g $_{straw}$	A.C.C. Chang et al. (2011)
Heat pretreated anaerobic sludge 105 °C, 2 h, batch 35 °C, pH 5.5	Steam exploded corn stover (200 °C, 1 min)	Furfural: 0.129 g L^{-1} 5-HMF: 1.74 g L^{-1}, concentration not available in fermentative process	Y_{H2} = 0.74 mol H_2 per liter of hydrolyzate, λ = 24 h	Datar et al. (2007)
Heat pretreated sludge, batch, 45 °C, pH = 6.5	Rice straw hydrolysate (various acids, 150 °C)	Removed by activated charcoal treatment Furfural: 0.044 g L^{-1} 5-HMF: 0.558 g L^{-1}, concentration not available in fermentative process	Y_{H2} = 0.74 mol H_2 per liter of hydrolyzate, λ = 12 h	A.C.C. Chang et al. (2011)
Elephant dung, Batch, 55 °C, pH = 5.5	Xylose + arabinose: 5 g L^{-1}each Sugar cane bagasse pretreated (1% H_2SO_4, 121 °C, 1 h) Sugars 10 g L^{-1}	None Furfural and acetate	Y_{H2} = 2.49 mol/$mol_{sugar\ cons}$ Y_{H2} = 1.48 mol/$mol_{sugar\ cons}$	Fangkum and Reungsang (2011)
Heat pretreated sludge (90 °C, 20 min), batch, 35 °C, pH = 7.4, I conc.: 1.65 gVS L^{-1}	Ultrasound pre-treatment on microalgae C. *vulgaris* (10,000 to 100,000 kJ/ kg TS)	Untreated samples 5-HMF: 0.02 to 0.41 g L^{-1} in pretreated sample, concentration not available in fermentative process	Y_{H2} = 31.1 mL/g_{TS} Y_{H2} = 31.9 to 37.9 mL/g_{TS}	Yun et al. (2013)
Heat pretreated sludge (90 °C, 20 min), batch, 35 °C, pH = 7.4, I conc.: 1.65 gVS L^{-1}	Acid pre-treatment (HCl) on microalgae C. *vulgaris*	Untreated samples 5-HMF: 0.23 to 1.51 g L^{-1} in pretreated sample, concentration not available in fermentative process 5-HMF: 3.12 to 4.30 g L^{-1} in pretreated sample, concentration not available in fermentative process	Y_{H2} = 31.1 mL/g_{TS} Y_{H2} = 29.3 to 35.7 mL/g_{TS} Y_{H2} = 25.3 to 13.6 mL/g_{TS}	
Heat pretreated sludge (90 °C, 20 min), batch, 35 °C, pH = 7.4, I conc.: 1.65 gVS L^{-1}	Acid pre-treatment (HCl) + ultrasound on microalgae C. *vulgaris*	Untreated samples 5-HMF: 0.15 to 2.95 g L^{-1} in pretreated sample, concentration not available in fermentative process 5-HMF: 3.40 g L^{-1} in pretreated sample, concentration not available in fermentative process	Y_{H2} = 31.1 mL/g_{TS} Y_{H2} = 34.7 to 29.7 mL/g_{TS} Y_{H2} = 24.2 mL/g_{TS}	

Y_{H2}: hydrogen yield λ: lag-phase time I conc.: Inoculum concentration in anaerobic fermenter.

acetate was not reported to inhibit specifically and significantly the growth of pure clostridial species involved in hydrogen production (Cao et al., 2009; Ezeji et al., 2007).

Main modes of action of by-products on microorganisms

Furanic compounds (i.e. furfural and 5-HMF) are known to have detrimental effects on microorganisms by inhibiting cell growth, induce DNA damage and inhibit several enzymes of the glycolysis pathway (Almeida et al., 2009; Palmqvist and Hahn-Hägerdal, 2000). Phenolic compounds damage microbial cells by altering selectively the membrane permeability, causing leakage of intracellular components and inactivation of essential enzymatic systems (Campos et al., 2009; Heipieper et al., 1994; Hierholtzer et al., 2013; Palmqvist and Hahn-Hägerdal, 2000). Low molecular weight phenolic compounds are considered as more toxic compounds to microorganisms than high molecular weight ones (Klinke et al., 2004). In *Escherichia coli*, phenolic compounds were found to be more toxic than furans (Mills et al., 2009). Both furans and phenols generate *Reactive Oxygen Species* (ROS) (i.e. H_2O_2, O_2^- and OH^-) that impact cell metabolism and induce apoptosis (Ibraheem and Ndimba, 2013). The individual effects of toxics on microbial cells are related to their structure and hydrophobicity. These characteristics determine the intrinsic ability of these compounds to penetrate cell membranes and cause cellular disturbances. High hydrophobic compounds are indeed suspected to affect cell membrane transporters and therefore compromise membrane integrity (Mills et al., 2009).

Microorganisms differ in their ability to adapt and grow in presence of toxic compounds and can use different adaptation mechanisms to avoid or repair damages caused by these toxics. Molecular adaptation mechanisms and activities of some bacterial species in response to lignocellulose-derived inhibitory compounds were recently reviewed (Lee et al., 2012; Ibraheem and Ndimba, 2013). In order to maintain the integrity of the cell membrane, some bacterial species may respond to the presence of toxic compounds by converting the cis-unsaturated fatty acids to trans-unsaturated ones at the cell membrane level (Heipieper et al., 1994; Palmqvist and Hahn-Hägerdal, 2000). Recently, variations in effect of inhibitory by-products on bacteria were also attributed to differences in cell surface structures between Gram-negative and Gram-positive species, but the effect observed was mainly species-dependent (Cueva et al., 2012). To better tolerate the stress generated by inhibitory by-products, some bacteria produce stress response proteins such as SOS response proteins and heat shock proteins, which repair the damaged DNA and maintain the structure of the enzymatic systems (Ibraheem and Ndimba, 2013). Some other microorganisms, mostly aerobic Gram-negative bacteria, can directly transform and/or degrade the furanic compounds, by utilizing them as a carbon source (Almeida et al., 2009; Wierckx et al., 2011). In particular, furfural degradation proceeds via 2-furoic acid, which is metabolised to the primary intermediate 2-oxoglutarate. HMF is converted, via 2,5-furandicarboxylic acid, into 2-furoic acid (Almeida et al., 2009). Under anaerobic conditions, some bacteria (e.g., *E. coli*, *Clostridium acetolyticum*) can convert furfural and 5-HMF to less inhibitory furfuryl compounds and HMF alcohols (Zaldivar et al., 1999; Zhang et al., 2012). As an illustration, in *E. coli* LYO1, furfural is converted more rapidly than 5-HMF and, since it is more toxic than 5-HMF, this selective transformation is beneficial for cell growth (Zaldivar et al., 1999).

Effect of by-products on dark fermentation process operated with mixed cultures

Effect on dark fermentation

Table 4 summarises the main results published in literature on the impact of furanic and phenolic compounds added separately or in combination (hydrolyzate) on dark fermentation process performances operated with mixed cultures. At a concentration of 1 g L^{-1}, Quémeneur et al. (2012) showed that furanic (furfural and 5-HMF) and phenolic compounds added separately decreased the hydrogen yield from xylose but did not lead to total inhibition. Increasing the 5-HMF concentration at around 1.5–2 g L^{-1} showed a severe decrease of hydrogen production down to zero (Park et al., 2011a). Among the by-products investigated, phenolic compounds (i.e. phenols, syringaldehyde and vanillin) were found to have less impact on hydrogen production than furanic compounds. The addition of 1 g L^{-1} of furan derivatives led to a reduction of the hydrogen yield of 68% (furfural) and 76% (5-HMF) compared to the control (Quémeneur et al., 2012). The effects of such by-products was also investigated using hydrogen-producing bacteria in pure cultures and similar trends to that in mixed cultures were reported (Cao et al., 2009; Ho et al., 2010; Tai et al., 2010). Indeed, total inhibition of hydrogen production in *Thermoanaerobacterium thermosaccharolyticum* was reported in presence of 1.8 g L^{-1} of 5-HMF or 2 g L^{-1} of furfural (Cao et al., 2009). *Clostridium butyricum* yielded H_2 at approximately 1.4 mol H_2 mol^{-1} glucose in presence of 200–400 mg L^{-1} phenol, but significant inhibition of cell metabolism was observed at phenol concentration higher than 1000 mg L^{-1} with total hydrogen pathway inhibition at concentrations higher than 1.5 g L^{-1} (Tai et al., 2010).

As shown in Table 4, the inhibition of hydrogen-producing mixed-cultures was reported with thermal or thermo-chemical hydrolyzates containing a mixture of by-products (A.C.C. Chang et al., 2011; Monlau et al., 2013b; Park et al., 2011a). Interestingly, Jung et al. (2011a) showed an inverse relationship ($R^2 = 0.84$) between the 5-HMF content and hydrogen yields. A.C.C. Chang et al. (2011) reported no hydrogen production after ten days from various dilute acid rice straw hydrolyzates, mainly due to the presence of by-products (i.e. furfural and 5-HMF). Indeed, by removing furfural and 5-HMF from the hydrolyzate, hydrogen was produced significantly. In addition, Monlau et al. (2013b) reported a total inhibition of fermentative hydrogen production after supplementation of the culture medium with 15% (v/v) of dilute-acid sunflower stalk hydrolysate, corresponding to 172 mg L^{-1} of furfural, 19 mg L^{-1} of 5-HMF and 3 mg L^{-1} of total phenolic compounds. Surprisingly, when the compounds were added separately at much higher amount of 1 g L^{-1} and under the same conditions, biohydrogen production was negatively affected but was not totally inhibited (Quémeneur et al., 2012). These observations suggest either the presence of other unknown inhibitors in hydrolyzates and/or a synergistic effect of the different by-products as their level of inhibition was much lower than when used separately (Monlau et al., 2013b; Quémeneur et al., 2012). Such synergy effect of by-products (furfural, 5-HMF, phenolic compounds) was previously reported on bioethanol fermentation by *S. cerevisiae*, on biohydrogen production by *T. thermosaccharolyticum* and lipid production by the oleaginous yeast *Rhodosporidium toruloides* (Cao et al., 2009; Larsson et al., 1999; Mussatto and Roberto, 2004).

Additionnally, the presence of by-products led also to an increase of lag-phase in dark fermentation, showing the necessity of microorganisms to adapt (Kongjan et al., 2009; Quémeneur et al., 2012). Datar et al. (2007) reported that, when steam exploded corn stover hydrolyzate (200 °C for 1 min) was treated with activated charcoal to remove inhibitory by-products, the hydrogen yield remained the same, but the lag phase decreased from 24 h to about 12 h suggesting a shorter adaptation time of microorganisms in absence of by-products. By using unadapted anaerobic mixed-cultures, Quémeneur et al. (2012) reported that the highest increase in lag-phase was observed with phenol, followed by furfural, vanillin, 5-HMF and syringaldehyde at 1 g L^{-1}. In particular, the lag-phase increased dramatically from 3 d to 23 d in presence of phenolic compounds (Quémeneur et al., 2012). Mainly, a negative correlation was observed between lag phase and molecular weight of furanic and phenolic compounds (Quémeneur et al., 2012). For instance, furans having molecular weight of 96 g mol^{-1} (furfurals) and 126 g mol^{-1} (5-HMF) exhibited a lag phase twice longer with furfurals than HMF-added cultures. Such differences can be explained by the intrinsic ability of these compounds to penetrate cell

Table 5
Summary of the main impact of by-products released during thermal and thermo-chemical pretreatments on anaerobic digestion using mixed cultures as inoculum.

Inoculum, fermentation process	Substrates	By-product concentration in fermentation process	Results	References
Anaerobic sludge, batch, 37 °C 50 d	Acetic and propionate	Phenol: 0 g L^{-1}	Control (Crt)	Fedorak and Hrudey (1984)
		Phenol: 0.50 g L^{-1}	Higher CH_4 production than Crt	
		Phenol: 1.2 g L^{-1}	Same CH_4 production as Crt	
		Phenol: 2 g L^{-1}	Lower CH_4 production than Crt	
		Phenol: 3 g L^{-1}	CH_4 production near 0	
Anaerobic sludge, batch, 37 °C, 140 d	Cellulose: 2.7 g L^{-1}	Phenol: 0 g/L	Control (Crt)	Chapleur et al. (2013)
		Phenol: 0.01 to 0.05 g L^{-1}	Same CH_4 production as Crt	
		Phenol: 0.5 to 1 g L^{-1}	Same CH_4 production as Crt, but two phases of degradation	
		Phenol: 2 g L^{-1}	CH_4 production near 0	
		Phenol: 4 g L^{-1}	No CH_4 production	
Granular sludge, batch, 35 °C, 35 d, I conc.: 4.5 gVSS L^{-1}	Acetate (AC) 3.0 gCOD L^{-1}	5-HMF: 0 g L^{-1}	Y_{CH4} = 320 mL/gCOD-AC; 3 d[a]	Park et al. (2011b)
		5-HMF: 1 g L^{-1}	Y_{CH4} = 400 mL/gCOD-AC; 17 d[a]	
		5-HMF: 2 g L^{-1}	Y_{CH4} = 480 mL/gCOD-AC; 15 d[a]	
		5-HMF: 3 g L^{-1}	Y_{CH4} = 550 mL/gCOD-AC, 32 d[a]	
		5-HMF: 5 g L^{-1}	Y_{CH4} = 710 mL/gCOD-AC, 30 d[a]	
		5-HMF: 10 g L^{-1}	Y_{CH4} = 0 mL/gCOD-AC, 35 d[a]	
Granular sludge, batch, 35 °C, 22 d, I conc.: 20 gVSS L^{-1}		5-HMF: 0 g L^{-1}	Y_{CH4} = 320 mL/gCOD-AC; 8 d[a]	
		5-HMF: 1 g L^{-1}	Y_{CH4} = 440 mL/gCOD-AC; 8 d[a]	
		5-HMF: 2 g L^{-1}	Y_{CH4} = 470 mL/gCOD-AC; 18 d[a]	
		5-HMF: 3 g L^{-1}	Y_{CH4} = 550 mL/gCOD-AC, 20 d[a]	
		5-HMF: 5 g L^{-1}	Y_{CH4} = 700 mL/gCOD-AC, 20 d[a]	
		5-HMF : 10 g L^{-1}	Y_{CH4} = 0 mL/gCOD-AC, 22 d[a]	
Anaerobic inoculum from a digester of a wastewater treatment plant, batch, 37 °C, 25 d, I conc.: 6 g VS L^{-1}	Cellulose: 12 g L^{-1}	None	Y_{CH4} = 352 mL/g_{VS}	Badshah (2012)
		Furfural: 1 g L^{-1}	Y_{CH4} = 345 mL/g_{VS}	
		Furfural: 2 g L^{-1}	Y_{CH4} = 384 mL/g_{VS}	
		Furfural: 4 g L^{-1}	Y_{CH4} = 338 mL/g_{VS}	
		5-HMF: 1 g L^{-1}	Y_{CH4} = 324 mL/g_{VS}	
		5-HMF: 3 g L^{-1}	Y_{CH4} = 353 mL/g_{VS}	
		5-HMF: 6 g L^{-1}	Y_{CH4} = 0 mL/g_{VS}	
		Furfural/5-HMF: 1–1 g L^{-1}	Y_{CH4} = 357 mL/g_{VS}	
		Furfural/5-HMF: 2–3 g L^{-1}	Y_{CH4} = 17 mL/g_{VS}	
		Furfural/5-HMF: 4–6 g L^{-1}	Y_{CH4} = 0 mL/g_{VS}	
Granular sludge, batch, 37 °C, 42 d, I conc.: 5 g VS L^{-1}	None	Furfural: 2 g L^{-1}	Y_{CH4} = 430 mL/g_{VS}, λ = 4 d	Barakat et al. (2012)
		5-HMF: 2 g L^{-1}	Y_{CH4} = 450 mL/g_{VS}, λ = 14 d	
		Vanillin: 2 g L^{-1}	Y_{CH4} = 105 mL/g_{VS}, λ = 4 d	
		Syringaldehyde: 2 g L^{-1}	Y_{CH4} = 453 mL/g_{VS}, λ = 4 d	
Granular sludge, batch, 37 °C, 20 d, I conc.: 5 g VS L^{-1}	Xylose: 1 g L^{-1}	None	Y_{CH4} = 300 mL/g_{VS}, λ = 0 d	
		Furfural: 1 g L^{-1}	Y_{CH4} = 300 mL/g_{VS}, λ = 1 d	
		5-HMF: 1 g L^{-1}	Y_{CH4} = 345 mL/g_{VS}, λ = 1 d	
		Vanillin: 1 g L^{-1}	Y_{CH4} = 225 mL/g_{VS}, λ = 0 d	
		Syringaldehyde: 1 g L^{-1}	Y_{CH4} = 400 mL/g_{VS}, λ = 0 d	
Predigested active sludge, batch, 35 °C, 250 d, I conc.: 1.3 gVSS L^{-1}	None	Phenol 100 mg L^{-1}	B = 21.7%, λ = 17 d, 38d[a]	Hernandez and Edyvean (2008)
		Phenol 200 mg L^{-1}	B = 27.3%, λ = 24 d, 45d[a]	
		Phenol 400 mg L^{-1}	B = 32.2%, λ = 31 d, 103d[a]	
		Phenol 800 mg L^{-1}	B = 1.1%, complete inhibition of the digestion process	
		Phenol 1600 mg L^{-1}	B = 1.7%, complete inhibition of the digestion process	
Rumen, batch	Filter paper cellulose 4 g L^{-1}	Vanilic acid: 6 to 30 mM	No methane inhibition compared to Crt	Op den Camp et al. (1988)
		Ferulic acid: 5 to 25 mM	No methane inhibition compared to Crt	
		p-coumaric acid: 6 to 30 mM	Total methane inhibition at 30 mM	
Municipal sewage sludge, batch, 35 °C, 21 d, I conc.: 4 g VS L^{-1}	Avicel cellulose: 2 g L^{-1}	None	Y_{CH4} = 730 mLbiogas/g_{VS},	Janzon et al. (2014)
		Medium 1:	Y_{CH4} = 705 mLbiogas/g_{VS},	
		Furfural: 5 mg L^{-1}		
		5-HMF: 30 mg L^{-1}		
		Medium 2:	Y_{CH4} = 670 mLbiogas/g_{VS},	
		Furfural: 5 mg L^{-1}		
		5-HMF: 60 mg L^{-1}		
Anaerobic inoculum from a digester of a wastewater treatment plant, batch, 37 °C, 25 d, I conc.: 6 g VS L^{-1}	Cellulose: 12 g L^{-1}	None	Y_{CH4} = 348 mL/g_{VS}	Badshah (2012)
		Medium 1:	Y_{CH4} = 359 mL/g_{VS}	
		Furfural: 0.13 g L^{-1}		
		5-HMF: 0.37 g L^{-1}		
		Medium 2:	Y_{CH4} = 369 mL/g_{VS}	
		Furfural: 0.80 g L^{-1}		
		5-HMF: 0.46 g L^{-1}		
Anaerobic inoculum from biogas plant treating pig manure and food wastes, batch, 37 °C, 18 d, I conc.: 6 g VS L^{-1}	Sugarcane bagasse hydrolyzate (2 g H_2SO_4/100 gTS, 121 °C, 15 min)	Furfural: 0.13 g L^{-1}	Y_{CH4} = 173 mL/g_{VS} (higher than raw sugarcane bagasse)	Badshah et al. (2012)
		5-HMF: not detected	Furfural was not detected at the end of anaerobic digestion process	
Granular sludge, bach, 37 °C, 35 d, I conc.: 5 gVS L^{-1}	Sunflower stalks pretreated (4 g HCl/100 gTS, 170 °C,1 h), 35 gTS L^{-1}	Furfural: 1.35 g L^{-1}	Y_{CH4} = 233 mL/g_{VS} (21% higher than raw sunflower stalks)	Monlau et al. (2012b)
		5-HMF: 0.13 g L^{-1}		
Anaerobic sludge from a wastewater treatment plant, batch, 35 °C, 60 d	Wet oxidation of newspaper wastes at different temperatures	Furans:0.005 to 0.065 g L^{-1}	No impact on methane production but lag phase of 10–15 d	Fox and Noike (2004)
		Phenols:0.441 to 0.552 g L^{-1}	Removal of lignin derivatives between 84% and 100% and furans removals varied between 87% and 96%.	

[a] Approximate time needed to reach methane production plateau, λ: lag-phase time, I conc.: Inoculum concentration in anaerobic fermenters, B: Anaerobic biodegradability.

membranes: the higher the molecular mass, the slower was the penetration into a cell and the shorter the lag phase (Quémeneur et al., 2012).

Effect of by-products on fermentative metabolic pathways and microbial communities

In the case of mixed cultures, furans and phenolic compounds may selectively affect the growth of individual species within the microbial consortium. Consequently, they may influence both metabolic pathways and bacterial population dynamics. Few studies investigated metabolic pathway and microbial community changes in presence of such by-products during dark fermentation (Kongjan et al., 2009; Park et al., 2011a; Quémeneur et al., 2012).

Quémeneur et al. (2012) reported acetate and butyrate as major metabolites in the soluble fraction associated with hydrogen production when using glucose as control. Significant changes in metabolic profiles were observed, depending on the nature of the inhibitory by-products added in the medium (i.e. furfural, 5-HMF, phenols, vanillin and syringaldehyde). Nevertheless, and whatever the inhibitor supplemented, the mixed-culture was dominated by *Clostridium* spp., especially *C. beijerinkii* more resistant to inhibitors and, thus, it can be considered as an ideal candidate for H_2 production from lignocellulosic hydrolyzates (Quémeneur et al., 2012). In contrast, the relative abundance of efficient hydrogen-producing bacteria *C. acetobutylicum* and *C. pasteurianum* were drastically affected by furanic and phenolic compounds (Quémeneur et al., 2012). In presence of such by-products, the emergence of competitive none-H_2 producing bacteria such as *C. cellulosi* and *Sporolactobacillus* sp. was observed (Quémeneur et al., 2012).

Interestingly, inhibition of biohydrogen production in presence of by-products does not mean the absence of bacterial activities since carbohydrates can be degraded through none-hydrogen-producing pathways such as lactacte, ethanol and propionate pathways (Kongjan et al., 2009; Monlau et al., 2013b; Park et al., 2011a; Quémeneur et al., 2012). That suggests that H_2-producing bacteria are more sensitive to the presence of by-products than other microorganisms. Furthermore, Park et al. (2011a) reported that when 1.5 g L^{-1} of 5-HMF was added to a galactose medium, no hydrogen was produced but propionate and mainly lactate were generated from carbohydrates through competing H_2 pathways (Park et al., 2011a). Similarly, Monlau et al. (2013b) observed a decrease in biohydrogen production from glucose by adding increasing volumes of dilute-acid sunflower stalk hydrolyzates containing by-products. In that case, for a volume lower than 7.5% (v/v), corresponding to concentration in fermenter of 86.2 mg L^{-1} of furfural, 9.5 mg L^{-1} of 5-HMF and 1.5 mg L^{-1} of phenolic compounds, no hydrogen inhibition was observed and acetate and butyrate were the main metabolites produced concomitantly with hydrogen. *Clostridium* genus, which plays a key role in fermentative mixed cultures producing H_2, was found to be dominant (Monlau et al., 2013b). In contrast, at a volume higher or equal to 15% (v/v), no hydrogen production was reported and this inhibition was accompanied to a shift from hydrogen-producing pathways (i.e. acetate/butyrate) to non-hydrogen-producing pathways (i.e. lactate/ethanol). Production of ethanol and lactate involved in zero-hydrogen balance pathways was also concomitant with a population shift from *Clostridium* sp. to *Sporolactobacillus* sp.

The inhibitory effect is strongly dependent of the initial adaptation of the initial microbial ecosystems. Kongjan et al. (2009) showed that 5-HMF and furfural at low concentration of 50 and 24 mg L^{-1}, respectively, were efficiently removed in a CSTR reactor using adapted hyperthermophilic microbial culture. Both furfural and 5-HMF can be transformed into less inhibitory furfuryl and HMF alcohols and then be degraded by clostridial species and facultative anaerobes (Wierckx et al., 2011; Zhang et al., 2012). At low concentrations, phenols were also reported to be degraded by many clostridial species generally involved in hydrogen production (Tai et al., 2010). Contrarily, Quémeneur et al. (2012) showed that no gas was produced during dark fermentation of inhibitor compounds such as furfural, 5-HMF, vanillin and syringaldehyde, as sole carbon source and at an initial concentration of 1 g L^{-1}. It is clear that the efficiency of H_2 production using mixed cultures is dependent on nature and concentration of toxic compounds but more investigations are still required to determine the exact impact of the origin of mixed cultures as well as the most adapted microbial community structures. Nonetheless, the presence of by-products during dark fermentation using mixed cultures may favour the production of other carboxylates (i.e. lactate and propionate) or biofuels (ethanol). However, supplementary investigations are needed to support this assumption. Recent advances in molecular techniques, such as functional community fingerprinting (Quéméneur et al., 2011), functional genomics (e.g., detection of genes related to the resistance or the degradation of the by-products) (Endo et al., 2008) and metagenomics (Chistoserdova, 2010), would be particularly applicable when combined to the analysis and monitoring of fermentative mixed cultures exposed to by-products, for better understanding of their influence on metabolic pathways and regulatory networks.

Effect on anaerobic digestion (AD)

Effect of individual by-products on AD

Table 5 shows the main data published about the impact of furanic and phenolic compounds on anaerobic digestion. The effects of such by-products were investigated on simple substrates (i.e. xylose, acetate and propionate) as well as more complex substrates (i.e. cellulose), allowing to have a global vision on their effect on the overall process.

At a concentration of 1 g L^{-1}, furanic compounds (i.e. 5-HMF and furfural) added to a growth medium containing xylose at 1 g/L did not reduce the methane yield (Barakat et al., 2012). Badshah (2012) investigated the degradation of cellulose during anaerobic digestion by adding separately various concentrations of furfural (1, 2 and 4 g L^{-1}) and 5-HMF (1, 3 and 6 g L^{-1}). At concentrations of 1 and 2 g L^{-1} of furfural and 1 and 3 g L^{-1} of 5-HMF, no methane production inhibition was observed. At 4 g $L^{-1}$of furfural, a moderate accumulation of acetate and propionate was found at the end of experiment (55 d) suggesting a partial inhibition of the methanogenic activity and likely no inhibition of hydrolysis and acidogenesis steps. At 6 g L^{-1} of 5-HMF, no biogas was produced suggesting that 5-HMF caused a total inhibition of AD. After 55 d of incubation, accumulation of fermentative metabolites in the liquid phase was found with mainly acetate (1 g L^{-1}) and propionate (0.09 g L^{-1}). This result suggest that methanogenesis was severely impacted (Badshah, 2012). Furthermore, total amounts of metabolic intermediates such VFAs, soluble sugars and methane were lower than if complete conversion of cellulose occurred, suggesting that hydrolysis was also severely affected at such concentration of 5-HMF (Badshah, 2012). Methanogenic activity from acetate and propionate was also investigated at several concentration levels of 5-HMF (Park et al., 2011b). Consistently, Park et al. (2011b) showed that the degradation of acetate is possible up to 5 g $L^{-1}$of 5-HMF, but a total inhibition of the methanogenic activity occurred at a concentration of 10 g L^{-1}.

Regarding the degradation of lignin-derived by-products, phenolic compounds such as vanillin and syringaldehyde were added at a concentration of 1 g L^{-1} to xylose at 1 g L^{-1} and the final methane yields were not reduced (Barakat et al., 2012). Chapleur et al. (2013) investigated the effect of increasing phenol concentrations on the anaerobic degradation of cellulose. The archaeal methanogenic and fermentative bacterial activities were inhibited at a threshold value of 1.5 g L^{-1} and 2 g L^{-1} of phenol, respectively (Chapleur et al., 2013). Similarly, Fedorak and Hrudey (1984) reported that methanogenic activity of anaerobic sludge was not affected at concentrations lower than 1.2 g L^{-1} of phenols, since acetate and propionate were fully degraded into methane. When phenol concentration exceeded 1.2 g L^{-1}, total methane production decreased sharply (Fedorak and Hrudey, 1984). Kayembe et al. (2013) showed a negative linear correlation between the toxicity of phenolic compounds and their hydrophobic properties. An increase

in the number of hydroxyl groups on aromatic compounds was indeed associated with a decrease of the compound toxicity on methanogenic microbial consortium (Kayembe et al., 2013). Additionnally, the toxic effects of phenolic compounds on anaerobic degradation of glucose were found to be dependent on many parameters such as the autoxidation level, the apolarity, as well as the type and number of substitutions of the phenolic compounds (Hernandez and Edyvean, 2008). Consistently with other by-products, the inhibitory level of the phenolic compounds was also linked to microbial ecosystem exposition to such compounds (Hierholtzer et al., 2013; Olguin-lora et al., 2003).

Effect of by-products combination on AD

As previously mentioned for hydrogen production, when by-products are present together, synergy effects may occur, reducing considerably the threshold value for inhibition compared if such by-products are added separately (Bellido et al., 2011; Larsson et al., 1999; Mussatto and Roberto, 2004). According to our knowledge, no study has reported until now the exact synergistic impact between phenolic compounds and furan derivatives on anaerobic digestion performances. Nonetheless, some authors already suggested a possible synergistic effect of simultaneous addition of furfural and 5-HMF on anaerobic digestion (Badshah, 2012; Janzon et al., 2014). When they were added in combination at a concentration of 1 g L^{-1} each, they did not show a synergistic inhibitory effect but affected the kinetics by increasing the lag phase, corresponding probably to the time of adaptation of the microbial community. In contrast, by adding 2 g L^{-1} of furfural and 3 g L^{-1} of 5-HMF in combination, the methane produced was lower than that obtained by adding furfural and 5-HMF individually (Badshah, 2012). To study the synergetic effect of by-products on AD and to compare the effect caused by the addition of the same compounds separately, the inocula were sampled from the same AD plant but at different times of sampling. Therefore it is difficult to conclude whether this inhibition was due to synergistic impact of by-products or due to the different inoculum microbial diversity (Badshah, 2012).

Badshah (2012) showed recently that addition of furfural and 5-HMF at concentrations generally found in hydrolyzates issued from thermal and thermo-chemical pretreatment of lignocellulosic substrates did not have any impact on anaerobic digestion of complex substrates such as cellulose. This suggests that neither hydrolysis nor methanogenesis step were inhibited in that case. By supplementing a solution of cellulose with two media containing both furfural and 5-HMF mixtures at concentrations higher than generally found in lignocellulosic hydrolyzates—Medium 1: furfural: 0.13 g L^{-1}; 5-HMF: 0.37 g L^{-1}; Medium 2: furfural: 0.80 g L^{-1}; 5-HMF: 0.46 g L^{-1}, no increase in the lag phase nor reduction of the methane yield was observed. These results are in agreement with studies that did not found apparent inhibition of anaerobic digestion after dilute-acid pretreatment of lignocellulosic biomass, such as sunflower stalks, sugarcane bagasse, mewsprint wates and besides the presence of furfural and 5-HMF in the hydrolyzate (Badshah, 2012; Badshah et al., 2012; Fox and Noike, 2004; Monlau et al., 2012b). As suggested by Vivekanand et al. (2012), it is difficult to establish clearly the absence of effect of by-products on anaerobic digestion as the beneficial effect of opening the plant cell structure and liberating sources of nutrition during pretreatments can cover partially or totally the chemical inhibitory effect of the by-products. Consequently, supplementary works on using by-products added separately or in mixtures, at a cellular level, are still required to state definitely their exact effects and their possible synergistic effect.

Degradation of by-products and microbial adaptation

In several studies, the necessity of adapting the microbial inoculum was shown through the increase of lag-phase or decrease of digestion rates in presence of pretreatment by-products (Barakat et al., 2012; Benjamin et al., 1984; Fox and Noike, 2004). Fox and Noike (2004) reported a long lag phase of 10–15 d during anaerobic digestion of newspapers waste hydrolyzate containing phenolic and furanic compounds. Such observation suggested that an appropriate period of adaption of the microbial ecosystems is required to enhance the development of specific microbial populations fermenting organic molecules to methane in presence of by-products (Fox and Noike, 2004). Rosenkranz et al. (2013) investigated this adaptation period by sequential addition of phenol at 200 mg L^{-1} in a batch anaerobic digester and they observed a reduction of the lag phase. Indeed, the lag phase was reduced from 20–25 d to 4 d after the third addition, showing an adaptation of the microbial inoculum to phenolic compounds. Park et al. (2013) showed that 5-HMF at 3 g L^{-1} extended the lag phase of anaerobic digestion of acetate with an initial granular sludge concentration of 4.5 g VSS L^{-1}. Interestingly, an increase of the inoculum concentration up to 20 g VSS L^{-1} completely overcame the lag phase period, emphasizing that the by-products/inoculum concentration ratio plays an important role in the adaptation process. Consequently, adaptation of inoculum or increase in its initial concentration seem to be two promising methods to overcome long lag phase that can occur during anaerobic digestion of hydrolyzates containing pretreatment by-products.

Contrarily to the dark fermentation process, anaerobic digestion seems more efficient to remove and degrade furan derivatives. Badshah et al. (2012) reported that furfurals generated during dilute-acid pre-treatment of sugarcane bagasse did not cause any apparent inhibition of methane production and were even degraded during the anaerobic process. Similarly, Barakat et al. (2012) investigated the anaerobic degradation of furfurals and 5-HMF at 2 g L^{-1} as sole carbon sources and reported methane yields corresponding to 74% and 78% of the theoretical values. Rivard and Grohmann (1991) showed previously that in a CSTR (Continuous Stirred Tank Reactor) system where furfural was continuously added, 80% of the biogas theoretically expected was recovered. In this case, furfural was converted into several intermediates, including furfuryl alcohol, furoic acid and acetate, before its final conversion to methane and carbon dioxide (Rivard and Grohmann, 1991). In general, microorganisms appear to have the ability to convert both 5-HMF and furfural into less inhibitory compounds. Inhibitory effects are therefore gradually reduced as long as initial concentrations are not too high (i.e. from 0 to 2 g L^{-1}) (Boyer et al., 1992).

Additionally, removal and degradation of phenolic compounds during anaerobic digestion were previously reported in several studies (Barakat et al., 2012; Rosenkranz et al., 2013; Fox et al., 2003). Barakat et al. (2012) investigated the anaerobic degradation of vanillin and syringaldehyde at 2 g L^{-1} as sole carbon sources. Vanillin was found to be recalcitrant to microbial degradation with a measured methane potentials representing 17% of the theoretical value compared to 84% for syringaldehyde. Fox et al. (2003) investigated the effect of phenolic and heterocyclic compounds during semi-continuous anaerobic digestion of news-print wastes pre-treated by alkaline subcritical water method. They found that phenolic compounds at a concentration of 7 mg L^{-1} were totally and rapidly degraded, except for 4-methylcatechol which needed around 200 d of microbial adaptation prior to any degradation (Fox et al., 2003). Adaptation of the mixed inoculum is also an important parameter to be considered when dealing with the degradation of phenolic compounds (Fang et al., 2004; Olguin-lora et al., 2003; Rosenkranz et al., 2013). By using phenol-adapted anaerobic sewage sludge, Fang et al. (2004) reported phenol degradation up to 2 g L^{-1} in a UASB (upflow anaerobic sludge blanket) reactor. Similarly, by a progressive increase of phenol concentration leading to microbial ecosystem adaptation, high rates of phenol removal were observed during anaerobic digestion (Rosenkranz et al., 2013). However, at a microbiological level, the increase of phenol concentration for inoculum adaptation was accompanied by a sharp decrease of microbial diversity and a progressive selection of the most adapted phylotypes (Rosenkranz et al., 2013). Main anaerobic microorganisms involved in degradation of phenolic compounds at mesophilic and thermophilic conditions were recently reviewed (Leven et al., 2012). Interestingly, Leven et al. (2012) concluded that the

degradation efficiency of different phenols correlated well inversely with the process temperature. A higher degradation efficiency was observed at mesophilic than at thermophilic temperature (Leven and Schnürer, 2005; Leven et al., 2012). Possible explanation was likely related to slight differences in microbial diversity, particularly in the abundance of phenol-degrading bacteria among the ecosystem and/or the presence of temperature-sensitive enzymes (Leven et al., 2012).

Benzoate was found to be a key intermediate of phenol degradation during anaerobic digestion at ambient and mesophilic temperature (Fang et al., 2004; Hoyos-Hernandez et al., 2013). Based on DNA cloning analysis, Fang et al. (2004) identified different groups of microoganisms involved in phenol degradation: *Desulfotomaculum* sp. and *Clostridium* sp. were found to be responsible for the conversion of phenols into benzoate, which was further degraded by *Syntrophus* sp. into acetate and H_2/CO_2. Methanogens lastly converted acetate and H_2/CO_2 into methane (Fang et al., 2004). Later, Fang et al. (2006) suggested that phenol could be transformed via a caproate pathway instead of benzoate pathway under thermophilic conditions.

Finally, the efficiency of phenolic compound removal during anaerobic digestion plays also an important role prior to reuse the digestate as fertiliser to avoid any environmental disturbance (Leven et al., 2006). Indeed, phenolic compounds, besides to affect sometimes downstream microbial processes, are also harmful and can affect the quality of the digestate, if not removed. They act negatively on soil microorganisms such as ammonia oxidizing bacteria and further reduce the productivity and sustainability of cultivated soils. (Leven et al., 2006, 2012; Pell and Torstensson, 2002).

Final remarks and future scope

In mixed microbial cultures, a thorough analysis of literature data showed that dark fermentation is more sensitive than anaerobic digestion to by-products generated during thermal and thermo-chemical pretreatments of lignocellulosic and algal biomass. Even though inhibition of methane production was observed in several cases, the minimal inhibitory concentration (MIC) of by-products for anaerobic digestion is far higher than the MIC for fermentative hydrogen production with 10 g/L against only 1.5–2 g/L for 5-HMF, respectively. Moreover, anaerobic digestion was found to be efficient to remove at moderate concentration most of the inhibitory by-products. These findings are surprising because the dark fermentation process corresponds to the first steps of the anaerobic digestion process. However, several differences between both processes can explain this observation: first, mixed-cultures used in dark fermentation are generally heat-treated and therefore are highly simplified and very specific for H_2 production. Comparatively, the anaerobic digestion inoculum has a better adaptability to environmental changes. Second, micro-organism concentrations are usually higher in methane potential tests (BMP) than in batch hydrogen production tests (BHP) since the ratio substrate/micro-organisms or by-product/micro-organisms is far higher in hydrogen tests, suggesting a higher and direct effect of by-products on the microbial growth. Moreover, a major impact of the presence of such pre-treatment by-products is the increase of lag-phase of biological processes. Microbial community adaptation is therefore recommended prior to inoculation. Although hydrogen production is strongly inhibited in presence of by-products, carbohydrates are nonetheless degraded during the process and converted into other metabolites such as propionate, ethanol or lactate. This metabolic shift is mainly due to microbial community changes from H_2 producers to H_2 consumers or competitors. These compounds can be further converted to methane and, therefore, the overall methane yields are not affected.

However, several bottlenecks remain to understand exactly the effect of such by-products on dark fermentation and anaerobic digestion processes. Some of the challenges that need to be addressed are listed below:

(1) More investigations have to been performed to determine exactly the Minimal Inhibitory Concentration (MIC) of each by-product (furfural, 5-HMF…) on both dark fermentation and anaerobic digestion processes.
(2) More investigations on the possible synergistic effect between the different by-products on the anaerobic fermentative processes represent also a challenging work for the future as information are clearly missing in the literature.
(3) Few studies have shown the degradation of by-products in continuous process. These results raise the questions of the impact of reactor mode (batch or continuous) and of inoculum adaptation

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References

Abatzoglou N, Chornet E, Belkacemi K. Phenomenological kinetics of complex systems: the development of a generalized severity parameter and its application to lignocellulosics fractionation. Chem Eng Sci 1992;47:1109–22.
Abbassi-Guendouz A, Trably E, Hamelin J, Dumas C, Steyer JP, Delgenès JP, et al. Microbial community signature of high-solid content methanogenic ecosystems. Bioresour Technol 2013;133:256–62.
Akpinar O, Erdogan K, Bostanci S. Enzymatic production of Xylooligosaccharide from selected agricultural wastes. Food Bioprod Process 2009;87(2):145–51.
Almeida JR, Bertilsson M, Gorwa-Grauslund MF, Gorsich S, Lidén G. Metabolic effects of furaldehydes and impacts on biotechnological processes. Appl Microbiol Biotechnol 2009;82(4):625–38.
Alvira P, Negro MJ, Ballesteros M. Effect of endoxylanase and α-l-arabinofuranosidase supplementation on the enzymatic hydrolysis of steam exploded wheat straw. Bioresour Technol 2011;102:4552–8.
Andrade LR, Salgado LT, Farina M, Pereira MS, Mourão P, Filho G. Ultrastructure of acidic polysaccharides from the cell walls of brown algae. J Struct Biol 2004;145:216–25.
Antonopoulou G, Gavala HN, Skiadas LV, Angelopoulos K, Lyberatos G. Biofuels generation from sweet sorghum: fermentative hydrogen production and anaerobic digestion of the remaining biomass. Bioresour Technol 2006;99(1):110–9.
Araque E, Parra C, Freer J, Contreras D, Rodrıguez J, Mendonca R, et al. Evaluation of organosolv pretreatment for conversion of *Pinus radiata* D don to ethanol. Enzym Microb Technol 2008;43:214–9.
Argun H, Kargi F, Kapdan IK, Oztekin R. Batch dark fermentation of powdered wheat starch to hydrogen gas: effects of the initial substrate and biomass concentrations. Int J Hydrogen Energy 2008;33(21):6109–15.
Badshah M. Evaluation of process parameters and treatments of different raw materials for biogas production [PhD Thesis] Sweden: University of Lunds; 2012.
Badshah M, Lam DM, Liu J, Mattiasson B. Use of an automatic methane potential test system for evaluating the biomethane potential of sugarcane bagasse after different treatments. Bioresour Technol 2012;114:262–9.
Banerjee S, Sen R, Mudliar S, Pandey RA, Chakrabarti T, Satpute D. Alkaline peroxide assisted wet air oxidation pretreatment approach to enhance enzymatic convertibility of rice husk. Biotechnol Prog 2011;27(3):691–7.
Barakat A, Monlau F, Steyer JP, Carrere H. Effect of lignin-derived and furan compounds found in lignocellulosic hydrolysates on biomethane production. Bioresour Technol 2012;104:90–9.
Becker EW. Microalgae: biotechnology and microbiology. Cambridge University Press; 1994.
Becker EW. Micro-algae as a source of protein. Biotechnol Adv 2007;25:207–10.
Bellido C, Bolado S, Coca M, Lucas S, González-Benito G, García-Cubero MT. Effect of inhibitors formed during wheat straw pretreatment on ethanol fermentation by *Pichia stipites*. Bioresour Technol 2011;102:10868–74.
Benjamin MM, Woods SL, Ferguson JF. Anaerobic toxicity and biodegradability of pulp-mill waste constituents. Water Res 1984;18(5):601–7.
Billa E, Monties B. Structural variability of lignins and associated phenolic acids in wheat straw. Cell Chem Technol 1995;29:305–14.
Boerjan W, Ralph J, Baucher M. Lignin biosynthesis. Annu Rev Plant Biol 2003;54:519–46.
Bondesson PM, Galbe M, Zacchi G. Ethanol and biogas production after steam pretreatment of corn stover with or without the addition of sulphuric acid. Biotechnol Biofuels 2013;6:11.
Boyer LJ, Vega K, Klasson KT, Clausen EC, Gaddy JL. The effects of furfural on ethanol production by *Saccharomyces cerevisiae*. Biomass Bioenergy 1992;3:41–8.
Brosse N, Sannigrahi P, Ragauskas A. Pretreatment of *Miscanthus* × *giganteus* using the ethanol organosolv process for ethanol production. Ind Eng Chem Res 2009;48(18):8328–34.

Campos FM, Couto JA, Figueiredo AR, Toth IV, Rangel AOSS, Hogg TA. Cell membrane damage induced by phenolic acids on wine lactic acid bacteria. Int J Food Microbiol 2009; 135(2):144–51.

Cantarella M, Cantarella L, Gallifuoco A, Spera A, Alfani F. Effect of inhibitors released during steam-explosion treatment of poplar wood on subsequent enzymatic hydrolysis and SSF. Biotechnol Prog 2004;20:200–6.

Cao GL, Ren NQ, Wang AJ, Guo WQ, Xu JF, Liu BF. Effect of lignocellulosederived inhibitors on growth and hydrogen production by *Thermoanaerobacterium thermosaccharolyticum* W16. Int J Hydrogen Energy 2009;35(24):13475–80.

Chang S, Li JZ, Liu F. Evaluation of different pretreatment methods for preparing hydrogen-producing seed inocula from waste activated sludge. Renew Energy 2011;36:1517–22.

Chang ACC, Tu YH, Huang MH, Lay CH, Lin CY. Hydrogen production by the anaerobic fermentation from acid hydrolysed rice straw hydrolysate. Int J Hydrogen Energy 2011; 36:14280–8.

Chapleur O, Civade R, Hoyos-Hernandez CF, Mazéas L, Bouchez T. Growing concentrations of phenols increasingly modify microbial communities dynamics and performances stability of anaerobic digesters. Proceedings of the 13th World Congress on Anaerobic Digestion, Santiago de Compostela, Spain, 25–28 June 2013, Paper IWA-11450 (Poster); 2013. p. 1–4. [on CD-ROM].

Chen CY, Zhao XQ, Yen HW, Ho SH, Cheng CL, Lee DJ, et al. Microalgae-based carbohydrates for biofuel production. Biochem Eng J 2013;78:1–10.

Chisti Y. Biodiesel from microalgae. Biotechnol Adv 2007;25:294–306.

Chisti Y. Biodiesel from microalgae beats bioethanol. Trends Biotechnol 2008;26:126–31.

Chistoserdova L. Recent progress and new challenges in metagenomics for biotechnology. Biotechnol Lett 2010;32:1351–9.

Cueva C, Mingo S, Muñoz-González I, Bustos I, Requena T, del Campo R, et al. Antibacterial activity of wine phenolic compounds and oenological extracts against potential respiratory pathogens. Lett Appl Microbiol 2012;54(6):557–63.

Datar R, Huang J, Maness PC, Mahagheghi A, Czernik S, Chounet E. Hydrogen production from the fermentation of corn stover biomass pretreated with a steam explosion process. Int J Hydrogen Energy 2007;32:932–9.

Delgenes JP, Moletta R, Navarro JM. Effects of lignocellulose degradation products on ethanol fermentations of glucose and xylose by *Saccharomyces cerevisiae*, *Zymomonas mobilis*, *Pichia stipitis*, and *Candida shehatae*. Enzym Microb Technol 1996;19:220–5.

Demirel B, Scherer P. The roles of acetotrophic and hydrogenotrophic methanogens during anaerobic conversion of biomass to methane: a review. Rev Environ Sci Biotechnol 2008;7:173–90.

Di Girolamo G, Grigatti M, Barbanti L, Angelidaki I. Effects of hydrothermal pre-treatments on Giant reed (*Arundo donax*) methane yield. Bioresour Technol 2013;147:152–9.

Diaz MJ, Cara C, Ruiz E, Perez-Bonilla M, Castro E. Hydrothermal pre-treatment and enzymatic hydrolysis of sunflower stalks. Fuel 2011;90(11):3225–9.

Du B, Sharma LN, Becker C, Chen SF, Mowery RA, van Walsum GP, et al. Effect of varying feedstock-pretreatment chemistry combinations on the formation and accumulation of potentially inhibitory degradation products in biomass hydrolysates. Biotechnol Bioeng 2010;107(3):430–40.

Emmel A, Mathias AL, Wypych F, Ramos LP. Fractionation of *Eucalyptus grandis* chips by dilute acid-catalysed steam explosion. Bioresour Technol 2003;86:105–15.

Endo A, Nakamura T, Ando A, Tokuyasu K, Shima J. Genome-wide screening of the genes required for tolerance to vanillin, which is a potential inhibitor of bioethanol fermentation, in *Saccharomyces cerevisiae*. Biotechnol Biofuels 2008;1:1–3.

Ezeji T, Qureshi N, Blaschek HP. Butanol production from agricultural residues: impact of degradation products on *Clostridium beijerinckii* growth and butanol fermentation. Biotechnol Bioeng 2007;97:1460–9.

Fang HHP, Liu Y, Ke SZ, Zhang T. Anaerobic degradation of phenol in wastewater at ambient temperature. Water Sci Technol 2004;49(1):95–102.

Fang HHP, Liang DW, Zhang T, Liu Y. Anaerobic treatment of phenol in wastewater under thermophilic condition. Water Res 2006;40:427–34.

Fangkum A, Reungsang A. Biohydrogen production from mixed xylose/arabinose at thermophilic temperature by anaerobic mixed cultures in elephant dung. Int J Hydrogen Energy 2011;36:13928–38.

Fedorak PM, Hrudey SE. The effects of phenol and some alkyl phenolics on batch anaerobic methanogenesis. Water Res 1984;18:361–7.

Feinberg D. Fuels options from microalgae with representative chemical compositions. Report, Solar Energy Research Institute, Colorado, United States; 1984.

Fengel D. Characterisation of cellulose by deconvoluting the OH valency range in FTIR spectra. Holzforschung 1992;46(4):283–8.

Fengel D, Wegener G. Wood: chemistry, ultrastructure, reactions, Wood: chemistry, ultrastructure, reactions. Berlin German Federal Republic: Walter de Gruyter; 1984. p. 613.

Fox M, Noike T. Wet oxidation pretreatment for the increase in anaerobic biodegradability of newspaper waste. Bioresour Technol 2004;91:273–81.

Fox MH, Noike T, Ohki T. Alkaline subcritical-water treatment and alkaline heat treatment for the increase in biodegradability of newsprint waste. Water Sci Technol 2003;48: 77–84.

Gnansounou E, Dauriat A. Techno-economic analysis of lignocellulosic ethanol: a review. Bioresour Technol 2010;101(13):4980–91.

Gonzalez-Fernández C, Sialve B, Bernet N, Steyer JP. Impact of microalgae characteristics on their conversion to biofuel Part II: focus on biomethane production. Biofuels Bioprod Bioref 2012a;6(2):205–18.

Gonzalez-Fernandez C, Sialve B, Bernet N, Steyer JP. Thermal pretreatment to improve methane production of *Scenedesmus*. Biomass Bioenergy 2012b;110:610–6.

Gonzalez-Fernandez C, Sialve B, Bernet N, Steyer JP. Comparison of ultrasound and thermal pretreatment of *Scenedesmus* biomass on methane production. Bioresour Technol 2013;129:219–23.

Guo XM, Trably E, Latrille E, Carrere H, Steyer JP. Hydrogen production from agricultural waste by dark fermentation: a review. Int J Hydrogen Energy 2010;35:10660–73.

Guo XM, Trably E, Latrille E, Carrere H, Steyer JP. Predictive and explicative models of fermentative hydrogen production from solid organic waste: role of butyrate and lactate pathways. Int J Hydrogen Energy 2014;39:7476–85.

Hawkes FR, Hussy I, Kyazze G, Dinsdale R, Hawkes DL. Continuous dark fermentative hydrogen production by mesophilic microflora: principles and progress. Int J Hydrogen Energy 2007;32(2):172–84.

Heipieper HJ, Weber FJ, Sikkema J, Keweloh H, de Bont JAM. Mechanisms of resistance of whole cells to toxic organic solvents. Trends Biotechnol 1994;12(10):409–15.

Hendriks ATWM, Zeeman G. Pretreatments to enhance the digestibility of lignocellulosic biomass. Bioresour Technol 2009;100(1):10–8.

Hernandez JE, Edyvean RGJ. Inhibition of biogas production and biodegradability by substituted phenolic compounds in anaerobic sludge. J Hazard Mater 2008;160: 20–8.

Hierholtzer A, Chatellard L, Kierans M, Akunna JC, Collier PJ. The impact and mode of action of phenolic compounds extracted from brown seaweed on mixed anaerobic microbial cultures. J Appl Microbiol 2013;114(4):964–73.

Ho K-L, Chen Y-Y, Lee D-J. Biohydrogen production from cellobiose in phenol and cresol-containing medium using Clostridium sp. R1. Int J Hydrogen Energ 2010;35: 10239–44.

Hoyos-Hernandez C, Limam I, Desmond F, Bouchez T, Mazéas L. Anaerobic biodegradation of 13C6-phenol: analysis of bacteria population involved in two different degradation kinetics. Proceedings of the 13th World Congress on Anaerobic Digestion, Santiago de Compostela, Spain, 25–28 June 2013, Paper IWA-12130 (Poster); 2013. p. 1–4. [on CD-ROM].

Hsu TC, Guo GL, Chen WH, Hwang WS. Effect of dilute acid pretreatment of rice straw on structural properties and enzymatic hydrolysis. Bioresour Technol 2010;101: 4907–13.

Hu Z, Foston M, Ragauskas AJ. Comparative studies on hydrothermal pretreatment and enzymatic saccharification of leaves and internodes of alamo switchgrass. Bioresour Technol 2011;14:7224–8.

Hu F, Jung S, Ragauskas A. Pseudo-lignin formation and its impact on enzymatic hydrolysis. Bioresour Technol 2012;117:7–12.

Ibraheem O, Ndimba BK. Molecular Aaptation meanisms employed by ethanologenic bacteria in response to lignocellulose-derived inhibitory compounds. Int J Biol Sci 2013; 9(6):598–612.

Illmer P, Reitschuler C, Wagner AO, Schwarzenauer T, Lins P. Microbial succession during thermophilic digestion: the potential of *Methanosarcina* sp. PLoS One 2014;9:e869.

Jackowiak D, Frigon JC, Ribeiro T, Pauss A, Guiot S. Enhancing solubilisation and methane production kinetic of switchgrass by microwave pretreatment. Bioresour Technol 2010;102(3):3535–40.

Jang JS, Cho YK, Jeong GT, Kim SK. Optimization of saccharification and ethanol production by simultaneous saccharification and fermentation (SSF) from seaweed, *Saccharina japonica*. Bioprocess Biosyst Eng 2012;35:11–8.

Janzon R, Schütt F, Oldenburg S, Fischer E, Körner I, Saake B. Steam pretreatment of spruce forest residues: optimal conditions for biogas production and enzymatic hydrolysis. Carbohydr Polym 2014;100:202–10.

John RP, Anisha GS, Nampoothiri KM, Pandey A. Micro and macroalgal biomass: a renewable source for bioethanol. Bioresour Technol 2011;102:186–93.

Jönsson LJ, Alriksson B, Nilvebrant NO. Bioconversion of lignocellulose: inhibitors and detoxification. Biotechnol Biofuels 2013;6:16.

Jorgensen H, Kristensen JB, Felby C. Enzymatic conversion of lignocellulose into fermentable sugars: challenges and opportunities. J Biofuels Bioprod Bioref 2007;1(2): 119–34.

Jung K, Kim D, Kim H, Shin H. Optimization of combined (acid + thermal) pretreatment for fermentative hydrogen production from *Laminaria japonica* using response surface methodology (RSM). Int J Hydrogen Energy 2011a;36:9626–31.

Jung K, Kim D, Shin Hang-Sik H. Fermentative hydrogen production from *Laminaria japonica* and optimization of thermal pretreatment conditions. Bioresour Technol 2011b;102:2745–50.

Jung KA, Lim SR, Kim Y, Park MP. Potentials of macroalgae as feedstocks for biorefinery. Bioresour Technol 2013;135:182–90.

Kampmann K, Ratering S, Baumann R, Schmidt M, Zerr W, Schnell S. Hydrogenotrophic methanogens dominate in biogas reactors fed with defined substrates. Syst Appl Microbiol 2012;35:404–13.

Kaparaju P, Serrano M, Thomsen AB, Kongjan P, Angelidaki I. Bioethanol, biohydrogen and biogas production from wheat straw in a biorefinery concept. Bioresour Technol 2009;100(9):2562–8.

Karakashev D, Batstone DJ, Trably E, Angelidaki I. Acetate oxidation is the dominant methanogenic pathway from acetate in the absence of Methanosaetaceae. Appl Environ Microbiol 2006;72(7):5138–41.

Kayembe K, Basosila L, Mpiana PT, Sikulisimwa PC, Mbuyu K. Inhibitory effects of phenolic monomers on methanogenesis in anaerobic digestion. Br Microbiol Res J 2013;3(1): 32–41.

Kelly C, Jones O, Barnhart C, Lajoie C. Effect of furfural, vanillin and syringaldehyde on *Candida guilliermondii* growth and xylitol biosynthesis. Appl Biochem Biotechnol 2008;148:97–108.

Keshwani DR, Cheng JJ. Switchgrass for bioethanol and other value-added applications. A review. Bioresour Technol 2009;100:1515–23.

Keymer P, Ruffell I, Pratt S, Lant P. High pressure thermal hydrolysis as pre-treatment to increase the methane yield during anaerobic digestion of microalgae. Bioresour Technol 2013;131:128–33.

Kim Y, Ximenes E, Mosier NS, Ladisch MR. Soluble inhibitors/deactivators of cellulase enzymes from lignocellulosic biomass. Enzym Microb Technol 2010;48:408–15.

Kim NJ, Li H, Jung K, Chang HN, Lee PC. Ethanol production from marine algal hydrolysates using *Escherichia coli* KO11. Bioresour Technol 2011;102:7466–9.

Klinke HB, Ahring BK, Schmidt AS, Thomsen AB. Characterization of degradation products from alkaline wet oxidation of wheat straw. Bioresour Technol 2002; 82(1):15–26.

Klinke HB, Thomsen AB, Ahring BK. Inhibition of ethanol-producing yeast and bacteria by degradation products produced during pre-treatment of biomass. Appl Microbiol Biotechnol 2004;66:10–26.

Kongjan P, O-Thong S, Kotay M, Min B, Angelidaki I. Biohydrogen production from wheat straw hydrolyzate by dark fermentation using extreme thermophilic mixed culture. Biotechnol Bioeng 2009;105:899–908.

Krakat N, Schmidt S, Scherer P. Mesophilic fermentation of renewable biomass: does hydraulic retention time regulate methanogen diversity? Appl Environ Microbiol 2010; 76:6322–6.

Kurakake M, Kisaka W, Ouchi K, Komaki T. Pretreatment with ammonia water for enzymatic hydrolysis of corn husk, bagasse, and switchgrass. Appl Biochem Biotechnol 2001;90:251–9.

Lapierre C, Monties B, Rolando C. Thioacidolysis of poplar lignins: identification of monomeric syringyl products and characterisation of guaiacylsyringyl lignins fractions. Holzforschung 1986;40:113–8.

Larsson S, Palmqvist E, Hahn-Hagerdal B, Tengbord C, Stenberg K, Zacchi G, et al. The generation of fermentation inhibitors during dilute acid hydrolysis of softwood. Enzym Microb Technol 1999;24(3–4):151–9.

Lay JJ, Fan KS, Chang J, Ku CH. Influence of chemical nature of organic wastes on their conversion to hydrogen by heat-shock digested sludge. Int J Hydrogen Energy 2003; 28(12):1361–7.

Lee J. Biological conversion of lignocellulosic biomass to ethanol. J Biotechnol 1997;56(1): 1–24.

Lee DH, Cho EY, Kim CJ, Kim SB. Pretreatment of waste newspaper using ethylene glycol for bioethanol production. Biotechnol Bioproc Eng 2010;15:1094–101.

Lee S, Monnappa AK, Mitchell RJ. Biological activities of lignin hydrolysate-related compounds. BMP Rep 2012;45(5):265–74.

Leven L, Schnürer A. Effects of temperature on biological degradation of phenols, benzoates and phthalates under methanogenic conditions. Int Biodegrad Biodeterior 2005; 55:153–60.

Leven L, Nyberg K, Korkea-Aho L, Schnürer A. Phenols in anaerobic digestion processes and inhibition of ammonia oxidising bacteria (AOB) in soil. Sci Total Environ 2006; 364:229–38.

Leven L, Nyberg K, Schnurer A. Conversion of phenols during anaerobic digestion of organic solid waste—a review of important microorganisms and impact of temperature. J Environ Manage 2012;95:S99–S103.

Li BZ, Balan V, Yuan YJ, Dale BE. Process optimization to convert forage and sweet sorghum bagasse to ethanol based on ammonia fiber expansion (AFEX) pretreatment. Bioresour Technol 2010;101(4):1285–92.

Manzanares P, Ballesteros I, Negro MJ, Oliva JM, Gonzalez A, Ballesteros M. Biological conversion of forage sorghum biomass to ethanol by steam explosion pretreatment and simultaneous hydrolysis and fermentation at high solid content. Biomass Convers Bioref 2012;2(2):123–32.

Mashevitskaya SG, Plevako EA. The decomposition products of sugars interfering with the development of fungi. J Appl Chem 1938;11:511–4.

Mata-Alvarez J, Macé S, Llabrés P. Anaerobic digestion of organic solid wastes. An overview of research achievements and perspectives. Bioresour Technol 2000;74:3–16.

Mills TY, Sandoval NR, Gill RT. Cellulosic hydrolysate toxicity and tolerance mechanisms in Escherichia coli. Biotechnol Biofuels 2009:2–6.

Monlau F, Sambusiti C, Barakat A, Guo XM, Latrille E, Trably E, et al. Predictive models of biohydrogen and biomethane production based on the compositional and structural features of lignocellulosic materials. Environ Sci Technol 2012a; 46(21):12217–25.

Monlau F, Barakat A, Steyer JP, Carrere H. Comparison of seven types of thermo-chemical pre-treatments on the structural features and anaerobic digestion of sunflower stalks. Bioresour Technol 2012b;120:241–7.

Monlau F, Barakat A, Trably E, Dumas C, Steyer JP, Carrere H. Lignocellulosic materials into biohydrogen and biomethane: impact of structural features and pretreatment. Crit Rev Environ Sci Technol 2013a;43(3):260–322.

Monlau F, Aemig Q, Trably E, Steyer JP, Carrere H. Specific inhibition of biohydrogen-producing *Clostridium* sp. after dilute-acid pretreatment of sunflower stalks. Int J Hydrogen Energy 2013b;38:12273–82.

Mosier N, Wyman C, Dale B, Elander R, Lee YY, Holtzapple M, et al. Features of promising technologies for pretreatment of lignocellulosic biomass. Bioresour Technol 2005; 96(6):673–86.

Mussatto SI, Roberto IC. Alternatives for detoxification of diluted-acid lignocellulosic hydrolyzates for use in fermentative process: a review. Bioresour Technol 2004;93:1–10.

Naseeruddin S, Srilekh Yadav K, Sateesh L, Manikyam A, Desai S, Venkateswar Rao L. Selection of the best chemical pretreatment for lignocellulosic substrate *Prosopis juliflora*. Bioresour Technol 2013;136:542–9.

Nath K, Das D. Improvement of fermentative hydrogen production: various approaches. Appl Microbiol Biotechnol 2004;65(5):520–9.

Nigam PS, Singh A. Production of liquid biofuels from renewable resources. Prog Energy Combust 2010;37(1):52–68.

Ntaikou I, Antonopoulou G, Lyberatos G. Biohydrogen production from biomass and wastes via dark fermentation: a review. Waste Biomass Valor 2010;1:21–39.

Olguin-Lora P, Puig-Grajales L, Razo-Flores E. Inhibition of the acetoclastic methanogenic activity by phenol and alkyl phenols. Environ Technol 2003;24:999–1006.

Op den Camp HJM, Verhagen FJM, Kivaisi AK, de Windt FE, Lubberding HJ, Gijzen HJ, et al. Effects of lignin on the anaerobic degradation of (ligno) cellulosic wastes by rumen microorganisms. Appl Microbiol Biotechnol 1988;29:408–12.

Overend RP, Chornet E. Fractionation of lignocellulosics by steamaqueous pretreatments [and discussion]. Philos Trans R Soc Lond A 1987;321:523–36.

Palmqvist E, Hahn-Hägerdal B. Fermentation of lignocellulosic hydrolysates. II: inhibitors and mechanisms of inhibition. Bioresour Technol 2000;74:25–33.

Panagiotopoulos IA, Bakker RR, Budde MA, de Vrije T, Claassen PA, Koukios EG. Fermentative hydrogen production from pretreated biomass: a comparative study. Bioresour Technol 2009;100(24):6331–8.

Panagiotopoulos IA, Bakker RR, de Vrije T, Koukios EG. Effect of pretreatment severity on the conversion of barley straw to fermentable substrates and the release of inhibitory compounds. Bioresour Technol 2011;102:11204–11.

Park YC, Kim JS. Comparison of various alkaline pretreatment methods of lignocellulosic biomass. Energy 2012;47(1):31–5.

Park JH, Yoon JJ, Park HD, Kim YJ, Lim DJ, Kim SH. Feasibility of biohydrogen production from *Gelidium amansii*. Int J Hydrogen Energy 2011a;36(21):13997–4003.

Park JH, Yong JJ, Park HD, Lim DJ, Kim SH. Anaerobic digestibility of algal bioethanol residue. Bioresour Technol 2011b;113:78–82.

Park JH, Cheon HC, Yoon JJ, Park HD, Kim SH. Optimization of batch dilute-acid hydrolysis for biohydrogen production from red algal biomass. Int J Hydrogen Energy 2013;38: 6130–6.

Pedersen M, Meyer AS. Lignocellulose pretreatment severity—relating pH to biomatrix opening. New Biotechnol 2010;27(6):739–50.

Pell M, Torstensson L. Toxicity testing in soil, use of microbial and enzymatic enzymes. In: Bitton G, editor. Encyclopedia of environmental microbiology. New York: Wiley & Sons Inc.; 2002. p. 3155–68.

Peng L, Chen Y. Conversion of paper sludge to ethanol by separate hydrolysis and fermentation (SHF) using *Saccharomyces cerevisiae*. Biomass Bioenergy 2011;35: 1600–6.

Persson T, Ren JL, Joelsson E, Jönsson AS. Fractionation of wheat and barley straw to access high-molecular-mass hemicelluloses prior to ethanol production. Bioresour Technol 2009;100(17):3906–13.

Prajapati SK, Kaushik P, Malik A, Vijay VK. Phycoremediation coupled production of algal biomass, harvesting and anaerobic digestion: possibilities and challenges. Biotechnol Adv 2013;31(8):1408–25.

Quéméneur M, Hamelin J, Latrille E, Steyer JP, Trably E. Functional versus phylogenetic fingerprint analyses for monitoring hydrogen-producing bacterial populations in dark fermentation cultures. Int J Hydrogen Energy 2011;36:3870–9.

Quémeneur M, Hamelin J, Barakat A, Steyer JP, Carrere H, Trably E. Inhibition of fermentative hydrogen production by lignocellulose-derived compounds in mixed cultures. Int J Hydrogen Energy 2012;37(4):3150–9.

Ras M, Lardon L, Sialve B, Bernet N, Steyer JP. Experimental study on a coupled process of production and anaerobic digestion of *Chlorella vulgaris*. Bioresour Technol 2010; 102(1):200–6.

Rasmussen H, Sorensen HR, Meyer AS. Formation of degradation compounds from lignocellulosic biomass in the biorefinery: sugars reaction mechanisms. Carbohydr Res 2014;385:45–57.

Rivard CJ, Grohmann K. Degradation of furfural (2-furaldehyde) to methane and carbon dioxide by an anaerobic consortium. Appl Biochem Biotechnol 1991;28(29): 285–95.

Rojan PJ, Anisha GS, Madhavan Nampoothiri K, Pandey A. Micro and macroalgal biomass: a renewable source for bioethanol. Bioresour Technol 2011;102:186–93.

Romani A, Garrote G, Alonso JL, Parajó JC. Bioethanol production from hydrothermally pretreated *Eucalyptus globulus* wood. Bioresour Technol 2010;101:8706–12.

Rosenkranz F, Cabrol L, Carballa M, Donoso-Bravo A, Cruz L, Ruiz-Filippi G, et al. Relationship between phenol degradation efficiency and microbial community structure in an Anaerobic SBR. Water Res 2013;47(17):6739–49.

Ruiz HA, Rodríguez-Jasso RM, Fernandes BD, Vicente AA, Teixeira JA. Hydrothermal processing, as an alternative for upgrading agriculture residues and marine biomass according to the biorefinery concept: a review. Renew Sust Energ Rev 2013;21:35–51.

Saha BC, Yoshida T, Cotta MA, Sonomoto K. Hydrothermal pretreatment and enzymatic saccharification of corn stover for efficient ethanol production. Ind Crop Prod 2013; 44:367–72.

Saidur R, Abdelaziz EA, Demirbas A, Hossain MS, Mekhilef S. A review on biomass as a fuel for boilers. Renew Sust Energ Rev 2011;15(5):2262–89.

Sambusiti C, Monlau F, Ficara E, Carrere H, Malpei F. A comparison of different pretreatments to increase methane production from two agricultural substrates. Appl Energy 2013a;104:62–70.

Sambusiti C, Ficara E, Malpei F, Steyer JP, Carrere H. Effect of sodium hydroxide pretreatment on physical, chemical characteristics and methane production of five varieties of sorghum. Energy 2013b;55:449–56.

Sannigrahi P, Kim DH, Jung S, Ragauskas A. Pseudo-lignin and pretreatment chemistry. Energy Environ Sci 2011;4:1306–10.

Sarkar O, Kannaiah Goud R, Venkata Subhash G, Venkata Mohan S. Relative effect of different inorganic acids on selective enrichment of acidogenic biocatalyst for fermentative biohydrogen production from wastewater. Bioresour Technol 2013;147:321–31.

Scordia D, Cosentino SL, Jeffries TW. Second generation bioethanol production from *Saccharum spontaneum* L. ssp. aegyptiacum (Willd.) Hack. Bioresour Technol 2010; 101(14):5358–65.

Shafiei M, Karimi K, Taherzadeh MJ. Palm date fibers: analysis and enzymatic hydrolysis. Int J Mol Sci 2010;11(11):4285–96.

Sialve B, Bernet N, Bernard O. Anaerobic digestion of microalgae as a necessary step to make microalgal biodiesel sustainable. Biotechnol Adv 2009;27(4):409–16.

Sills DL, Gossett JM. Using FTIR spectroscopy to model alkaline pretreatment and enzymatic saccharification of six lignocellulosic biomasses. Biotechnol Bioeng 2012; 109(4):894–903.

Sun Y, Cheng J. Hydrolysis of lignocellulosic materials for ethanol production: a review. Bioresour Technol 2002;83(1):1–11.
Sun R, Tomkinson J. Separation and characterization of cellulose from wheat straw. Sep Sci Technol 2005;39(2):391–411.
Sydney EB, Sturm W, de Carvalho JC, Thomaz-Soccol V, Larroche C, Pandey A, et al. Potential carbon dioxide fixation by industrially important microalgae. Bioresour Technol 2010;101(15):5892–6.
Sze P. A biology of the algae. 2nd ed. Wm. C. Brown Publishers; 1993.
Taherzadeh MJ, Karimi K. Acid-based hydrolysis processes for ethanol from lignocellulosic materials: a review. Bioresources 2007;2:472–99.
Taherzadeh MJ, Karimi K. Pretreatment of lignocellulosic wastes to improve ethanol and biogas production: a review. Int J Mol Sci 2008;9(9):1621–51.
Tai J, Adav SS, Su A, Lee DJ. Biological hydrogen production from phenol-containing wastewater using Clostridium butyricum. Int J Hydrogen Energy 2010;35(24):13345–9.
Talebnia F, Karakashev D, Angelidaki I. Production of bioethanol from wheat straw: an overview on pretreatment, hydrolysis and fermentation. Bioresour Technol 2010;101:4744–53.
Theerarattananoon K, Xu F, Wilson J, Staggenborg S, Mckinney L, Vadlani P, et al. Effects of the pelleting conditions on chemical composition and sugar yield of corn stover, big bluestem, wheat straw, and sorghum stalk pellets. Bioprocess Biosyst Eng 2012;35:615–23.
Torry-Smith M, Sommer P, Ahring BK. Purification of bioethanol effluent in an UASB reactor system with simultaneous biogas formation. Biotechnol Bioenergy 2003;84:7–12.
Vancov T, Alston AS, Brown T, McIntosh S. Use of ionic liquids in converting lignocellulosic material to biofuels. Renew Energy 2012;45:1–6.
Vanholme R, Demedts B, Morreel K, Ralph J, Boerjan W. Lignin biosynthesis and structure. Plant Physiol 2010;153(3):895–905.
Veeravalli SS, Chaganti SR, Lalman JA, Heath DD. Effect of furans and linoleic acid on hydroge production. Int J Hydrogen Energy 2013;38:12283–93.
Velasquez JA, Ferrando F, Salvado J. Effects of kraft lignin addition in the production of binderless fiberboard from steam exploded Miscanthus sinensis. Ind Crop Prod 2003;18:17–23.
Vivekanand V, Ryden P, Horn SJ, Tapp HS, Wellner N, Eijsink VG, et al. Impact of steam explosion on biogas production from rape straw in relation to changes in chemical composition. Bioresour Technol 2012;123(11):608–15.
Von Sivers M, Zacchi G, Olsson L, Hahn-Hugerdal. Cost analysis of ethanol production from willow using recombinant *Escherichia coli*. Biotechnol Prog 1994;10(5):555–60.
Wei N, Quarterman J, Jin YS. Marine macroalgae: an untapped resource for producing fuels and chemicals. Trends Biotechnol 2013;31:70–7.
Wei WQ, Wu SB, Liu LG. Combination of liquid hot water pretreatment and wet disk milling to improve the efficiency of the enzymatic hydrolysis of eucalyptus. Bioresour Technol 2013;128:725–30.
Whyte J, Englar JR. The agar component of the red seaweed. Phytochemistry 1981;20:237–40.
Wierckx N, Koopman F, Ruijssenaars HJ, de Winde JH. Microbial degradation of furanic compounds: biochemistry, genetics, and impact. Appl Microbiol Biotechnol 2011;92(6):1095–105.
Ximenes E, Kim Y, Mosier N, Dien B, Ladisch M. Inhibition of cellulases by phenols. Enzym Microb Technol 2010;46:170–6.
Yadav KS, Naseeruddin S, Prashanthi GS, Sateesh L, RaoL V. Bioethanol fermentation of concentrated rice straw hydrolysate using co-culture of *Saccharomyces cerevisiae* and *Pichia stipites*. Bioresour Technol 2011;102:6473–8.
Yamada T, Sakaguchi K. Comparative studies on Chlorella cell walls: induction of protoplast formation. Arch Microbiol 1982;132:10–3.
Yoshizawa N, Watanabe N, Yokota S, Idei T. Distribution of guaiacyl and syringyl lignins in normal and compression wood of *Buxus Microphylla* Var. *Insularis Nakai*. IAWA J 1993;14(2):139–51.
Yun YM, Jung KW, Kim DH, Oh YK, Cho SK, Shin HS. Optimization of dark fermentative H2 production from microalgal biomass by combined (acid + ultrasonic) pretreatment. Bioresour Technol 2013;141:220–6.
Zaldivar J, Martinez A, Ingram LO. Effect of selected aldehydes on the growth and fermentation of ethanologenic *Escherichia coli*. Biotechnol Bioeng 1999;65(1):24–33.
Zhang Y, Han B, Ezeji TC. Biotransformation of furfural and 5-hydroxymethyl furfural (HMF) by *Clostridium acetobutylicum* ATCC 824 during butanol fermentation. N Biotechnol 2012;29(3):345–51.