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Review

Use of microalgae to recycle nutrients in aqueous phase derived from hydrothermal liquefaction process

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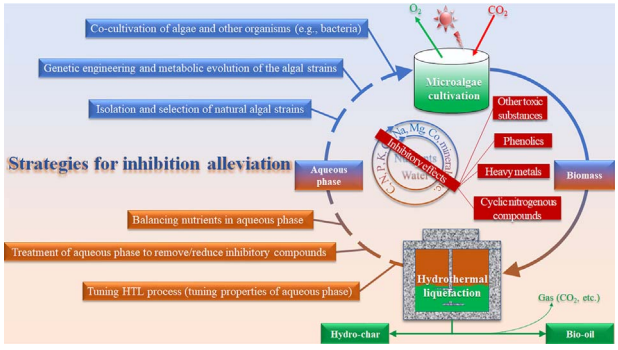
GRAPHICAL ABSTRACT



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ABSTRACT

Hydrothermal liquefaction (HTL) of microalgae biomass generates an aqueous phase (AP) byproduct with limited energy value. Recycling the AP solution as a source of nutrients for microalgae cultivation provides an opportunity for a cost-effective production of HTL based biofuel and algal biomass feedstock for HTL, allowing a closed-loop biofuel production in microalgae HTL biofuel system. This paper aims to provide a comprehensive overview of characteristics of AP and its nutrients recycling for algae production. Inhibitory effects resulted from the toxic compounds in AP and alleviation strategies are discussed.

1. Introduction

Hydrothermal liquefaction (HTL) of wet biomass such as microalgae is one of the promising ways to produce renewable and sustainable energy alternatives to fossil fuels. HTL is a thermal depolymerization process converting wet biomass into crude-like oil (bio-oil) under moderate temperature 200–380 °C and high pressure 5–20 MPa (Huang and Yuan, 2015; Peterson et al., 2008). Water is used as the reaction solvent during HTL processes, with or without organic solvent participation as co-solvent. The products from HTL of biomass contain multiple phases including oil phase (bio-oil, the main product), solid phase (hydrochar), gas phase, and aqueous phase (AP). Under milder conditions (temperature of 180–260 °C and pressure of 2–5 MPa), this process produces hydrochar as the main product because of carbonization (Du et al., 2012; Leng et al., 2015b; Yao et al., 2016a).

When wet biomass such as microalgae is used as the feedstock for fuel production, HTL is a superior technology for the conversion as this technology does not require energy intensive dewatering and drying of

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Table 1
Characteristics of aqueous phase produced from hydrothermal liquefaction of microalgae.

Process[a]	Feedstock[b]	Production conditions[c]	AP yield (carbon %)[d]	Organic compounds (major components, ammonia is not organic)	Wastewater properties (g/L, except pH which has no unit)[c]	Remark[e]	Ref.
HTL; CF; BS	*Tetraselmis* from 4 different sources (marine MA, n = 4)	T: 343–350 °C; AF SL: 17.0–18.1%; P: 20.2–20.9 MPa; FR: 1.5–3.0 L/h	22–33%	(Ammonia), acetic acid, propanoic acid, ethanol, acetone, etc.	pH 7.6–7.9; COD 43.8–94.9; PO_4^{3-} BDL	• Marine MA produced AP with low phosphate • High feed load led to high COD in AP • Fresh water MA of high lipid content produced AP with low pH and COD	Maddi et al. (2016)
	Scenedesmus obliquus or *Chlorella* from 4 different sources (freshwater MA, n = 4)	T: 340–350 °C; AF SL: 13.4–19.4%; P: 20.1–20.6 MPa; FR: 1.5–2.0 L/h	10–34%	(Ammonia), acetic acid, propanoic acid, acetamide, methyl pyrazine, 2-pyrrolidinenone, ethanol, acetone, etc.	pH 3.7–8.8; COD 44.6–84.8; PO_4^{3-} 0.044–0.687		
HTL; CF, BS	Algae slurries (from 4 different source) of *Nannochloropsis* sp. (n = 4)	T: 344–362 °C; P 2966–3020 psi (about 20 MPa); SL:17–35%; FR: 1.5–2.2 L/h	15.2–43.9%	Methanol, ethanol, glycerol, acetic and glycolic acids, etc.	pH 7.48–7.72; COD 59.9–125.5; TN 5.4–11.0 (for three of the sample); TP 0.015 (for one of the sample)	• About half (47–51%) of the nitrogen transformed to AP • 28–39% of the nitrogen was detected as ammonia in the gas phase	Elliott et al. (2013)
HTL; batch; BS	*Chlorella pyrenoidosa*	T: 260/280/300 °C; SL: 15%/25%/35%; RT: 30/60/90 min	–[f]	Fatty acid, phenolics, esters, ketones and alcohols, amides and N&O-heterocyclic compounds.	pH 7.77–8.29; COD 62.7–104; TN 11.0–31.7; TP 5.4–18.9	• S/L ratio was dominant factor affecting the concentration of nutrients in AP • Very high TP in AP	Gai et al. (2015)
HTL; batch; BS	*Nannochloropsis gaditana* (marine MA)	T: 350 °C; SL: 10%; RT: 15 min	26.8–31.0%	Acetic acid, glycolic acid, formic acid, etc.	pH 8.2–8.6; TOC 11.37–14.10; TN 4.22–5.42; NH_4^+ 3.92–4.47; PO_4^{3-} **2.65–2.72**	• Marine MA produced AP with very high phosphate • Organic solvent (dichloromethane) assisted phase separation reduced TOC in AP and increased bio-oil yield but with high N and O content	López Barreiro et al. (2015b)
	Scenedesmus almeriensis (freshwater MA)	T: 350 °C; SL: 10%; RT: 15 min	18.7–23.3%	Acetic acid, glycolic acid, formic acid, etc.	pH 8.4–8.6; TOC 10.11–12.55; TN 3.90–4.04; NH_4^+ 2.72–3.19; PO_4^{3-} 0.037–0.040		
HTL; batch; BS	24 different feedstocks (12 batches of MA with their defatted analogues, n = 24)	T: 300 °C; RT: 30 min	4.6–31.2% (total dissolved solids)	–	TOC about 8–39; TN about 1–24	• AP yield positively correlated to feedstock protein content and ash content, respectively	Li et al. (2017a)
HTC; batch; BS	MA and MA mixtures (n = 3)	T: 125–225 °C; RT: 0.5–15 min		Acetic acid, propanoic acid, pyrazines, etc.	pH 4.7–6.8; TN 3.6–14.6; NH_4^+ 0.58–4.05; TP 0.32–1.05	• HTC could be used as a denitrification pretreatment process before HTL for biocrude production	Costanzo et al. (2015)
HTL; batch; BS	*Chlorella vulgaris*, *Scenedesmus dimorphous* or *Spirulina platensis* (n = 4)	T: 300/350 °C; SL: 10%; RT: 60 min	46–68%	Acetic acid; phenols, etc.	pH 8.4–9.2; TOC 9.06–15.12; TN 3.13–8.14; NH_4^+ 4.75–6.30; PO_4^{3-} 0.28–2.16	AP yield is the total mass percentage of AP including water	Biller et al. (2012)
HTL; batch; BS	*Chlorella pyrenoidosa* (freshwater MA)	T: 220–300 °C; RT: 0–120 min; S/L: 6.3/75–50.0/75 g/mL; ethanol content in water: 0–100%	–	Cyclic amine derivatives, straight amine derivatives, phenols, ketone & alcohol derivatives, esters, etc.	–	• Ethanol – water promoted N-containing compounds into aqueous phase	Peng et al. (2016a,b)
HTL; CF, pilot-scale	*Spirulina*	T: 300 °C; SL: 20–30%; RT: 30 min	–	–	pH 7.5; COD 128; TOC 41.1; TN 5.48; NH_4^+ 3.23; TP 1.86	• High COD in AP	(Zhou et al., 2011a,b,2013)
HTL; batch; BS	Algae-bacteria biomass mixtures (n = 3)	T: 300 °C; S/L:1/4; RT: 30 min; P: 10–12 MPa	15–26%	–	pH 7.89; COD 85.2–121; TOC 23.2–39.4; TN 10.2–20.3; TP 0.68–1.56	• More than half (51–64%) of the nitrogen transformed to AP	
HTL; CF; BS	Mixed algae	T: 329 °C; AF SL: 14.4%; P: 20.0 MPa; FR: 1.5 L/h	32%	(Ammonia), acetic acid, N-methyl acetamide, acetamide, acetone, etc.	pH 7.9; COD 68.1; PO_4^{3-} BDL	–	Maddi et al. (2017)

[a] HTL: hydrothermal liquefaction; HTC: hydrothermal carbonization; HTG: hydrothermal gasification; CF: continuous flow; BS: bench scale.
[b] MA: microalgae.
[c] T: temperature; AF: ash-free; SL: solid load; P: pressure; FR: feed rate; S/L: solid/liquid mass ratio; RT: residence time.
[d] AP: aqueous phase.
[e] BDL: below detection limit. TOC: total organic carbon; COD: chemical oxygen demand; TN: total nitrogen; TP: total phosphorus; PO_4^{3-}: phosphate; NH_4^+: ammonium.
[f] Not reported.

algal biomass prior the treatment. Due to this energy-saving feature, HTL of microalgae has received increasing interest as a viable route for producing algae-based biofuel (Chen et al., 2015b; Elliott et al., 2013,2015). Currently HTL is not commercialized due to several challenges such as low efficiency of heat transfer and recovery for HTL reactor, low yield and poor fuel properties of bio-oil such as corrosivity, high nitrogen content, and difficulty with upgrading, and lack of effective utilization of HTL by-products such as hydrochar and AP (Lee et al., 2016).

During HTL, AP is produced in large amount due to the high-moisture (> 80%) biomass used. In general, AP contains high contents of organic carbon and nitrogen as well as toxic components such as heavy metals and cyclic oxygen and nitrogen compounds. Currently, HTL of biomass as an emerging area has not been fully explored for its scaling up and commercialization, therefore, the safe disposal of the large amount of AP generated from HTL process has been rarely reported. However, some researches have been attempted to explore the utilization of this underutilized stream as a resource and feedstock for various processes. For example, AP can be recirculated for use as co-solvent for HTL of biomass but with limited bio-oil enhancement, and the concentrated organic carbon content and toxic substances would be accumulated which makes AP more recalcitrant to the treatment (Biller et al., 2016; Madsen et al., 2016; Pedersen et al., 2016). AP can also be used as a resource for energy recovery by processes such as anaerobic digestion (Chen et al., 2017) or supercritical gasification (Elliott et al., 2013). However, the energy yield of these processes is low due to low energy content of the AP liquid. Additionally, other elements such as phosphorus and nitrogen cannot be utilized during energy recovery. These nutrient elements may be adsorbed by adsorbents such as zeolite (Ran et al., 2015) or recovered as struvite (Barbera et al., 2017; Shanmugam et al., 2017a) before or after energy recovery. But the applicability and effectiveness of these nutrient recovery strategies remain to be further examined.

It should be noted that the AP actually contains various essential nutrients that could support plant and microorganism growth. When using microalgae as biomass feedstock for HTL, for example, about 20% of carbon and more than 50% of nitrogen in the feed were transferred into AP, mainly in the form of short-chain organic acids (such as acetic acid) and ammonia/ammonium, respectively (Elliott et al., 2013; López Barreiro et al., 2015b; Lu et al., 2017; Zhou et al., 2011b, 2013). Orthophosphate and potassium ions also abundantly exist in AP (Bagnoud-Velásquez et al., 2015; López Barreiro et al., 2015a). These chemical characteristics indicate that AP may serve as a good nutrients source for growing microorganisms such as microalgae.

On the other hand, mass production of the microalgae as feedstock for HTL will need a large amount of nutrient supply (Lee et al., 2016; Pate et al., 2011; Wijffels and Barbosa, 2010). The nutrient-rich AP may provide an ideal nutrient source for mass microalgae production. It is estimated that 25 million tons of nitrogen and 4 million tons of phosphorus are needed to produce microalgae to replace all transportation fuel in the EU each year (Wijffels and Barbosa, 2010). In the U.S., this scenario will need a 400% increase of nitrogen and 200% phosphorus fertilizers (Pate et al., 2011). The sustainable biofuel system is therefore demanding the production of microalgae on nutrients-rich wastewater, and in fact, algae production coupling with wastewater treatment has been widely reported (Chen et al., 2015a; Reddy et al., 2016; Selvaratnam et al., 2016; Zhou et al., 2011a, 2014, 2017).

Considering the problems with AP disposal in HTL and the nutrients contained in AP that meet the requirement for mass algae production, it is ideal to create a synergy and win-win scenario by using the AP from HTL for algal production. The aim of this work is to provide a comprehensive review of AP derived from HTL of microalgae biomass, and the microalgae cultivation on AP. This will help create a close loop of nutrient cycle as the AP will be in turn used for growing new algal biomass. It should be noted that HTL has been used for processing a variety of biomass feedstock, and the compositions of the AP streams derived from different biomass feedstock are quite different. For example, AP derived from HTL of lignocelluloses has a more acidic pH, higher phenolic content, and lower phosphorus content (Maddi et al., 2017; Madsen et al., 2016; Weiner et al., 2014) compared to the AP derived from microalgae. In this work, we focus on microalgae cultivation in AP derived from microalgae-based HTL process.

2. Chemical characteristics of AP derived from HTL

AP is generated during HTL of wet biomass with water in supercritical state being the reaction medium. During processing, hundreds of compounds are produced from hydrolysis, dehydration, decarboxylation and deamination of biomass compounds such as lipids, proteins, cellulose, hemicellulose and lignin (Lu et al., 2017). Table 1 shows the dominant components in microalgae derived AP. Short-chain organic acid such as acetic acid and propanoic acid and ammonia are the major components identified in most studies (Biller et al., 2012; Cherad et al., 2016; Jena et al., 2011; Maddi et al., 2016). High protein content results in high concentration of these components in AP (Lu et al., 2017; Madsen et al., 2016). These compounds can serve a good nutrients source for algae cultivation (Alba et al., 2013; Perez-Garcia et al., 2011). However, it should also be noted that other compounds such as phenols, indoles, cyclic amides, piperidinones, amino-phenols, pyrazines also exist in AP, which could be toxic to algal growth (Biller et al., 2012; Gai et al., 2015; Jena et al., 2011; Maddi et al., 2016; Tommaso et al., 2015). Fig. 1 summarizes the quantitative characteristics of the AP such as pH levels and the concentrations of various compounds. These characteristics are described as follows.

2.1. pH of AP

As seen in Fig. 1, the pH of AP produced from HTL are commonly within the range of 7–9, but can vary widely from 3.7 to 10.0. In general, the pH of AP highly depends on the biomass composition. For example, HTL of algae with high-protein content tends to result in a higher AP pH (7.6–8.8) due to high content of ammonia derived from protein hydrolysis and deamination (Maddi et al., 2016; Zhang et al., 2016). A low AP pH (pH 3.7) was reported from HTL of heterotrophically-grown *Chlorella* containing high lipid but low protein contents (Maddi et al., 2016). A similar low pH range of AP (4.42–4.79) was also reported from HTL of *Chlorella* sp. with low-protein (9.3%), while AP from high-protein (52.4%) containing *Nannochloropsis* sp. had a much higher pH (7.55–9.20) (Zhang et al., 2016). In addition to biomass composition, AP pH also depends on the operation conditions used in HTL. For example, a pH 10.0 was observed for AP from HTL of *Nannochloropsis* sp. at 350 °C for 60 min; at a reduced reaction temperature (300 °C) and time (5 min), HTL of the same biomass reduced the pH to 7 (Patel et al., 2016). In another study, pH of AP increased with increasing temperature in the range of 180–260 °C, which was due to the decarboxylation of organic acids and deamination of protein (Yu et al., 2011).

2.2. Carbon

Protein content and loading of algae feedstock affect carbon distribution during HTL. Fig. 1 shows that carbon-based AP yield or the percentage of carbon in AP relative to the total carbon in HTL feedstock ranges from 4.6 to 43.9 with an average of 20% (Fig. 1). Protein content in microalgae feedstock was found positively correlated with AP yield (Li et al., 2017a). Chemical oxygen demand (COD) and total organic carbon (TOC) contents of AP follow a similar trend as the AP yield. As shown in Fig. 1, most studies reported COD in the range of 60–100 g/L with an average of 85 g/L; the values for TOC seem more widely distributed from 3 to 80 g/L but mainly in the range of 10–30 g/L. A TOC value as low as 3.07 g/L was due to low feedstock load (1.9%, wt%) (Teymouri et al., 2017). The highest TOC (80 g/L) was obtained when

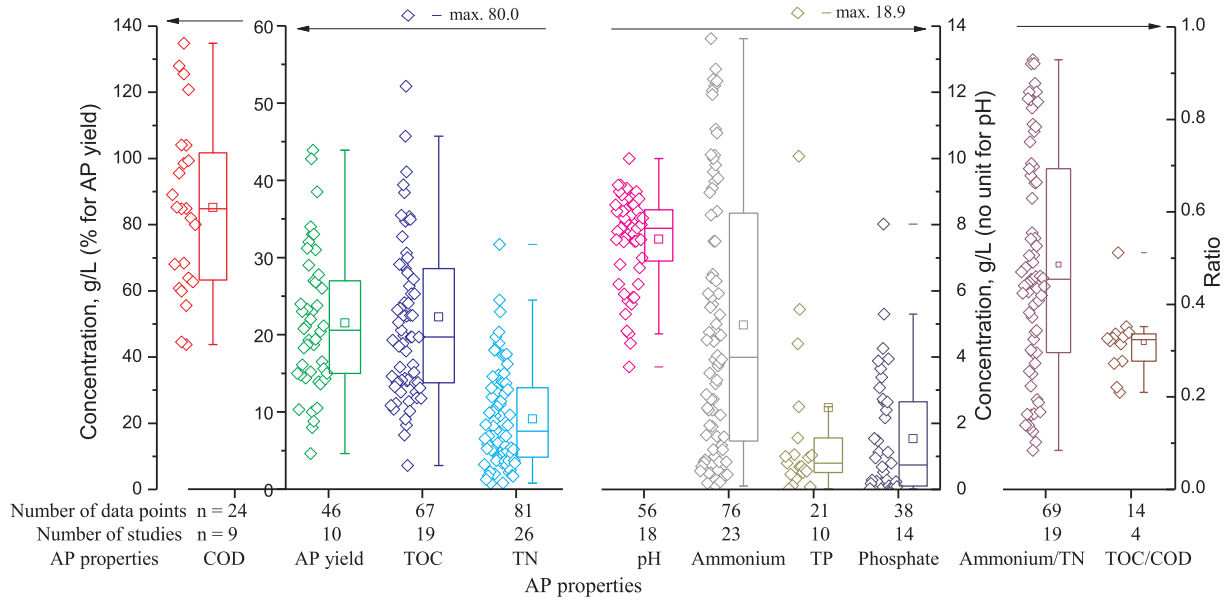

Fig. 1. Wastewater properties of aqueous phase produced from hydrothermal treatment of microalgae. Data collected from 31 studies (Bagnoud-Velásquez et al., 2015; Biller et al., 2012; Broch et al., 2013; Cherad et al., 2016; Costanzo et al., 2015; Du et al., 2012; Elliott et al., 2013; Gai et al., 2015; Hognon et al., 2015; Jena et al., 2011; Li et al., 2017a; López Barreiro et al., 2015b; Maddi et al., 2017, 2016; Madsen et al., 2016; Martinez-fernandez and Chen, 2017; Nelson et al., 2013; Patel et al., 2016; Reddy et al., 2016; Selvaratnam et al., 2015a, 2015b; Teymouri et al., 2017; Wang et al., 2016; Yao et al., 2016b; Yu et al., 2011; Zhang et al., 2016; Zhang et al., 2017; Zheng et al., 2017; Zhou et al., 2015, 2013, 2011b). Data obtained at different processing conditions from microalgae of a certain biochemical compositions were collected with quota to avoid data disguise by curtain source of data pools; only the maximum, median and minimum values were collected when more than 3 sets of data for each property were available. For example, the number of TP data available in Ref. (Gai et al., 2015) is 20 with TP ranging from 5.44 to 18.9 g/L, only the maximum (18.9 g/L), median (10.1 g/L) and minimum (5.44 g/L) values were collected and used in this figure.

high protein-containing *Nannochloropsis* sp. was processed (Zhang et al., 2016). In general, proteins in algae feedstock contribute more TOC to AP compared to carbohydrate and lipids (Li et al., 2017a; Madsen et al., 2016).

2.3. Nitrogen

Nitrogen content in AP highly depends on the protein content and mass loading of algae feedstock used in HTL (Li et al., 2017a; Madsen et al., 2016). Generally, more than half of the nitrogen in microalgae is transferred to AP during HTL; the concentrations of total nitrogen (TN) and ammonium vary from 0.77 to 31.7 g/L and from 0.10 to 13.6 g/L, respectively (Fig. 1). Fig. 1 also shows that the ratio of ammonium to TN ranges widely, with half of reported data are within 0.3–0.7. The highest TN content in AP was obtained from *Chlorella pyrenoidosa* biomass with a protein content up to 71% (Gai et al., 2015). On the contrary, low protein containing (11.4%) *Scenedesmus* resulted in the lowest TN and ammonium content (Li et al., 2017a). The processing conditions also affect the TN content. A low TN value (0.77 g/L) was obtained from HTL of *Nannochloropsis gaditana* due to low biomass loading (Teymouri et al., 2017). Similar variation trend of TN vs biomass loading was also reported by (Gai et al., 2015). Longer reaction time greatly increased nitrogen content in AP (Cherad et al., 2016; Gai et al., 2015). For example, 30-min residence time resulted in an AP with 11.7 g/L TN, while 90 min resident time increased TN to 31.7 g/L (Gai et al., 2015).

2.4. Phosphorus

The fate of phosphorus (P) during HTL of algae feedstock depends on phosphorus and metal contents in the algae biomass. For biomass with low content of metals such as calcium (Ca), magnesium (Mg), copper (Cu), ferrum (Fe) and zinc (Zn), the majority (85–100%) of P was transferred into AP after HTL process (Bagnoud-Velásquez et al., 2015; Valdez et al., 2012). On the contrary, algae with high content of metals (Ca, Mg, and Fe) led to a low P recovery (< 30%) in AP (Jena et al., 2011).

Mass loading also affects P transformation. Reducing biomass loading from 35% to 15% resulted in a reduction of the total phosphorus (TP) concentration in AP from 18.9 to 5.44 g/L (Gai et al., 2015). The separation method used to obtain AP may lead to difference in AP phosphate content. The direct separation of bio-oil from the reaction matrix without use of solvent led to high phosphate (PO_4^{3-}) concentration (8.02 g/L) in AP when HTL of *Chlorella vulgaris* at 350 °C (Cherad et al., 2016). On the contrary, the use of organic solvent dichloromethane reduced 50% phosphate content in AP, which may due to the extraction of organophosphates such as phospholipids to the solvent (Cherad et al., 2016).

2.5. Macro-/micro-nutrients

Alkaline metals such as potassium (K) and sodium (Na) in microalgae usually exist in AP due to their high solubility. For example, about 80% of the Na and K in the biomass were found in AP after HTL of *Laminaria Saccharina* (Anastasakis and Ross, 2011). López Barreiro et al. (2015a,b) and Bagnoud-Velásquez et al. (2015) reported a complete recovery of K and Na in AP. Some major elements such as sulphur (S) and chloride (Cl) were also mainly extracted into AP phase (Bagnoud-Velásquez et al., 2015; Elliott et al., 2013; Maddi et al., 2016). Other elements such as Ca, Mg, and Fe also exist in AP although their concentrations were relatively low (less than 1% or even several mg/L) (Bagnoud-Velásquez et al., 2015; López Barreiro et al., 2015a).

3. Recycling nutrients in AP for microalgae production

3.1. Recycling AP as a carbon source

In a typical algae-based wastewater treatment process, mixotrophic algal growth mode is preferred as the algae can use both organic carbon in wastewater and CO_2 from the atmosphere. Many algae species can grow mixotrophically (Perez-Garcia et al., 2011) and thus, those species can be used for recycling carbons from AP of HTL (Table 2).

Table 2
Microalgae cultivation in aqueous phase obtained from hydrothermal treatment of microalgae.

Source of AP[a]	Aim of the work	Cultivation conditions[b]	● Cultivation species ■ Photobioreactor	Performance	Inhibitory effect	Ref.
HTL; T: 350 °C, RT: 60 min, SF: 20%; *Arthrospira* (*Spirulina*) *platensis*	Whole nutrients utilization; inhibitory effect	M: diluted AP with water by 10×, 100×, 300× or 500×; pH: 7.5; T: 25 °C; D: 12 days (batch); ECS: aeration (air with 5% CO_2); LS: 24 h illumination (80–110 $\mu mol \cdot m^{-2} \cdot s^{-1}$); BA: total chlorophyll, cell density.	● *Chlorella minutissima* ■ 250 mL Erlenmeyer flask	● Mixotrophic mode ● Best growth (biomass productivities 0.035 $g\,L^{-1}\,d^{-1}$, concentration 0.52 g/L) was obtained in medium diluted by 500×; only 50% of productivities of that in (BG 11) ● No growth in medium diluted by 10×	● Inhibition happened for all cases ● Inhibitory from phenols in diluted AP could be excluded for the > 10× diluted growth media ● Phenols (5.09 mg/L) and high concentrations of secondary and micronutrients may be toxic in 10× diluted medium	Jena et al. (2011)
HTL; T: 300/350 °C, RT: 60 min, SF: 10%; *Chlorella vulgaris*, *Scenedesmus dimorphous* or *Spirulina platensis* (n = 3)	Whole nutrients utilization; inhibitory effect	M: diluted AP with water by 50×, 100×, 200×, 400 × or 600× (*Spirulina* cultures supplemented with $NaHCO_3$); D: 12 days (batch); ECS: aeration (air, CO_2 390 mg/L); LS: 24 h illumination; BA: chlorophyll *a* and cell count by haemocytometer	● *Chlorella vulgaris*, *Scenedesmus dimorphous* and *Spirulina platensis* inoculated to their corresponding AP (n = 3) ■ 500 mL Conical flask	● Mixotrophic mode ● Completely inhibited in 50× diluted AP except for *Chlorella vulgaris* grew in AP from HTL of *Chlorella vulgaris* at 300 °C. Optimum dilution ranging between 200 and 400× for the three strains obtained biomass concentration ranging from 0.05 to 0.88 g/L ● Algae grew slower and reached a lower final concentration than standard media (e.g., 3 N-BBM + V or BG 11)	● Inhibition happened for all cases ● Smallest inhibition happened for *Chlorella vulgaris* ● Inhibition happened in AP diluted by 50× or even up to 400× depend on species ● Ni (leached from reactor wall), phenols and fatty acids may pose inhibition	Biller et al. (2012)
HTC; T: 200 °C; RT: 40 min; *Nannochloropsis oculata*	Whole nutrients utilization; inhibitory effect	M: diluted AP with water by 50×, 100 × or 200×; pH: about 8.5–11; T: 25 °C; D: 5 days; ECS: no aeration, 100 rpm rotation; LS: 24 h illumination (100 $\mu mol \cdot m^{-2} \cdot s^{-1}$); BA: total volatile suspended solids.	● *Chlorella vulgaris* (isolated from local freshwater) ■ 250 mL Erlenmeyer flask	● Mixotrophic mode (autotrophic mode for control) ● Growth rates in media containing only AP showed higher growth than the standard growth medium (**BG 11**) ● Lower dilution for AP (or high carbon content) led to higher final biomass concentrations of 0.8 (day 4), 0.5 and 0.3 g/L and productivity (0.160, 0.092 and 0.054 $g\,L^{-1}\,d^{-1}$) ● TN removal rate of 45.5–59.9%, COD of 50.0–60.9% and TP of 85.8–94.6%	● No inhibition happened	Du et al. (2012)
HTL; T: 300 °C; RT: 30 min; SF: 20–30%; *Spirulina*	Whole nutrients utilization; heterotrophic growth; inhibitory effect	M: diluted AP with filtered MWW by 10×, 20×, 50×, 100× or 200×; T: 25 °C; D:10 days; LS: one series with 24 h illumination (50 $\mu mol \cdot m^{-2}\,s^{-1}$) and one without illumination; BA: chlorophyll *a* and dry cell weight	● Bacteria from MWW and a mixed algal culture obtained from MWW mainly *Chlorella* spp. (dominant strain) ■ 250 mL Pyrex flasks	● Two different primary modes of biomass growth depending on the AP dosage: heterotrophic mode dominant media diluted by 10×, 20× and 50× and autotrophic mode dominant media diluted by 100× and 200×, and the MWW without AP	● Inhibitory effect was found in AP diluted by < 200× (completely inhibited for 10×, 20×, 50× and partly inhibited for 100×) ● High concentrations of ammonia may account for part of the inhibitory effect	Zhou et al. (2013)
HTL; T: 300 °C; RT: 5 min; SF: 7.66%; *Desmodesmus* sp.	Whole nutrients utilization; inhibitory effect	M: diluted AP with water by 20×; pH: 7.4; T: 27 °C; D: 4 days; ECS: aeration (1.8 vvm, air with 2.0% CO_2); LS: 24 h illumination (247 $\mu mol \cdot m^{-2} \cdot s^{-1}$); BA: optical density.	● *Desmodesmus* sp. ■ 2 L glass vessel	● Growth rate (0.14 $g\,L^{-1}\,d^{-1}$) significantly slower than that on standard medium (COMBO, 0.70 $g\,L^{-1}\,d^{-1}$)	● The inhibition from ammonia, phenols, metals (e.g. Ni, from reactor wall corrosion) and fatty acids may be excluded ● Short of NO_3-N may inhibit the growth	Alba et al. (2013)
	Nitrogen utilization	M: diluted AP with standard medium (COMBO) by 20×				

(*continued on next page*)

Table 2 (*continued*)

Source of AP[a]	Aim of the work	Cultivation conditions[b]	● Cultivation species ■ Photobioreactor	Performance	Inhibitory effect	Ref.
				○ Growth rate (0.62 g L^{-1} d^{-1}) comparable to that on COMBO (0.70 g L^{-1} d^{-1}) ● Autotrophic/phototrophic mode ● Organic nitrogen and TOC remain constant and were not consumed, no mixotrophic growth ● Five times more algae produced in media enriched with COMBO ● Microalgae cells prefer NH_3-N than NO_3-N	○ Slightly longer lag phase was observed (> day) (had potential inhibitors) ● Inhibition happened in AP diluted with only water ● High concentration of NH_3-N had no inhibitory effect ● A lack of other essential nutrients (e.g. Mg) seems to be the primary cause of the growth reduction observed	
	Inhibition from high ammonia or low (macro-/micro-) nutrients content in AP	M: diluted AP with water by 160× or 311×, or with mixtures of water and COMBO by 320× or 632× (to reach the exact same N concentration as that in COMBO); D: 3 days.				
HTL; T: 350 °C, RT: 15 min, SF: 10%; *Nannochloropsis gaditana*	Nitrogen (NH_3-N, 50%/75%) utilization; inhibitory effect	M: diluted AP with standard medium (F/2) by 377 × or 571×; pH: 7.8; T: 21 °C (25 °C for *Nannochloropsis gaditana*); D: 14 days (batch); ECS: ambient air; LS: 24 h illumination (125 μmol·m^{-2}·s^{-1}); BA: optical density.	● *Nannochloropsis gaditana* or *Phaeodactylum* inoculated individually (n = 2) ■ 500 mL Erlenmeyer flask	● Mixotrophic mode ● *Phaeodactylum tricornutum* could not grow satisfactorily (with only 30% of productivities in standard medium) ● *Nannochloropsis gaditana* could grow well in all diluted medium comparable to standard medium	● No inhibition happened for *Nannochloropsis gaditana*; inhibition happened for *Phaeodactylum tricornutum* ● Inhibitory from metals (e.g., Ni) leached from reactor wall and from phenols in AP could be excluded; other inhibitors were not identified in the study	López Barreiro et al. (2015a)
HTL; T: 350 °C, RT: 15 min, SF: 10%; *Scenedesmus almeriensis*	Nitrogen (NH_3-N, 50%) utilization; inhibitory effect	M: diluted AP with standard medium (COMBO) by 392× (supplemented with P); pH: 7.8; T: 25 °C; D: 14 days (batch); ECS: ambient air; LS: 24 h illumination (125 μmol·m^{-2}·s^{-1}); BA: optical density.	● *Chlorella vulgaris* or *Scenedesmus almeriensis* inoculated individually (n = 2) ■ 500 mL Erlenmeyer flask	● Mixotrophic mode ● *Scenedesmus almeriensis* could not grow satisfactorily (with only 30% of productivities in standard medium) ● *Chlorella vulgaris* could grow well comparable to standard medium	● No inhibition happened for *Chlorella vulgaris*; inhibition happened for *Scenedesmus almeriensis* ● Inhibitory from metals (e.g., Ni) leached from reactor wall and from phenols could be excluded; other inhibitors were not identified in the study	López Barreiro et al. (2015a)
HTL; T: 400 °C, RT: ~50 min (from 300 to 400 °C), SF: 20%; *Phaeodactylum tricornutum*	Whole nutrients utilization; inhibitory effect	M: diluted AP with water by 25× [supplemented with SO_4^{2+}, Mg, Ca and Fe salts according to standard medium]; pH: 7.3–7.5; T:°C; D: 33 days (semi-continuous, 3 growth cycles); ECS: aeration (200 L/h, air with 2.5–3.5% CO_2); LS: 24 h illumination (100–400 μE·$m^{-2}$$s^{-1}$); BA: optical density.	● *Phaeodactylum tricornutum* ■ 5 L Flat panel airlift-photobioreactor	● Mixotrophic mode ● Productivity and biomass concentration were higher than those obtained by them with conventional photobioreactors. Maximum biomass concentration of 13.4 g/L (biomass productivities ~1 g L^{-1} d^{-1}) was obtained, close to the standard culture medium ● Photosynthetic efficiency was up to ~9%, close to the standard culture medium (ca. 10%)	● No inhibition happened ● A short lag (4 days) observed (had potential inhibitors)	Bagnoud-Velásquez et al. (2015)
HTL; T: 180–300 °C, RT: 30 min, SF: 10%;*Galdieria sulphuraria*	Nitrogen utilization by heterotrophic growth; inhibitory effect; effect of AP from varied temperature	M: diluted AP with standard medium (Modified Cyanidium medium, without nitrogen addition) by 12.5×, 25×, 50× or 100×; T: 40 °C; D: 3 days; ECS: 2–3% CO_2 in the headspace of the microplate assay; LS: 14 h on/10 h off illumination; BA: optical density	● *Galdieria sulphuraria* (originated in geothermal springs adapted to pH of 1.0–4.0 and temperatures of 25–56 °C) ■ Microplate assay (culture volume of 250 μL)	● Mixotrophic mode (autotrophic mode for control) ● Biomass density increased with the AP concentration (carbon source) increased in the media ● Biomass density decreased dramatically with the AP production temperature increased from 180 to 300 °C because of reduced carbohydrates (carbon source) in AP	● Inhibition only happened in AP produced at high temperature which had deficient carbohydrates ● Carbon source inhibited the growth for media without enough carbon source	Selvaratnam et al. (2015b)
HTL; T: 220/310 °C; SF: 14%; *Chlamydomonas reinhardtii*	Whole nutrients utilization; effect of	M: diluted AP with water by 140× (supplemented with NH_4^+ and PO_4^{3-});	● *Chlamydomonas reinhardtii* (one adapted with AP for	● Mixotrophic mode (autotrophic mode for control)		Hognon et al. (2015)

(*continued on next page*)

Table 2 (*continued*)

Source of AP[a]	Aim of the work	Cultivation conditions[b]	● Cultivation species ■ Photobioreactor	Performance	Inhibitory effect	Ref.
	adaptation on inhibitory effect	pH: 7.2–7.4; T: 25 °C; D: 7 days; ECS: aeration (air with 2.0% CO_2); LS: 24 h illumination (130 μE·m^{-2}s^{-1}); BA: cell amount and volume by automated cell counters and dry cell weight (end).	10 days and another without adaptation) ■ Flasks	● With adaptation, comparable biomass concentration (about 0.9 g/L for AP from 310 °C) or higher (about 1.7 g/L for 220 °C) than the control in a conventional autotrophic medium (1.0 g/L) ● The cells grew in diluted AP are larger and aggregate more easily (sign of un-healthiness)	● No inhibition was found for culture that experienced a 10-day adaptation ● Strong inhibitory effect found for the culture without adaptation with high reduction of the growth rates and the final dry weights ● High organic carbon in the diluted aqueous phases (235/172 mg/L) might be toxic to the microalgae	
HTL; T 300 °C; RT 60 min; SF 25%; *Nannochloropsis* sp. or *Chlorella* sp. (processed with two different AP separation methods)	Whole nutrients utilization; inhibitory effect	M: diluted AP with water by 3.5–52.6 × (TN 500, 250, 150 or 50 mg/L); pH: 7.0–7.5 (re-adjusted daily); T: 26 °C; D: 11 days; ECS: no aeration, shaken 3 times a day; LS: 12 h on/off illumination (170 μmol m^{-2}s^{-1})	● *Chlorella vulgaris* 1067 ■ 500-mL Erlenmeyer flasks	● Mixotrophic mode ● All grew well except the case in diluted AP from *Chlorella* sp. using ethyl ether extraction for AP separation ● Growth rate dependent on raw feedstock and AP separation during HTL	● Almost no inhibition happened ● A lag phase found in diluted AP from *Nannochloropsis* sp. (had potential inhibitors) ● The inhibition from NH_3-N might be excluded as the grow in media with NH_3-N 343.14 mg/L was good	Zhang et al. (2016)
HTL; T 280 °C; RT 30 min; SF 8.7%/FH; T 280 °C; RT 9 s; SF 7–8%;*Scenedesmus*	Utilization of phosphorus; inhibitory effect; hydrolysate vs. AP for algae cultivation	M: diluted AP with a control medium AM-14 to achieve 8%, 10%, 20%, 25% or 50% phosphorus replacement (supplemented with nitrogen); T: 24–30 °C; D: 22 days; ECS: aeration (air, air stone); LS: 12 h on/off illumination (100 μmol m^{-2} s^{-1}); BA: total suspended solids	● *Scenedesmus* or *Oocystis* inoculated individually ■ 3-L plastic bottle	● Much lower growth found than that of the control (AM-14, without P replacement) ● Hydrolysate from flash hydrolysis could satisfy 50% of the nitrogen and phosphorus demand in the culture media	● Inhibition happened for all cases which used AP from HTL ● Almost no inhibition happened for cases which use hydrolysate from flash hydrolysis ● Ammonia was identified as one potential inhibitor	Talbot et al. (2016)
HTC; T 190/210 °C; RT 2/3/4h; SF 9.1%; algae residue from *Arthrospira platensis*	Nitrogen utilization; compare cultivation performance between N-repletion and N-limitation modes	M: diluted AP with a nitrogen-deprived LFY medium and water by to obtain TN 122.6–143.8 mg/L (N-repletion) or 14–17 mg/L (N-limitation); T: 28 °C; D: 6 days; ECS: no aeration, shaken 3 times a day; LS: 14 h on/10 h off illumination (40 μmol m^{-2}s^{-1}); BA: dry cell weight	● *Arthrospira platensis* ■ 500 mL Erlenmeyer flasks	o Biomass accumulation declined with the increase of HTC operation temperature or reaction time o The AP could completely substitute conventional nitrate as N source for *A. platensis* ● Protein content of *Arthrospira platensis* cultivated in N-repletion medium can be increased by 22% compared with $NaNO_3$ ● Carbohydrate content in N-limitation medium can be increased by 14% compared with $NaNO_3$	● No inhibition happened for most cases ● AP obtained under these relatively severe conditions exerted toxic effects on algae ● Inhibitory effect from phenols in AP (< 70 mg/L) may be excluded because most AP had a such high concentration, including those with no inhibition happened ● There were inhibitors, but were not identified in the study	Yao et al. (2016b)
HTL;Nannochloropsis sp.	Whole nutrients utilization	M: diluted AP with water by 40× (to obtain TN 250 mg/L in the media); pH: 7.0–7.5 (re-adjusted daily); T: 26 °C; D: 12 days; ECS: no aeration, shaken ≥ 3 times a day; LS: 12 h on/off illumination (170 μmol m^{-2}s^{-1}); BA: optical density	● Five species inoculated individually ■ 2 L Erlenmeyer flasks	● Mixotrophic mode ● Daily productivity ranged from 0.0022 g L^{-1} d^{-1} (*Chlorella regularis* var. *minima*) to 0.031 (*Chlorella vulgaris* 1067), utilization range of substances were different between species ● *Chlorella vulgaris* 1067 had the best performance		Zhang et al. (2017)[c]
	Inhibitory effect	M: diluted AP **with water** by 13×, 20×, 28 × or 40× (to obtain TN 750, 500, 350 or 250 mg/L in the media)	● *Chlorella vulgaris* 1067 ■ 2 L *Erlenmeyer* flasks	● Mixotrophic mode ● Higher TN in the medium led to higher productivity except AP diluted by 13× (inhibition)	● Inhibition happened for AP diluted by 13× ● The dominant inhibitor could be by NH_3-N	

(*continued on next page*)

Table 2 (*continued*)

Source of AP[a]	Aim of the work	Cultivation conditions[b]	● Cultivation species ■ Photobioreactor	Performance	Inhibitory effect	Ref.
					● Lag phase found in AP diluted by 20× and 28× (had potential inhibitors)	
	Inhibitory effect	M: diluted AP with water by 20× (to obtain TN 500 mg/L in the media); Inoculum size: 0.017, 0.060, 0.103, 0.135 or 0.160 g/L	● *Chlorella vulgaris* 1067 ■ 2 L Erlenmeyer flasks	● Higher productivity for larger inoculum sizes ● Growth potential (calculated) for high-inoculum size case reduced; inoculum sizes between 0.103 and 0.135 g/L was recommended	● Large inoculum sizes help to reduce or even remove the lag phase	
HTL; T 350 °C; RT 20 min; SF 5%; 6 species processed individually or in combination of any of 2, 4 or all 6	Using polycultures to alleviate the high inhibitory effect happened in monocultures	M: diluted AP with nutrient-replete medium by 50× to 1000× (7 concentrations); T: 20 °C; D: 18–20 days; ECS: no aeration, shaker with 120 rpm; LS: 16 h on/8 h off illumination (100 μmol $m^{-2} s^{-1}$); BA: chlorophyll *a*	● Six microalgae species inoculated individually or in combination of 2, 4 or all 6	● Polycultures outperformed even the best single species in terms of coproduct tolerance and productivity ● Growth rate increased up to 25% and biomass production increased by 53% for polycultures ● Polycultures could require less dilution or purging in a recycling pathway	● Inhibition happened in monoculture cases when AP was diluted by 50× (2% AP) or lower ● Polycultures of the same species can tolerate a dilution by 10× (10% AP)	Godwin et al. (2017)[d]

[a] AP: aqueous phase; HTL: hydrothermal liquefaction; T: temperature; SF: solid in feed; RT: residence time.
[b] M: medium; T: temperature; D: duration; ECS: extra carbon source; LS: light source; BA: biomass accumulation; MWW: municipal wastewater.
[c] Five species: *Chlorella vulgaris* 1067, *Chlorella regularis* var. *minima, Chlorella pyrenoidosa, Scenedesmus quadricauda* and *Maeruginosa.*
[d] Six species: *Ankistrodesmus falcatus, Chlorella sorokiniana*, *Pediastrum duplex*, *Scenedesmus acuminatus*, *Scenedesmus ecornis*, and *Selenastrum capricornut.*

Selvaratnam et al., (2015b) reported that mixtrophic growth of *Galdieria sulphuraria* in BG-11 medium blended with AP led to much higher algal biomass productivity than autotrophic grow of this species, with more addition of AP in BG11 medium leading to higher cell density. Similarly, *Chlorella vulgaris* cultivated in media containing AP reduced influent COD from about 2700 to 1100 mg/L, 1330 to 510 mg/L, or 640 to 300 mg/L, depending on the dilution rate used (Du et al., 2012). A 69% reduction of soluble COD in influent of municipal wastewater-diluted AP (1% AP) was reported by a consortium of algae (mainly *Chlorella* sp.) and bacteria, with the un-utilized carbon being the recalcitrant or slow-degrading compounds such as ring structures and nitrogen heteroatoms (Zhou et al., 2013).

3.2. Recycling AP as a phosphorus source

Phosphorus is essential for the formation of DNA, RNA, Adenosine Triphosphate (ATP), and phospholipids in algae biomass. In AP, phosphorus is mainly in the readily available form orthophosphate (Huang et al., 2017). Du et al. (2012) reported that *Chlorella vulgaris* removed TP from 2.0–6.3 mg/L to < 0.5 mg/L in AP-containing medium. The TP removal efficiencies attained 85–95%, while that of TP in the standard medium BG-11 was as low as 40% (TP reduced from 5 to about 3 mg/L) (Du et al., 2012). Zhou et al. (2013) found that 95% of phosphate in wastewater (supplemented with 1% AP) was assimilated by algae (mainly *Chlorella* spp.) and bacteria consortium. The TP concentration in the influent was reduced from about 22 to < 1 mg/L. Talbot et al. (2016) replaced 8–50% phosphorus in a standard AM-14 medium with AP produced from a fast pacing flash hydrolysis of *Scenedesmus* as the synthetic medium, and found a normal growth of *Scenedesmus* or *Oocystis*. However, algal growth in AP from HTL encountered inhibition, probably due to the high ammonia content in AP (Talbot et al., 2016).

3.3. Recycling AP as a nitrogen source

AP can be used as a nitrogen source to completely or partially replace the nitrogen in standard algal culture medium. For example, *Galdieria sulphuraria* grew normally in medium containing 8% AP as the sole nitrogen source with 320 mg/L TN (Selvaratnam et al., 2015b). 50–70% replacement of nitrogen by AP also supported the growth of several other algal species (López Barreiro et al., 2015a). The nitrogen concentration in AP can cause different nitrogen utilization mode and the compositions of the resulted algal biomass. For example, when AP was used as the sole nitrogen source for *Arthrospira platensis* in a N-rich medium (TN 122.6–143.8 mg/L) and a N-limitation medium (14–17 mg/L), protein content of algae grown in N-rich medium increased by 22% while carbohydrate content of algae in N-limitation medium increased by 14% compared to the control medium culture which used potassium nitrate as nitrogen source (Yao et al., 2016b). Yao et al. (2016a) demonstrated feasible a pilot-scale culture of *Arthrospira platensis* using AP as nitrogen source in a N-limitation condition.

Nitrogen species is very important for AP utilization by microalgae. For example, species such as *Desmodesmus* sp. and *Phaeodactylum tricornutum* preferred ammonium to nitrate (Alba et al., 2013; Meiser et al., 2004). As seen in Fig. 1, about half of the nitrogen in AP is in the form of ammonium, which is more bioavailable than nitrate or organic-N. For example, ammonium was consumed completely by a consortium of algae (mainly *Chlorella* spp.) and bacteria, while there was still residual total soluble nitrogen (30 mg/L) existing at the end of culture (Zhou et al., 2013). When the ammonium/TN ratio was as low as 0.14, the removal efficiency of TN from AP-containing medium became considerably low (< 50%) (Du et al., 2012). The growth of algae can be enhanced with the increasing ammonia/ammonium concentration (at low concentration range) (Tsukahara et al., 2001; Zhang et al., 2017; Zhang et al., 2016). But high concentration is known to result in inhibitory effect. *Chlorella vulgaris* 1067 can grow normally in medium with 5% AP (500 mg/L TN) but the growth was inhibited when AP addition increased to 7.7% (750 mg/L TN), probably due to ammonium inhibition at higher concentration (Zhang et al., 2017). Free NH_3 (ammonia) can easily pass through the cell membrane and bind with the thylakoids to inhibit photosynthesis (Azov and Goldman, 1982). High culture temperature and/or pH could lead to equilibrium of free ammonia (NH_3) and ammonium (NH_4^+) shift towards ammonia production and thereafter the algal growth inhibition. For example, López Barreiro et al. (2015a) found drastic growth difference when *Chlorella vulgaris* was cultivated in AP-containing COMBO with different initial pH (one at 7.8 and another at 9.0). The biomass concentration obtained in medium at pH 7.8 was ~0.25 g/L, which was comparable to that in COMBO and was much higher than that in the latter (~0.10 g/L) (López Barreiro et al., 2015a). The daily pH regulation to maintain a steady pH of 7.0–7.5 supported the normal growth of *Chlorella vulgaris* 1067 in medium of TN 500 mg/L which contained 28.6% AP (Zhang et al., 2016).

Nitrogen assimilation from AP varies significantly among algae species and the resistance to high concentration of ammonia/ammonium is also different. Generally, the assimilated percentage of nitrogen from AP-containing medium to biomass could be 50% or higher (Yao et al., 2016b), with a relatively high value of 78% being reported by Jena et al. (2011). It is worth noting that ammonia emission during algal cultivation may distort nitrogen recovery; ammonia vaporization from the algal growth system can range from 17% to 80% (Markou et al., 2014).

3.4. Recycling AP as a multiple nutrients source

When AP is used as the only nutrients source, an appropriate AP concentration is crucial for algal growth performance, low AP concentration leads to low nutrients available for algae, while high AP concentration may result in growth inhibition due to toxic compounds in AP. At an appropriate concentration, AP may simultaneously provide multiple nutrients for algal growth while minimizing the toxic compound inhibition. For example, Jena et al. (2011) cultivated *Chlorella minutissima* in medium containing AP without supplementation of any external nutrients; the biomass production can reach 50% of those obtained in a synthetic medium (BG 11 medium). Similarly, Biller et al. (2012) also successfully grew *Chlorella vulgaris, Scenedesmus dimorphous*, and *Spirulina platensis* in media containing only AP (Biller et al., 2012). Other species including *Chlorella regularis* var. *minima*, *Chlorella pyrenoidosa*, *Scenedesmus quadricauda*, *Maeruginosa*, and *Chlorella vulgaris* 1067 also grew successfully with varied productivity in medium containing AP (Zhang et al., 2017).

In general, algae grow in AP-containing medium have a lower growth rate and cell density than the culture in the synthetic medium. For example, significantly slower growth rate ($0.14\ g\ L^{-1}\ d^{-1}$) was observed when *Desmodesmus* sp. was inoculated in 5%-AP containing medium than that obtained in standard medium (COMBO, $0.70\ g\ L^{-1}\ d^{-1}$) (Alba et al., 2013). Increasing AP content from 0.5% to 2% led to incremental biomass production of *Chlorella vulgaris* (Du et al., 2012). The productivity for 2%-AP containing medium was comparable to that obtained in BG 11 medium (Du et al., 2012). *Chlorella vulgaris* 1067 can be cultivated in media containing 1.9–28.6% of AP in water (Zhang et al., 2016). Biomass productivities and concentration reached $0.12\ g\ L^{-1}\ d^{-1}$ and 1.44 g/L, respectively (Zhang et al., 2016). Biomass productivity can reach as high as $\sim 1\ g\ L^{-1}\ d^{-1}$ and 13.4 g/L when *Phaeodactylum tricornutum* was grown in medium containing 4%-AP supplemented with SO_4^{2-}, Mg, Ca and Fe salts in a 5-L flat panel airlift bioreactor (Bagnoud-Velásquez et al., 2015).

The combination of multiple microalgae species can promote the nutrient utilization from AP. A recent study showed that polyculture of 2, 4, or 6 algal species from *Ankistrodesmus falcatus*, *Chlorella sorokiniana*, *Pediastrum duplex*, *Scenedesmus acuminatus*, *Scenedesmus ecornis*, and *Selenastrum capricornutum* in media containing AP produced

from HTL of the combination of those algae species outperformed the monoculture of algal species using the same AP-containing media (Godwin et al., 2017). The AP content in the algal polyculture for supporting normal growth can be as high as 10%, compared to 2% AP in monoculture (Godwin et al., 2017).

To ensure sufficient nutrient supply is another way to support normal growth of algae in media containing only AP. Macro-nutrients such as K, S, Ca, Mg, Na, and Cl and micro-nutrients such as Fe, Mg, Cu, molybdenum (Mo), and cobalt (Co) are significantly important during algal metabolism and growth. For example, Co is essential for vitamin B_{12} synthesis and Mg is essential for chlorophyll production and photosynthesis. The growth of *Dunaliella tertiolecta* was greatly inhibited when the culture medium was depleted of Fe, Co, Mg, or Mo compared with the medium contained these nutrients (Chen et al., 2011). Unsatisfactorily, imbalanced distributions of these nutrients in AP were reported (Anastasakis and Ross, 2011; Christensen et al., 2014; Lu et al., 2017; Toufiq Reza et al., 2016). Many of these elements present in trace amount in AP (Bagnoud-Velásquez et al., 2015; López Barreiro et al., 2015a) and thus, supplementary nutrients may be added to AP based media to support long term normal growth of algae. Deficiencies of other essential elements such as carbon (Selvaratnam et al., 2015b) and phosphorus (Tsukahara et al., 2001) would also result in similar inhibition.

4. Inhibitory effects of AP for algal cultivation

HTL-derived AP commonly contains various compounds such as furans and phenolics (Toufiq Reza et al., 2016), toluene, benzene, 2-methylarizidine, aziridine (Elliott, 1991), 2-Methylbenzofuran (Becker et al., 2014), and nitrogenous compounds such as amino-phenol, 2-pi-peridione, 2-pyrrolidinone, pyridine and its derivatives, and piperidinone and its derivatives (Pham et al., 2013). These compounds can be inhibitory to algal growth when crude AP solution is added to the culture medium, and thus limit the utilization of AP as a nutrient source for algae cultivation (Fig. 2).

4.1. Phenolics

Phenolics as a group compounds in AP can significantly inhibit algal growth. For example, 400 mg/L of phenol led to 40% reduction in the growth of *Chlorella* VT-1 or complete inhibition to the growth of *Chlorella vulgaris* (Scragg, 2006). *Chlorella* VT-1 can metabolize some phenols heterotrophically whereas *C. vulgaris* cannot, and the growth inhibition was less severe when 100 mg/L phenol was presented in the medium (Scragg, 2006). No inhibition was observed when *Arthrospira platensis* was grown in AP-containing medium with ~70 mg/L of phenols (Yao et al., 2016b). Aruoja et al. (2011) reported an EC_{50} value (concentration of the inhibitory compounds resulting half of the maximal cell density) of 197 mg/L for phenol in the culture of *Pseudokirchneriella subcapitata*.

In general, a higher AP addition to the medium leads to a higher toxicity to algal growth and many phenol derivatives were more toxic than phenol (Aruoja et al., 2011). For example, 29 phenol derivatives substituting phenol with chloro-, methyl- or ethyl-groups significantly reduced EC_{50} values for the culture of *Pseudokirchneriella subcapitata* (Aruoja et al., 2011). The EC_{50} values of these 29 compounds ranged from 2.10 mg/L (3,5-dichlorophenol) to 145 mg/L (3-methylphenol) with 10 of these having an EC_{50} < 10 mg/L (Aruoja et al., 2011). Nakai et al. (2001) reported that the algae *Microcystis aeruginosa* can be inhibited by polyphenols such as catechol and hydroquinione at a concentration as low as 7.5 mg/L, due to the formation of reactive radicals through auto-oxidation of the polyphenols. Those polyphenols were mainly observed from HTL of lignocellulosic biomass such as wood and corn stove (Panisko et al., 2015). HTL of model protein (soy protein) also produced high concentrations of phenol (139 mg/L) and p-cresol (28.2 mg/L) (Madsen et al., 2016). However, some phenolics such as caffeic, p-coumaric, ferulic, protocatechuic, sinapic, syringic and vanillic acids had limited growth inhibition to *Microcystis aeruginosa* (Nakai et al., 2001).

4.2. (Hetero-) cyclic nitrogenous compounds

Various (hetero-) cyclic nitrogenous compounds such as anilines methylaminos, piperidones, and pyridines and their congeners have been identified in AP produced from HTL of protein rich microalgae (Gai et al., 2015; Maddi et al., 2016; Peng et al., 2016a; Pham et al., 2013). Many of these (hetero-) cyclic nitrogenous compounds are toxic to bacteria (Zhao and Liu, 2016) and mammalian cells (Pham et al., 2013). In the culture of *Pseudokirchneriella subcapitata*, 28 anilines were found toxic to the cell growth with EC_{50} ranging from 1.43 mg/L (3,4,5-trichloroaniline) to 109 mg/L (2-methylaniline). Eleven of those anilines had a EC_{50} value less than 10 mg/L (Aruoja et al., 2011). Pham

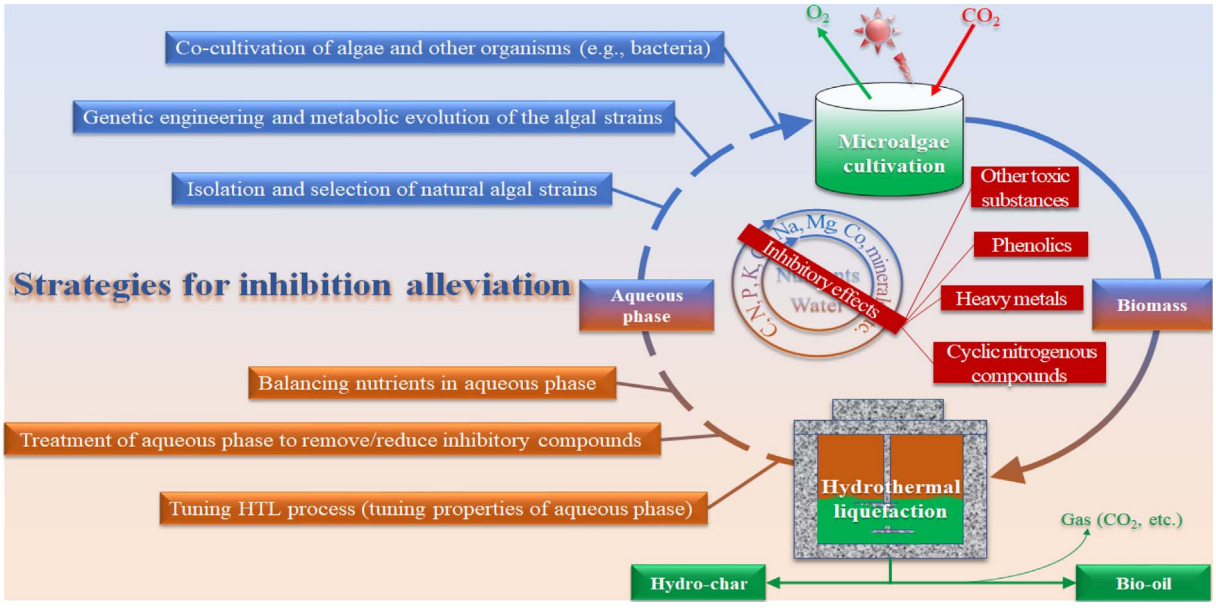

Fig. 2. Strategies proposed for the alleviation of inhibitory effects on microalgae cultivation in AP derived from microalgae-based HTL process.

et al. (2013) identified the inhibitory effects of nine nitrogenous compounds (ranging from 0.052 to 139 mg/L) on algae. The authors reported that the compounds with more methyl groups (e.g., 3-dimethylamino-phenol, 2,2,6,6-tetramethyl-4-piperidone and 2,6-dimethyl-3-pyridinol) were more toxic to algal growth (Pham et al., 2013). A possible synergistic toxicity effect among these components were also reported (Pham et al., 2013).

4.3. Heavy metals

The presence of heavy metals such as nickel (Ni) in AP is inhibitory to algal growth (Biller et al., 2012). Ni has proven toxic to many microalgae species isolated from soft or hard water environment (Deleebeeck et al., 2009). Nickel ion (Ni^{2+}) inhibited the growth of *Chlorella vulgaris* in a concentration-dependent manner when the algae was cultivated in a synthetic medium containing Ni^{2+}, and Ni^{2+} at 100 mg/L led to 50% reduction of biomass productivity (Tsukahara et al., 2001). Although Ni concentration in AP of HTL was only scarcely reported, high concentration of Ni (240 mg/L) presented in AP produced from algae hydrothermal gasification of *Chlorella vulgaris* (Tsukahara et al., 2001).

Other metals such as Cu, Cr, Pb, Zn, and Cd can present in AP when biomass rich in these metals was used as feedstock for HTL process (Huang and Yuan, 2016; Leng et al., 2016,2014). These metals are likely to present in AP that is obtained through phase separation solvent extraction or centrifugation rather than evaporation. Though the concentrations of those metals would be low, their toxicity could be significant. For example, aluminium ions at 0.02 mg/L inhibited growth of *Chlorella vulgaris* by up to 70% (Bagnoud-Velásquez et al., 2014). This aluminium based toxicity may particularly be an issue as aluminium salt is often used for harvesting of algal biomass through flocculation.

4.4. Other toxic substances

Other substances in AP may also inhibit the algal growth. For example, the growth of *Scenedesmus obliquus* and *Chlorella pyrenoidosa* was significantly inhibited by dibutyl phthalate at 2–20 mg/L (Gu et al., 2017). Dibutyl phthalate is an emerging new pollutant found in soil/water, which was also detected in bio-oils (Leng et al., 2015a; Yuan et al., 2009) and AP from HTL (Shen et al., 2017). Biomass reduction of ~30% was observed in culture of *Chlamydomonas reinhardtii* in media containing furfural (0.6 g/L) or acetol (3.2 g/L) (Liang et al., 2013). In addition, AP may also contain numerous unidentified compounds which inhibit algal growth (Pham et al., 2013).

5. Strategies for alleviation of inhibitions of AP

5.1. Tuning HTL process

Various strategies have been proposed to alleviate the inhibitions from toxic substances (Fig. 2). Controlling HTL process parameters such as feedstock compositions, temperature and temperature ramping rate, retention time, pressure, solid feeding rate, and AP separation method can significantly affect the properties of AP and therefore, the usability for algal cultivation. For instance, heavy metals in AP could probably be influenced by tuning HTL process conditions (e.g., change of HTL temperature) (Leng et al., 2014; Yuan et al., 2015) or manipulating properties of feedstock (e.g., pretreatment of heavy metal contaminated biomass) (Leng et al., 2016; Huang and Yuan, 2016). However, the processing parameters should be skilfully optimized to balance the trade-off between AP usability and bio-oil yields and properties. For example, Patel et al. (2016) reported that HTL of *Nannochloropsis* sp. at a processing temperature of 275 °C (within the range of 275–350 °C) and a residence time of 30 min (within the range of 5–60 min) recovered most nutrients in AP for algal growth, however, the energy recovery under this condition was unsatisfactory due to low bio-oil yield. On the other hand, higher temperature favoured bio oil yield, but led to higher toxicity of AP for algal culture.

Understanding the mechanisms and kinetics of microalgae-based HTL process is crucial to provide a rational guidance to tune this process. Algae biomass with different chemical compositions leads to variations in yield and properties of both bio-oil and AP (Li et al., 2017a; Madsen et al., 2016). Understanding the mechanisms of HTL reaction of the main components in biomass can help to predict the chemical compositions of AP based on the actual chemical compositions of the feedstock and the process conditions used (Madsen et al., 2016). It should be noted that processing of multiple biomass species (meaning mixtures of multiple biomass components) may make the prediction less feasible. However, co-processing of algal polyculture (Godwin et al., 2017; Newby et al., 2016) or a mixture of algae with other biomass feedstock (e.g. lignocellulosic biomass) (Sohail et al., 2011) may be an effective way to tune the AP properties. Co-processing can not only produce AP with lower toxic compounds because of dilution (Madsen et al., 2016), but also enhance the bio-oil yield and properties (Coma et al., 2017; Leng et al., 2018).

5.2. Treatment of AP to remove or reduce inhibitory compounds

Removal or reduction of toxic compounds in AP is another strategy to alleviate the AP-caused inhibition. A specific compound can be added to or stripped from AP solution to identify its toxicity for algal growth. A treatment process can then be developed to remove or reduce this compound is deemed toxic. In general, toxic substances can be removed from AP by adsorbents such as activated carbon and zeolite or extracted by petroleum ether, and these practices have been applied for pretreatment of AP before anaerobic digestion of AP (Chen et al., 2016; Li et al., 2017b; Shanmugam et al., 2017a,b; Zheng et al., 2017). Shanmugam et al. (2017b) reported that increasing activated carbon loading significantly removed various organic compounds in AP such as nitrogenous compounds. Phenolics in AP can be adsorbed by resins (Chen et al., 2015c). Furfural can be removed completely from acetic-rich bio-oil fraction from pyrolysis of softwood by activated carbon at carbon loading higher than 0.7 g/mL bio-oil (Liang et al., 2013). Pham et al. (2013) reported that the toxicity of AP (assessed by LC_{50}, a median lethal concentration value) decreased significantly after removal of nitrogenous compounds by activated carbon. In addition to the above detoxification methods, other methods such as precipitation and membrane filtration may also be used to remove the inhibitory compounds, but the practice of these methods have been rarely reported.

In addition to the toxic compounds, imbalanced nutrients compositions, e.g., excessive ammonia, may also cause algal growth inhibition; thus, appropriate treatment of AP is needed to reduce this inhibition. Air stripping is an approach commonly used to reduce the ammonia inhibition. This approach has been used to alleviate bacteria inhibition during landfill leachate treatment (Renou et al., 2008), and it can be used to treat AP containing high level of ammonia. Addition of ammonium adsorbent to AP-containing media is another strategy to reduce ammonia inhibition and produce slow-release nitrogen source for algal growth (Xie et al., 2013). Maintaining a neutral pH of the algal growth medium also helps to slow ammonium release (Zhang et al., 2016). Alternatively, nitrogen and phosphorus in AP can be recovered as struvite (Barbera et al., 2017; Shanmugam et al., 2017a). As high as 99% of phosphorus and 40–100% of ammonium can be recovered by struvite precipitation (Shanmugam et al., 2017a). The recovered struvite can then be used for various applications including algal culture (Barbera et al., 2017).

5.3. Developing robust algae strains that tolerate AP inhibitions

5.3.1. Isolation and selection of natural strains

Isolation and selection of robust algal species that can tolerate the

toxic compounds in AP is another approach to mitigating toxicity in AP. Microalgae as one of the oldest forms of original life have more than 40,000 strains which provide a large pool of candidates for the toxicity tolerance selection (Zhou et al., 2017). The nutrients utilization efficiency and tolerance to inhibitory compounds vary significantly between different strains. However, it should be noted that other than nutrients utilization and toxicity tolerance inhibitions, other traits associated with the algal strains such as growth rate, growth conditions, easiness of biomass harvesting, and biomass usability also should to be considered during strain isolation and selection (Zhou et al., 2017).

Microalgae strains vary in chemical compositions, metabolisms, requirements of growth conditions (e.g., temperature and light), and sensitivity to different toxic compounds. A polyculture of multiple strains may be more resistant to toxicity through synergism of those strains. From this perspective, a multi-species culture (polyculture) is a promising approach for an effective AP utilization. In addition, polyculture of algae communities, if designed properly, can also improve bio-oil quality and yield when the biomass is used as feedstock for HTL (Godwin et al., 2017; Newby et al., 2016). To date, however, researches on the algal polyculture (with 2–6 species) for AP utilization are very limited (Godwin et al., 2017).

5.3.2. Genetic engineering and metabolic evolution of the algal strain

Development of toxicity-tolerant algal strains are desirable and these strains may be obtained by rational genetic engineering. For instance, engineering enzyme systems into a target algal biomass can enhance algae toxicity tolerance. Ascorbate peroxidase (AsPOX, which detoxifies peroxides using ascorbate as a reductant in ascorbate-glutathione cycle) can be used for this purpose. The expression of AsPOX in *Picochlorum* sp. increased significantly in response to the toxic compounds in AP-containing media (Wang et al., 2016). Accumulation of carotenoid pigments and increased AsPOX activity were also reported in several other strains as a mechanism to tolerate the toxic compounds (Osundeko et al., 2014). Furfural-tolerant bacteria due to the presence of some certain string of genes were also reported (Shen et al., 2015). It is noteworthy that genetic engineering of high-lipid microalgae has been widely applied to enhance microalgae biodiesel industry (Tabatabaei et al., 2011).

Directed evolution is another approach to increase the resistance of microalgae to toxic compounds (Hognon et al., 2015; Liang et al., 2013; Wang et al., 2016). For example, the alga *Chlamydomonas reinhardtii* was used as a model strain to enhance tolerance to acetic-acid-rich aqueous phase of biomass pyrolysis (Liang et al., 2013). Hognon et al. (2015) reported that the inhibition on growth of *C. reinhardtii* in media containing AP supplemented with NH_4^+ and PO_4^{3-} can be alleviated after a stepwise increment of AP content in the medium. The authors reported 1.7 g/L biomass concentration, which was even higher than that in the standard medium (~1.0 g/L) (Hognon et al., 2015).

5.3.3. Co-cultivation of algae and bacteria

Co-cultivation of bacteria and microalgae has been widely used for municipal wastewater treatment. Enhanced removal of ammonium and phosphorus was found in co-cultivation compared with that in microalgae cultivation alone (Lima et al., 2004; Mujtaba and Lee, 2017). O_2 required by bacteria to degrade those inhibitory compounds may be provided by microalgae (Muñoz and Guieysse, 2006). Algal-bacterial consortium was effective when treating effluent of the anaerobically digested swine manure centrate (Wang et al., 2015). For the treatment of AP-based wastewater, a similar concept of bacteria-algae co-culture may be used to treat contaminants such as polycyclic aromatic hydrocarbons and phenolics in AP stream (Muñoz and Guieysse, 2006).

In general, bacteria have a higher tolerance to AP than algae. For example, *Escherichia coli* and *Pseudomonas putida* can grow in medium with 40% AP produced as the sole source of C, N, and P (Nelson et al., 2013). In another study, *E. coli* and *Pseudomonas putida* grown in medium with up to 30% of the AP and exhibited a high cell density (Pirwitz et al., 2016).

The growth of algae-bacteria consortium in AP-containing wastewater was tested with success, which could achieve a net positive energy yield (Zhou et al., 2013). Continuous cultivation of algae-bacteria consortium in diluted AP solution achieved a stable organic removal (Zhou et al., 2011b). In the algae-bacteria consortium, bacteria can degrade organic pollutants which are difficult to be degraded by autophototrophic algae strains (Zhou et al., 2011b).

6. Conclusions

Protein-rich microalgae tends to produce AP of alkaline and contains high contents of total carbon, organic acids, and total nitrogen. Cultivation of microalgae in AP containing media generally has lower growth rate and biomass concentration compared with those from the synthetic media. Growth inhibitions are mainly due to the presence of toxic compounds such as phenolics, cyclic nitrogenous compounds, and heavy metals. Various strategies can be developed to alleviate these inhibitions, including tuning HTL process, de-toxification of AP, strain improvement through selection of robust natural strains or metabolic evolution, and co-culture. Combining multiple strategies can help realize highly efficient detoxification.

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