The Variation of Growth Rate, Photosynthetic Activity, and Biodiesel Productivity in *Synechocystis* sp. PCC 6803 under Antibiotic Exposure

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Abstract

Enrichment of biomass containing high lipid content is the key limiting step for the utilization of cyanobacterial feedstock in biodiesel production. This study investigated the influence of antibiotics on the biodiesel productivity of a model biodiesel-producing cyanobacterium (*Synechocystis* sp. PCC 6803) through a 18-day exposure test and observed that 100 ng/L of ciprofloxacin, amoxicillin, and spiramycin significantly ($p < 0.05$) increased biomass, chlorophyll a content, and F_v/F_m value and $rETR_{max}$ value in *Synechocystis* sp. PCC 6803. Due to the stimulation of photosynthesis, the 18-day dry weights of the cyanobacterial cells increased from 0.354 ± 0.039 to 0.508 ± 0.048, 0.58 ± 0.028, and 0.66 ± 0.028 g/L under exposure to ciprofloxacin, amoxicillin, and spiramycin, respectively. As a stress response to antibiotics, the lipid content in *Synechocystis* sp. PCC 6803 increased from 14.71 to 20.92%, 20.59%, and 15.36% under exposure to ciprofloxacin, amoxicillin, and spiramycin, respectively. Due to the increase of biomass and lipid content, the lipid productivity of *Synechocystis* sp. PCC 6803 increased from 2.89 to 5.90, 6.63, and 5.63 mg/L/d under exposure to ciprofloxacin, amoxicillin, and spiramycin, respectively. Exposure to each target antibiotic increased the proportion of monounsaturated fatty acids in the lipid, while exposure to spiramycin reduced the proportion of saturated fatty acid. Antibiotics regulated the lipid composition of *Synechocystis* sp. PCC 6803 towards an increase of combustion property. This study proved that antibiotic exposure increased the lipid productivity of cyanobacteria through hormesis, which provided new insights for promoting the production of cyanobacteria-based biodiesel.

Keywords Cyanobacteria · Biodiesel feedstock · Biomass · Lipid accumulation · Hormesis

Introduction

Due to excessive consumption and increased demand of conventional fossil fuel resources, the development of alternative energy has attracted great attention. Biodiesel is a promising substitute for fossil fuel, because of its renewable and environmentally friendly features [1]. Compared with crops and animal fats, microalgae present many advantages as feedstocks for biodiesel production, including short harvesting life, fast growth rate, and high lipid content [2, 3].

Utilization of microalgae as feedstocks for biodiesel production could also avoid the occupation of farmland and reduce the emission of sulfoxide [4]. At present, eukaryotic microalgae are commonly used for the production of microalgae-based biodiesel, while less attention was paid to cyanobacteria. Cyanobacteria are a large group of fast-growing prokaryotic microalgae with great tolerance to extreme condition and variable illumination [5], which show excellent ability for the production of bioenergy, including ethanol, hydrogen, butanol, and various triglyceride lipids [6]. For instance, Vargas et al. observed a hydrogen production ability of 4.1 μmol per mg chlorophyll a per day in *Anabaena* sp. PCC 7120 [7]. *Synechocystis* sp. PCC 6803 showed a good performance in the production of both ethanol and triglycerides. Triglycerides could be further transesterified into fatty acid methyl esters (FAMEs) that have good combustion properties [8].

Cost-effective production of high-quality biodiesel is the major challenge for the commercialization of microalgae-based biodiesel [9]. Various efforts have been made to

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increase the lipid production ability of cyanobacteria, including the optimization of culture conditions [10], the exposure to exogenous stresses [11], the construction of mixed microalgae consortia [12–14], the improvement of lipid extraction and transesterification [15], as well as the application of genetic modification [16]. Antibiotics are a large group of chemicals highly effective against bacteria, which are widely used for the protection of human and animal health and the promotion of plant growth [17]. Recent studies observed that cyanobacterial cells were sensitive to antibiotic stress due to their bacterial-like structure [18]. Antibiotics are toxic to cyanobacteria at high concentrations while generate various stimulatory effects in cyanobacteria at low concentrations, including the promotion of growth, photosynthesis, and carbohydrate synthesis [19]. For instance, 100–300 ng/L of amoxicillin, ciprofloxacin, and sulfamethoxazole were found to increase growth rate and polysaccharide content as well as induce over-expression of proteins related to carbohydrate synthesis in *Microcystis aeruginosa*. Erythromycin was found to increase cell density and photosynthetic activity in *Microcystis flos-aquae* at low concentrations of 1–100 ng/L [20, 21]. The above studies suggested that antibiotic stress had the potential to simultaneously increase biomass and lipid content in cyanobacteria, which might contribute to a better biodiesel production ability. However, the influence of antibiotics on biodiesel-producing cyanobacteria has not been reported by previous studies.

In order to test the above hypothesis, the influence of three commonly used antibiotics (ciprofloxacin, amoxicillin, and spiramycin) on biomass, photosynthetic activity, lipid content, and fatty acid composition in a model biodiesel-producing cyanobacterium, *Synechocystis* sp. PCC6803, was investigated in this study. To date, this is the first study evaluating the possibility of introducing antibiotic stress into cyanobacteria-based biodiesel production for the promotion of biodiesel productivity.

Materials and Methods

Antibiotic Exposure

Synechocystis sp. PCC 6803 was supplied by Pasteur Culture Collection of Cyanobacterial Strains (France). Ciprofloxacin (CIP, purity ≥ 98.0%), amoxicillin (AM, purity ≥ 98.7%), and spiramycin (SPI, purity ≥ 95.0%) were obtained from Dr. Ehrenstorfer, Inc. (Germany). Antibiotic stock solution (1 mg/L) was prepared by dissolving each antibiotic in methanol (Merck Co., Ltd., Germany). The stock solutions were stored in − 20 °C before use. Four test groups were prepared for evaluating the effects of antibiotics on *Synechocystis* sp. PCC 6803, including the CIP-treated group, the AM-treated group, the SPI-treated group, and the solvent control. In the exposure test, the cyanobacterial cells were cultivated in 250-mL flasks containing 150 mL standard BG11 medium. The initial biomass characterized by OD_{730} (optical density value at 730 nm) was 0.05. The stock solution of each target antibiotic was added into the culture medium at the beginning of cyanobacterial cultivation. The test concentration for each target antibiotic was 100 ng/L. Due to the photolysis and hydrolysis of antibiotics, the stock solution of each antibiotic was daily replenished into the culture medium, in order to maintain a stable exposure dose. The replenishing amount was determined in a preliminary experiment according to a previously reported method [22]. The final concentration of methanol in the culture medium was controlled below 0.005% (v/v). The BG11 medium containing cyanobacterial cells and 0.005% (v/v) methanol was prepared as the solvent control. Three replicates were prepared for each test group. Four test groups were cultured for 18 days under continuous fluorescent light at an irradiance of 2000 lx. The light:dark cycle was maintained as 16 h:8 h. The cultivation temperature was 25 °C.

Analysis of Cellular Responses

The OD_{730} value of the culture medium was measured every day with a TU-1810 UV–Vis spectrophotometer (Persee Co., Ltd., China). The growth rate was calculated according to the slope of the linear regression between the natural logarithm of OD_{730} value and the cultivation time in the exponential phase [23]. 5 mL of cyanobacterial culture medium were sampled and centrifuged at 6000×g for 10 min every 3 days using a TG-16 high-speed centrifuge (Bioridge Co., Ltd., China). The cyanobacterial cells were extracted by 90% (v/v) ethanol aqueous solution, and the supernatant was subjected to a TU-1810 UV–Vis spectrophotometer for analyzing the absorbance at 630 nm, 647 nm, 664 nm, and 750 nm. The content of chlorophyll a was calculated according to the method of Bland and expressed in μg/L [24].

The measurement of photosystem II (PSII) activity was conducted every 3 days using a Dual-PAM-100 fluorometer (Walz Co., Ltd., Germany). 5 mL of cyanobacterial cells were dark-adapted for 10 min prior to the measurement. The minimum fluorescence (F_0) was obtained by applying light pulses at low frequency (1 Hz). The maximum fluorescence (F_m) was determined by applying a saturation pulse (0.6 s, 10 Hz) [25]. The maximum photochemical quantum yield of PSII (F_v/F_m) was calculated as Eq. (1):

$$\frac{F_v}{F_m} = \frac{F_m - F_0}{F_m} \tag{1}$$

The rapid light curve (RLC) was obtained by applying a series of 20 s light exposures with increasing photosynthetically active radiation (PAR) values [25]. The maximum relative electron transport rate ($rETR_{max}$) was defined as the value of the plateau phase in the rapid light curve.

Analysis of Total Lipid Content

At the end of the cultivation period, 50 mL cyanobacterial culture medium was sampled and centrifuged at 6000×g for 15 min. The precipitate was rinsed with distilled water and centrifuged twice to remove the inorganic salt in the medium. The pellet was frozen dried with a Scientz-10N lyophilizer (Scientz Biotechnology Co., Ltd., China) for 48 h. The dry weight of the cyanobacterial cells (M) was obtained. The dry cyanobacterial cells were ground to powder and extracted with the mixture of chloroform and methanol (2:1, v/v) according to the method of Folch [26]. The supernatant was collected by centrifugation (6000×g, 15 min), transferred to a 10 mL centrifuge tube, and mixed with 2 mL of 0.9% sodium chloride solution, and the weight of the centrifuge tube (m_0) was obtained prior to use. The supernatant was removed, and the lower solution was dried under a nitrogen flow. The tubes with extracted lipid were weighed (m_1), and the total lipid content and lipid productivity were calculated according to Eqs. (2) and (3), respectively.

$$\text{Lipid content} = \frac{m_1 - m_0}{M} \times 100\% \qquad (2)$$

$$\text{Lipid productivity (mg/L/d)} = \frac{m_1 - m_0}{100 \times 10^{-3} \times 18} \qquad (3)$$

Measurement of Fatty Acid Methyl Ester (FAMEs)

Fatty acids in cyanobacterial cells were methylated, and the contents of fatty acid methyl ester (FAMEs) were analyzed. 2 mL of 40 g/L KOH-CH$_3$OH was used to dissolve 10 mg dry cyanobacterial cells. After that, the mixture was homogenized with a JY92-II ultrasonic cell pulverizer (Scientz Biotechnology Co., Ltd., China) for 2 min. Then the mixture was incubated in a water bath at 75 °C for 15 min and then was cooled to room temperature. The mixture was further mixed with 2 mL of 14% BF$_3$-CH$_3$OH solution (Sigma-Aldrich Co., Ltd., USA) and incubated in a water bath at 75 °C for 15 min. After cooling, 1 mL saturated NaCl solution and 2 mL n-hexane (Sigma-Aldrich Co., Ltd., U.S.A.) were added to extract FAMEs. The mixed solution was centrifuged at 4000×g for 8 min. The upper hexane layer was used for the analysis of FAMEs through an Agilent 7890A-5975C gas chromatography coupled to mass spectrometer (Agilent Co., Ltd., USA) according to the method of Anahas [27].

Statistics Analysis

A repeated measured ANOVA was used to determine the differences in biomass (OD$_{730}$), chlorophyll a content, and F_v/F_m and rETR$_{max}$ between each antibiotic-treated group and the solvent control during the whole cultivation period. A Student's t test was used to determine the differences in dry weights, lipid contents, lipid productivity, and FAME contents between each antibiotic-treated group and the solvent control. All the statistics analysis were conducted through the SPSS software (version 22.0).

Results

Cellular Responses to Antibiotics

The effect of each antibiotic on the biomass of *Synechocystis* sp. PCC6803 was illustrated in Fig. 1. In each antibiotic-treated group, the biomass was significantly ($p < 0.05$) higher than that in the solvent control. The exponential growth rate of *Synechocystis* sp. PCC 6803 in the solvent control was 0.057 ± 0.0004 per day. The exponential growth rates in CIP-, AM-, and SPI-treated groups increased to 0.102 ± 0.002, 0.101 ± 0.002, and 0.107 ± 0.002 per day, respectively. On the last day of the culture period, the OD values in CIP-, AM-, and SPI-treated groups were 1.44-, 1.49-, and 1.52-fold higher than that in the solvent control, respectively.

The chlorophyll a content in the culture medium increased with culture time (Fig.2). Addition of antibiotics into the culture medium also significantly ($p < 0.05$) increased the chlorophyll a content. The highest chlorophyll a content was observed in the AM-treated group on the last day of the culture period, which was 1.76-fold higher than that in the solvent control. During the 18-day culture period, F_v/F_m and rETR$_{max}$ values increased firstly and then decreased (Fig.3). This result was in accordance with the life cycle of cyanobacteria, in which cyanobacterial cells first grow slowly for adapting to new environment and then grow exponentially for rapid multiplication of biomass, followed by a stationary
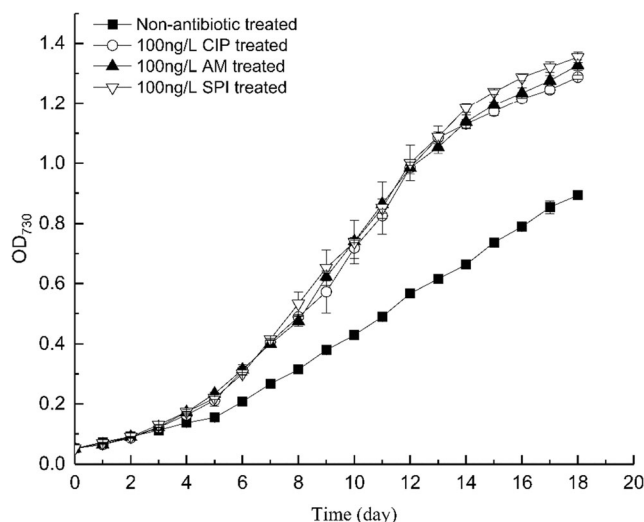

Fig. 1 Effects of ciprofloxacin (CIP), amoxicillin (AM), and spiramycin (SPI) on the biomass of *Synechocystis* sp. PCC 6803 (mean ± standard deviation of three replicates is shown for each value)
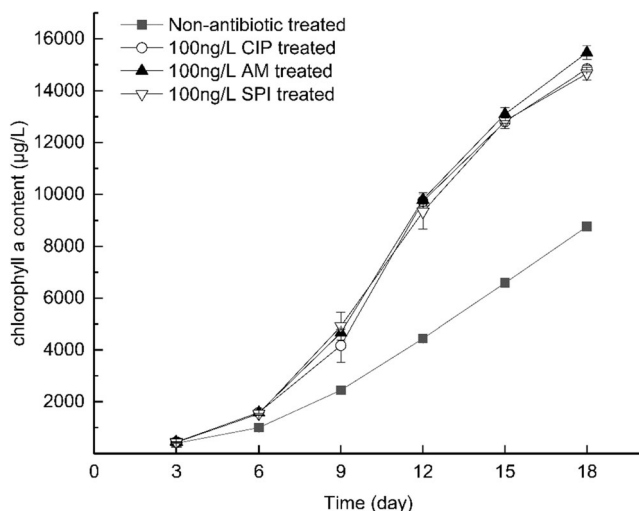
Fig. 2 Effects of ciprofloxacin (CIP), amoxicillin (AM), and spiramycin (SPI) on the chlorophyll a content of *Synechocystis* sp. PCC 6803 (mean ± standard deviation of three replicates is shown for each value)

Fig. 3 Effects of ciprofloxacin (CIP), amoxicillin (AM), and spiramycin (SPI) on the (**a**) F_v/F_m value and (**b**) the rETR$_{max}$ value of *Synechocystis* sp. PCC 6803 (mean ± standard deviation of three replicates is shown for each value)

phase presenting low or zero growth rate. The highest F_v/F_m and rETR$_{max}$ values in the solvent control were observed on the 12th day of the culture period. Compared with the solvent control, the F_v/F_m values were significantly ($p < 0.05$) increased by 9.8%–27.3%, 34.4%–53.4%, and 20.1%–56.4% following exposure to CIP, AM, and SPI, respectively. The rETR$_{max}$ values in CIP-, AM-, and SPI-treated groups were 1.42–1.62, 1.28–1.93, and 1.26–1.91-fold higher ($p < 0.05$) than that in the solvent control, respectively. The above results indicated that each target antibiotic induced the stimulation of photosynthetic activity in *Synechocystis* sp. PCC 6803.

Influence of Antibiotics on Lipid Synthesis and FAME Composition

The dry weight, total lipid content, and the composition of FAMEs in each group are shown in Table 1. Significant increase ($p < 0.05$) of dry weight was observed in *Synechocystis* sp. PCC 6803 under exposure to each target antibiotic, which was in accordance with the responses of OD$_{730}$ values. The total lipid content in the solvent control accounted for 14.71% of the dry weight. Exposure to CIP, AM, and SPI significantly increased ($p < 0.05$) the total lipid content, which accounted for 20.92%, 20.59%, and 15.36% of the dry weight, respectively. Furthermore, the lipid productivity of *Synechocystis* sp. PCC 6803 in CIP-, AM-, and SPI-treated groups was 2.04-, 2.29-, and 1.95-fold higher ($p < 0.05$) than that in the solvent control, respectively.

In the solvent control, eight fatty acids were successfully identified in cyanobacterial cells, including C15:0, C16:0, C16:1, C17:0, C18:0, C18:1, C18:2, and C18:3. Compared with the solvent control, C15:0 was not detected in the CIP-treated group, but C14:0 was detected in this group. In AM-
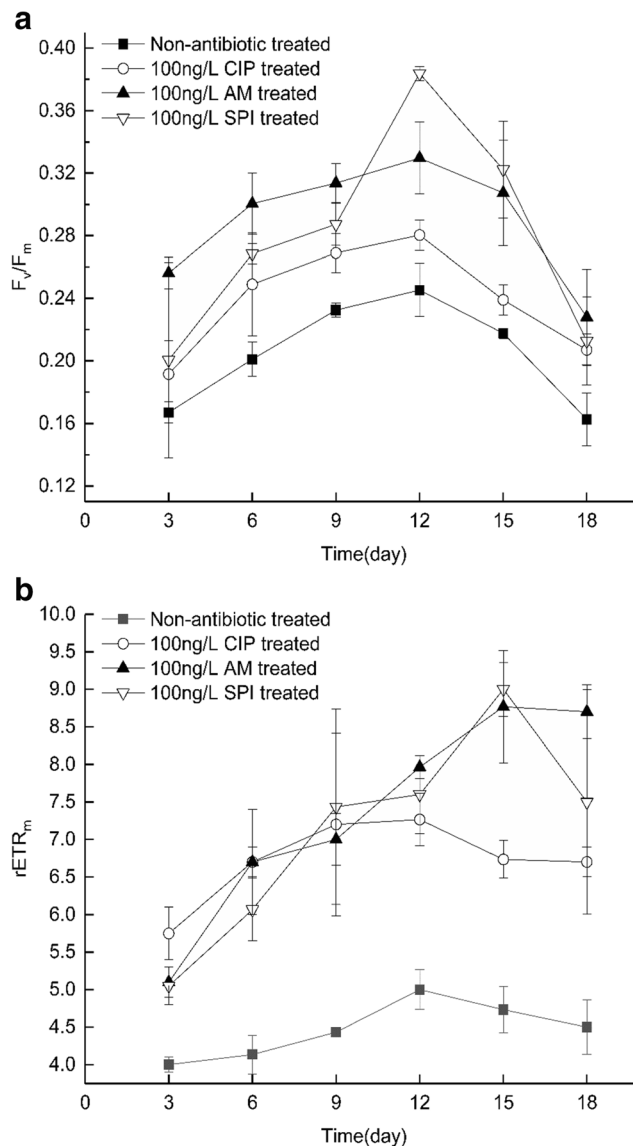
and SPI-treated groups, C17:0 was not detected. In each test group, C16:0 and C18:2 were the major component of FAMEs. The proportion of saturated fatty acid (SFA) was significantly reduced ($p < 0.05$) in *Synechocystis* sp. PCC 6803 under exposure to SPI. The proportion of monounsaturated fatty acids (MUFA) in CIP-, AM-, and SPI-treated groups were 1.34-, 1.28-, and 1.58-fold higher than that in the solvent control, respectively. The proportion of unsaturated fatty acid (UFA) in *Synechocystis* sp. PCC 6803 increased significantly ($p < 0.05$) following exposure to CIP, AM, and SPI, respectively. The proportion of polyunsaturated fatty acid (PUFA) in *Synechocystis* sp. PCC 6803 was not significantly ($p > 0.05$) affected by antibiotic exposure.

Table 1 Comparison of total lipid content and FAME composition between the solvent control and each antibiotic-treated group (mean ± standard deviation of three replicates is shown for each value)

Parameters		Test groups			
		Solvent control	100 ng/L CIP-treated group	100 ng/L AM-treated group	100 ng/L SPI-treated group
Dry weight (g/L)		0.354 ± 0.039	0.508 ± 0.048*	0.58 ± 0.028*	0.66 ± 0.028*
Lipid content(%DW)		14.71	20.92*	20.59*	15.36*
Lipid productivity (mg/L/d)		2.89	5.90*	6.63*	5.63*
FAME composition (%)	C14:0	ND	ND	0.33	0.50
	C15:0	0.61	ND	2.34	4.45*
	C16:0	65.29	63.32	63.48	59.53
	C16:1	5.79	8.25*	7.74*	8.92*
	C17:0	0.94	0.55	ND	ND
	C18:0	1.72	3.35*	1.01	1.72
	C18:1	1.79	1.93	1.97	3.09*
	C18:2	21.98	20.34	20.36	19.45
	C18:3	1.88	2.25	2.77*	2.43*
	SFA	68.57	67.23	66.83	65.70*
	UFA	31.43	32.77*	32.83*	33.80*
	MUFA	7.58	10.18*	9.71*	11.92*
	PUFA	23.86	22.59	23.13	21.88

*Significant difference between each antibiotic-treated group and the solvent control at $p < 0.05$ according to the Student's t test

ND not detected, *SFA* saturated fatty acid, *UFA* unsaturated fatty acids, *MUFA* monounsaturated fatty acid, *PUFA* polyunsaturated fatty acid

Discussion

The total lipid productivity of microalgae is determined by biomass × lipid content. Culture of microalgae under stress conditions may facilitate lipid accumulation, while the biomass may not increase in that case. For instance, Casazza et al. observed that ultraviolet stress increased the lipid content of *Chlorella* sp. by 29.5%, reduced the FAME fraction by 67.3%, and caused no influence on biomass [28]. Two previous studies observed that the lipid content in *Chlorella* sp. increased from 11.5 to 21.8% due to the decrease of nitrogen supply in the culture medium, but the influence of nitrogen starvation on biomass was not mentioned in these studies [29, 30]. Recent studies observed that certain exogenous chemicals had the potential to simultaneously increase biomass and lipid content in biodiesel-producing microalgae. For instance, high bicarbonate concentration (HCO_3^- 171.2 mM) induced 37.9% increase of biomass and 32.5% increase of lipid content in *Arthrospira* ZJU9000, which corresponded to 82.7% increase of total lipid productivity [31]. Addition of kinetin into nitrogen-deficient culture medium led to an increase of 61.8% in the lipid productivity of *Acutodesmus obliquus*, compared with the microalgal cells cultured in standard BG11 medium [32]. This study proved that antibiotics also effectively increased the lipid productivity in *Synechocystis* sp. PCC 6803 through the increase of both biomass and lipid content.

Antibiotics were observed to generate hormesis effect in photosynthetic organisms, including plants, eukaryotic microalgae, and cyanobacteria [33]. Hormesis is a biphasic dose-dependent effect of toxicants or stressors, which is characterized by high-dose inhibition and low-dose stimulation [34]. For instance, Xie et al. found that chlortetracycline stimulated the growth of root in wheat (*Triticum aestivum L.*) through promoting the cell mitotic division at low concentrations of 0.125–0.5 mg/L while inhibiting the above physiological processes at high concentrations of 25–300 mg/L [35]. Liu et al. observed that amoxicillin inhibited the growth of a cyanobacterium (*Microcystis aeruginosa*) at high concentrations of ≥ 6.88 μg/L while stimulating cyanobacterial growth at low concentrations of 100–600 ng/L [36]. In this study, the increase of growth rate and biomass in *Synechocystis* sp. PCC 6803 was also supposed to be a typical hormesis effect under a moderate stress generated by antibiotics at low exposure doses. Results of previous studies and this study suggested that the growth stimulation effect of antibiotics due to hormesis was a universal phenomenon in photosynthetic organisms. In this study, all of the three target antibiotics with different antibacterial mechanisms were effective in stimulating the growth of *Synechocystis* sp. PCC 6803, suggesting that hormesis effects of antibiotics in cyanobacteria were not restricted by the category of antibiotics.

In photosynthetic organisms, the photosynthesis system was supposed to be the action target of antibiotics, which

consequently triggered various downstream responses [37]. Direct evidence has been observed in plants. For instance, elevated root activity was coupled to increased leaf chlorophyll content in *Phragmites australis* exposed to 0.1–1 μg/L of ciprofloxacin, oxytetracycline, and sulfamethazine [38]. Gomes et al. observed that ciprofloxacin induced hormesis in duckweed (*Lemna minor* L.) through regulating photosynthesis [39]. Several studies also observed the positive correlation between photosynthetic parameters and growth parameters in eukaryotic microalgae and cyanobacteria under exposure to antibiotics. Wang et al. observed that the increase of cell density was coupled to the raise of chlorophyll a content in *Microcystis aeruginosa* exposed to the binary mixture of spiramycin and ampicillin at test concentrations of 300 ng/L [40]. Wan et al. [21] observed that exposure to 0.001–0.1 g/L of erythromycin increased biomass and chlorophyll a content in *Microcystis flos-aquae*. In this study, ciprofloxacin, amoxicillin, and spiramycin increased growth rate, chlorophyll a content, light energy conversion efficiency (F_v/F_m), and photochemical electron transport ($rETR_{max}$) in *Synechocystis* sp. PCC6803 at a low concentration of 100 ng/L. Increased chlorophyll a content may promote the capture of light energy, and increased photosynthetic activity may produce extra energy for cyanobacterial growth and the synthesis of cellular substances including lipid. Besides antibiotics, auxins were also found to cause hormesis in *Scenedesmus* sp. through the increase of photosynthetic activity and chlorophyll content, which consequently promoted growth and FAME accumulation [41]. Addition of exogenous chemicals that generate hormesis effects during the cultivation of microalgae may be a promising route for increasing the lipid productivity during the production of microalgae-based biodiesel.

C16-C18 FAMEs are the most important chemical composition in biodiesel [42]. In this study, C16-C18 FAMEs accounted for the largest proportion of the total FAME content in the solvent control and each antibiotic-treated group. The FAME profile of the biodiesel produced by *Synechocystis* sp. PCC6803 was similar to that produced by *Chlorella* sp. [29]. Besides, the proportion of linolenic acid (C18:3) was lower than 12% in the solvent control and each antibiotic-treated group, which met the requirements of EN 14214 Standard for biodiesel [43]. The above results proved that *Synechocystis* sp. PCC 6803 was a qualified feedstock for biodiesel production. Treatment with antibiotic showed beneficial effects on the lipid accumulation in *Synechocystis* sp. PCC 6803. Lipid accumulation was supposed to be a stress response in eukaryotic microalgae and cyanobacteria under exposure to exogenous stresses. For instance, higher lipid content was observed in *Scenedesmus* SDEC-8 and *Chlorella* SDEC-18 under nitrogen-deficient conditions, possibly due to the alteration of cellular substance synthesis towards a preference of carbohydrate and a limitation of nitrogenous compounds [44]. Longworth et al. also observed that nitrogen

starvation induced increased lipid accumulation in *Phaeodactylum tricornutum* [45]. Furthermore, the synthesis of lipid is correlated with the carbon fixation process of photosynthesis [46]. The antibiotic-induced stimulation of photosynthesis may also contribute to increased lipid accumulation.

Several studies focused on the regulation of the FAME composition in biodiesel-producing microalgae. For instance, Udayan et al. observed that addition of kinetin and gibberellic acid (GA3) during the cultivation of *Nannochloropsis oceanica* CASA CC201 resulted in a high proportion of MUFA and a low proportion of SFA [47]. Gao et al. found that the increase of C:N ratio slightly increased the saturation degree of FAMEs in *Chlorella* sp. [48]. The degree of saturation and the length of the carbon chain in the lipid affect the combustion property of microalgae-based biodiesel. A low proportion of SFA and PUFA and a high proportion of MUFA are more favorable for oxidation stability and cold flow property [49]. In this study, exposure to each target antibiotic increased the proportion of MUFA in the lipid of *Synechocystis* sp. PCC 6803, while exposure to spiramycin reduced the proportion of SFA. This result indicated that antibiotic exposure improved the combustion property of the biodiesel produced by *Synechocystis* sp. PCC 6803. Further studies were still required for exploring the action mechanisms of antibiotics in biodiesel-producing cyanobacteria during the regulation of FAME composition. Besides, the influence of more antibiotics on the lipid productivity of more biodiesel-producing cyanobacterial species deserves further investigation to fully evaluate the possibility for utilizing antibiotics in the production of cyanobacteria-based biodiesel .

Conclusions

This study introduced antibiotics into the culture medium of the biodiesel-producing cyanobacterium *Synechocystis* sp. PCC 6803 and observed a significant increase of lipid productivity under antibiotic exposure. Ciprofloxacin, amoxicillin, and spiramycin effectively promoted cyanobacterial growth, photosynthesis, and lipid accumulation in *Synechocystis* sp. PCC 6803 and changed the composition of FAMEs towards an increase of unsaturation degree, which may improve the combustion property of the biodiesel. Antibiotics had a promising potential to be used as a positive regulator in the cultivation of cyanobacteria for biodiesel production.

Data Availability All data generated or analyzed during this study are included in this published article.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Informed Consent All authors were informed and consented to the manuscript publishment.

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