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Impact of Neurotransmitters on the Photosynthetic Pigment Content of the Green Microalga *Haematococcus lacustris* (Strains IPPAS H-239 and BM-1)

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Abstract—The effects of the neurotransmitters serotonin (5-HT), histamine, dopamine (DA), norepinephrine (NE), and acetylcholine (ACh) at concentrations of 0.1–10 μM on the contents of chlorophylls (*a* and *b*) and carotenoids in strains IPPAS B-239 and BM-1 of the microalga *Haematococcus lacustris* are considered. In the strain *H. lacustris* BM-1, all tested neurotransmitters except serotonin were found to stimulate carotenoid formation with an increase in the carotenoid content in the cells. The stimulatory effect was quite significant with acetylcholine and especially histamine and was manifested less with dopamine and norepinephrine. Carotenoid formation by strain IPPAS H-239 was only stimulated by acetylcholine and, to a lesser extent, by norepinephrine. The other neurotransmitters inhibited carotenoid formation. The total chlorophyll *a* and *b* content increased in the presence of all tested neurotransmitters except serotonin in strain BM-1. As for strain IPPAS H-239, its chlorophyll content was increased by acetylcholine and norepinephrine, whereas histamine and serotonin lowered the chlorophyll content. It is suggested that the tested neurotransmitters influence the vegetative cell—palmelloid cell—encysted cell transition, fixing it at the intermediate brown palmelloid stage characterized by significant chlorophyll and carotenoid contents.

Keywords: neurotransmitters, biogenic amines, serotonin, histamine, dopamine, norepinephrine, acetylcholine, astaxanthin, chlorophylls, carotenoids, *Haematococcus lacustris*

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INTRODUCTION

Haematococcus lacustris (= *pluvialis*) is a freshwater microalga that is characteristic of temperate climate habitats. It inhabits rainwater pools and natural and artificial ponds [1]. The microalga performs its ecological function as a component of the phytoplankton that enter into complex interaction with its other components. For instance, representatives of the genus *Haematococcus* are exposed to the destructive effects of toxins (allomones) produced by the cyanobacterium *Anacystis nidulans* [2]. In addition, the species *H. lacustris* is of paramount biotechnological importance since it produces valuable substances such as polyunsaturated fatty acid (PUFA)–enriched lipids and especially the carotenoid astaxanthin. It is envisaged as a "superantioxidant" with a system of 13 conjugated double bonds. "As societies nowadays are looking toward "green" solutions, natural astaxanthin from *H. pluvialis* seems to be more favorable than its synthetic counterpart due to its structure, function, application, and security" [1, pp. 6–7]. Of significant importance are the applications of astaxanthin in health care, the food industry, and cosmetics. Unlike other carotenoids, astaxanthin is not a vitamin precursor; therefore, even its long-term intake does not result in hypervitaminosis (excessive vitamin production) [3]. It has been estimated that the global astaxanthin market has the potential to reach a valuation of US $2.57 billion in 2025 and $ 3.40 billion by 2027 [4].

Active astaxanthin accumulation by encysted cells is preceded by stress-stimulated transformation of the "green" cells to nonmotile palmelloid cells containing an increased amount of astaxanthin against the background of a still significant chlorophyll content (referred to as "brown" cells) [3]. Thereupon, they convert to "reddish" (encysted) cells containing up to 3–5% of astaxanthin by dry weight, which corresponds to 80–99% of the total carotenoid content [1].

The substances that were tested in the present work with respect to their impact on the photosynthetic pigments of *H. lacustris*, such as acetylcholine and biogenic amines (BAs), are termed neurotransmitters due to one of their functions in the animal (human) organism where they are responsible for impulse transmis-

sion between nervous cells. However, along with this function, many neurotransmitters also perform regulatory and communicative roles in various types of animals, plants, fungi, and protozoans. In a recent work [5], it was suggested that neurotransmitters form a part of the ecosystem signal pool that is produced and sensed by many ecosystem components. Therefore, they are not only involved in pairwise parasite–host or predator–prey interaction; they also work at the global level corresponding to the functioning of a whole ecosystem. For this reason, such neurotransmitters can be referred to as ecomones.

According to relevant literature data, acetylcholine stimulates the growth of the green microalgae *Chlorella* spp. [6, 7]. It also promotes the accumulation of monosaccharides and water-soluble proteins in *C. vulgaris* [6] and lipid synthesis in *C. sorokiniana* [7].

It was established, in the authors' earlier work [8, 9], that serotonin facilitated biomass accumulation in a *C. vulgaris* culture at a concentration of 10 μM but not at 1 and 100 μM. Dopamine concentrations of 1 and 10 μM promoted the growth of *C. vulgaris* but no growth stimulation occurred with 100 μM dopamine. Norepinephrine insignificantly stimulated *C. vulgaris* growth, whereas histamine (1 and 10 μM) exerted a strong stimulatory effect on it. Low concentrations of the tested neurotransmitters also facilitated biomass accumulation in *Scenedesmus quadricauda* [8, 9].

In *H. lacustris,* dopamine enhanced the yield of the biotechnologically valuable carotenoid astaxanthin against the background of saline stress (which boosts astaxanthin production per se) that was caused by adding 1 g/L NaCl. Dopamine also increased the biomass yield of *H. lacustris* [4].

The goal of this work was to investigate the impact of the neurotransmitters serotonin (5-HT), histamine, dopamine (DA), norepinephrine (NE), and acetylcholine (ACh) on the contents of the photosynthetic pigment during the cultivation of *H. lacustris*, strains IPPAS H-239 and BM-1.

MATERIALS AND METHODS

The green microalga *Haematococcus lacustris (=pluvialis),* strain IPPAS H-239, was obtained from the Institute of Plant Physiology, Russian Academy of Sciences. The *H. lacustris* strain BM-1 was isolated from the brackish coastal water of a White Sea bay [10]. The strains were axenically cultivated in 25 mL tubes at a PAR photon light intensity of 65 μmol m^{-2} s^{-1} at 24°C in the BG-11 medium with the following composition (g/L): $NaNO_3$, 1.5; K_2HPO_4, 0.04; $MgSO_4 \cdot 7H_2O$, 0.075; $CaCl_2 \cdot 2H_2O$, 0.05; Na_2CO_3, 0.02; citric acid, 0.006; Na_2EDTA, 0.001; $FeC_6H_5O_7$, 0.006; and microelement solution, 1 mg/L. The microelement solution was as follows (g/L): H_3BO_3, 2.86; $MnCl_2 \cdot 4H_2O$, 1.81; $ZnSO_4 \cdot 7H_2O$, 0.22; $Na_2MoO_4 \cdot 2H_2O$, 0.4; $CuSO_4 \cdot 5H_2O$, 0.08; $Co(NO_3)_2 \cdot 7H_2O$, 0.05.

An *H. lacustris* culture precultivated to the stationary growth stage was grown at 24°C for two weeks; samples were taken on days 7 and 14 of cultivation. The neurotransmitters serotonin, dopamine, norepinephrine, histamine, and acetylcholine were used in the form of hydrochlorides (all neurotransmitters were obtained from Sigma, United States); they were added at concentrations of 0.1, 1, or 10 μM as aqueous solutions; the control cultures were supplemented with an equivalent volume of distilled water.

The total chlorophyll and carotenoid fraction was extracted with dimethylsulfoxide (DMSO) for five minutes at 70°C. 2 mL of the culture was precentrifuged for ten minutes at 8000 *g* to obtain a pellet that was treated with 2 mL DMSO. The pigment concentrations were determined in DMSO extracts spectrophotometrically with a Cary 300 Bio spectrophotometer (Varian, United States) according to the following equations [11].

$$\text{Chlorophyll } a \text{ concentration } C_{\text{Chl}\,a}\,(\text{mg/L}) = 13.34A_{666} - 4.85A_{650},$$

$$\text{Chlorophyll } b \text{ concentration } C_{\text{Chl}\,b}\,(\text{mg/L}) = 24.58A_{650} - 6.65A_{666},$$

$$\text{Carotenoid concentration Car}\,(\text{mg/L}) = \left(1000A_{480} - 1.29\text{CChl}\,a - 53.76,\ \text{CChl}\,b\right)/220,$$

where A is the light absorption at the respective wavelength.

RESULTS AND DISCUSSION

All tables given here below (Tables 1–10) include data on the dynamics of change in the chlorophyll and carotenoid contents during the cultivation period of strains IPPAS H-239 and BM-1. Comparison of the data corresponding to days 0 (immediately after the inoculation), 7, and 14 of cultivation reveals a gradual decrease in the content of chlorophyll *a* and *b* with a concomitant increase in the carotenoid concentration. What is the impact of neurotransmitters on these dynamics?

Serotonin. This biogenic amine inhibits the synthesis of carotenoids and chlorophylls on days 7 and 14 of cultivation of strain *H. lacustris* IPPAS H-239, compared to the control (Table 1). In contrast, serotonin virtually does not influence the carotenoid content and slightly increases the chlorophyll content in strain BM-1 (Table 2).

Histamine was also revealed to inhibit carotenoid and chlorophyll synthesis in strain IPPAS H-239 (Table 3). Unlike serotonin, histamine brought about a significant stimulation of carotenoid and chlorophyll formation in strain BM-1 (Table 4); i.e., the effects of histamine proved to be strain-specific.

Dopamine. The effect of dopamine on carotenoid synthesis in IPPAS H-239 was analogous to those of

Table 1. Influence of serotonin on the carotenoid and chlorophyll content in *H. lacustris* IPPAS H-239* cells on days 7 and 14 of cultivation

Photosynthetic pigments	Content, mg/g of biomass								
	upon inoculation	control		5-HT, 0.1 μM		5-HT, 1 μM		5-HT, 10 μM	
		7	14	7	14	7	14	7	14
Chlorophyll *a*	1.9 ± 0.15	1.29 ± 0.15	1.12 ± 0.10	1.30 ± 0.10	1.13 ± 0.10	1.29 ± 0.10	1.05 ± 0.10	1.35 ± 0.10	1.29 ± 0.15
Chlorophyll *b*	0.97 ± 0.10	0.66 ± 0.10	0.59 ± 0.10	0.66 ± 0.10	0.61 ± 0.10	0.65 ± 0.10	0.55 ± 0.10	0.67 ± 0.10	0.64 ± 0.10
Chlorophyll *a* + *b*	2.87 ± 0.20	1.95 ± 0.15	1.71 ± 0.15	1.97 ± 0.15	1.74 ± 0.20	1.95 ± 0.20	1.60 ± 0.20	1.40 ± 0.15	1.05 ± 0.15
Carotenoids	2.86 ± 0.20	2.71 ± 0.20	5.18 ± 0.25	2.65 ± 0.20	5.91 ± 0.25	2.59 ± 0.20	5.26 ± 0.25	2.65 ± 0.20	3.39 ± 0.20

* Averaged results of three repeats.

Table 2. Influence of serotonin on the carotenoid and chlorophyll content in *H. lacustris* BM-1* cells on days 7 and 14 of cultivation

Photosynthetic pigments	Content, mg/g of biomass								
	upon inoculation	control		5-HT, 0.1 μM		5-HT, 1 μM		5-HT, 10 μM	
		7	14	7	14	7	14	7	14
Chlorophyll *a*	2.97 ± 0.20	1.38 ± 0.15	0.85 ± 0.15	1.50 ± 0.20	0.86 ± 0.10	1.63 ± 0.20	0.98 ± 0.155	1.34 ± 0.20	0.98 ± 0.15
Chlorophyll *b*	1.30 ± 0.10	0.60 ± 0.10	0.39 ± 0.10	0.60 ± 0.15	0.43 ± 0.10	0.69 ± 0.15	0.44 ± 0.10	0.55 ± 0.10	0.47 ± 0.15
Chlorophyll *a* + *b*	4.27 ± 0.25	1.98 ± 0.20	1.23 ± 0.20	2.09 ± 0.25	1.29 ± 0.25	2.32 ± 0.25	1.42 ± 0.15	1.88 ± 0.15	1.44 ± 0.15
Carotenoids	0.69 ± 0.10	2.01 ± 0.20	2.23 ± 0.20	2.13 ± 0.20	2.21 ± 0.25	2.44 ± 0.25	2.42 ± 0.25	2.11 ± 0.20	2.24 ± 0.20

* Averaged results of three repeats.

serotonin (Table 5) but, in contrast to serotonin and histamine, dopamine somewhat increased the chlorophyll content in IPPAS H-239 cells on days 7 and 14 of cultivation. As for BM-1 (Table 6), dopamine stimulated chlorophyll and carotenoid synthesis to some extent (by approximately 15%).

Norepinephrine is only distinguished from dopamine by the presence of an extra hydroxy group in the side chain, but its effect on *H. lacustris* significantly differed from that of dopamine. Norepinephrine stimulated chlorophyll and carotenoid synthesis in both tested strains (Tables 7, 8).

Acetylcholine (Tables 9, 10) considerably stimulated chlorophyll and carotenoid synthesis in strains IPPAS H-239 and BM-1 of *H. lacustris*.

The difference between the neurotransmitter effects on the two tested strains of *H. lacustris* is attributable to the different conditions of their habitats: strain BM-1 was isolated from the brackish coastal water of one of the bays of the White Sea, and strain IPPAS H-239 was obtained from the collection of the Institute of Plant Physiology, Russian Academy of Sciences. Despite the interstrain differences, some common patterns were revealed. For instance, acetylcholine and norepinephrine increase the chlorophyll and carotenoid contents of both strains.

The above data on the effects of neurotransmitters on the pigment content of *H. lacustris* are comparable to the results of earlier studies on their impact on other green microalgae. Of relevance are recent data on the influence of neurotransmitters on the photosynthetic

Table 3. Influence of histamine on the carotenoid and chlorophyll content in *H. lacustris* IPPAS H-239* cells

Photosynthetic pigments	Content, mg/g of biomass								
	upon inoculation	control		5-HT, 0.1 μM		5-HT, 1 μM		5-HT, 10 μM	
		7	14	7	14	7	14	7	14
Chlorophyll *a*	1.82 ± 0.15	1.23 ± 0.15	2.46 ± 0.15	1.23 ± 0.15	1.35 ± 0.15	1.22 ± 0.10	1.36 ± 0.10	1.18 ± 0.10	1.38 ± 0.15
Chlorophyll *b*	1.11 ± 0.15	0.69 ± 0.10	1.26 ± 0.10	0.66 ± 0.10	0.82 ± 0.10	0.66 ± 0.10	0.79 ± 0.10	0.67 ± 0.10	0.77 ± 0.10
Chlorophyll *a* + *b*	2.93 ± 0.20	1.92 ± 0.20	3.72 ± 0.25	1.89 ± 0.15	2.17 ± 0.20	1.88 ± 0.15	2.15 ± 0.20	1.84 ± 0.15	2.15 ± 0.20
Carotenoids	0.64 ± 0.10	2.94 ± 0.20	6.57 ± 0.30	2.96 ± 0.20	5.61 ± 0.25	3.15 ± 0.20	4.99 ± 0.20	2.90 ± 0.20	5.35 ± 0.25

* Averaged results of three repeats.

Table 4. Influence of histamine on the carotenoid and chlorophyll content in *H. lacustris* BM-1* cells on days 7 and 14 of cultivation

Photosynthetic pigments	Content, mg/g of biomass								
	upon inoculation	control		5-HT, 0.1 μM		5-HT, 1 μM		5-HT, 10 μM	
		7	14	7	14	7	14	7	14
Chlorophyll *a*	1.93 ± 0.10	1.20 ± 0.10	1.13 ± 0.10	1.47 ± 0.10	1.89 ± 0.15	1.77 ± 0.15	1.88 ± 0.15	1.86 ± 0.15	1.96 ± 0.15
Chlorophyll *b*	1.06 ± 0.10	0.50 ± 0.10	0.59 ± 0.10	0.62 ± 0.10	1.08 ± 0.15	0.80 ± 0.15	1.07 ± 0.15	0.85 ± 0.10	1.03 ± 0.15
Chlorophyll *a* + *b*	2.99 ±	1.70 ±	1.73 ±	2.09 ±	2.97 ±	2.57 ±	2.94 ±	2.71 ±	2.98 ±
Carotenoids	0.57 ± 0.10	1.86 ± 0.10	3.36 ± 0.20	2.25 ± 0.20	6.40 ± 0.20	2.25 ± 0.20	6.54 ± 0.20	2.25 ± 0.15	7.09 ± 0.15

* Averaged results of three repeats.

Table 5. Influence of dopamine on the carotenoid and chlorophyll content in *H. lacustris* IPPAS H-239* cells

Photosynthetic pigments	Content, mg/g of biomass								
	upon inoculation	control		DA, 0.1 μM		DA, 1 μM		DA, 10 μM	
		7	14	7	14	7	14	7	14
Chlorophyll *a*	1.83 ± 0.15	1.76 ± 0.15	1.33 ± 0.15	1.22 ± 0.10	1.26 ± 0.10	1.30 ± 0.10	1.26 ± 0.10	1.26 ± 0.15	1.33 ± 0.10
Chlorophyll *b*	0.65 ± 0.10	0.68 ± 0.10	0.62 ± 0.10	0.22 ± 0.05	0.44 ± 0.10	0.30 ± 0.10	0.51 ± 0.10	0.48 ± 0.15	0.55 ± 0.15
Chlorophyll *a* + *b*	2.48 ± 0.20	2.45 ± 0.20	1.95 ± 0.20	2.45 ± 0.15	1.70 ± 0.20	1.59 ± 0.20	1.77 ± 0.20	1.74 ± 0.25	1.88 ± 0.20
Carotenoids	2.85 ± 0.20	3.26 ± 0.20	3.09 ± 0.20	2.04 ± 0.15	2.66 ± 0.20	2.52 ± 0.20	2.86 ± 0.15	2.28 ± 0.20	2.85 ± 0.20

* Averaged results of three repeats.

pigment content and the fatty-acid composition of the lipids of *Chlorella vulgaris* (unpublished) and *Scenedesmus quadricauda* [12]. The data obtained permitted classifying the tested neurotransmitters into two main subroups [12]: (1) Acetylcholine and histamine increased the percentage of polyunstaturated fatty acids (PUFAs) in the lipids and elevated the chlorophyll and carotenoid contents of microalgal cells; and (2) dopamine and norepinephrine (in *C. vulgaris* but not in *S. quadricauda*), in contrast, increased the share of saturated fatty acids. Importantly, serotonin increased the percentage of unsaturated fatty acids in *C. vulgaris* and decreased it in *S. quadricuada*.

Interestingly, acetylcholine and histamine, which increase the share of unsaturated fatty acids in both microalgae, also elevate the levels of chlorophyll *a*, plausibly resulting in the increased photosynthetic activity that is characteristic of the early culture development stages of microalgae. Conversely, dopamine augmented the percentage of saturated fatty acids in the lipid fraction while decreasing the photosynthetic pigment levels, at least with *S. quadricauda* [12].

Batch cultures, such as those used in the present work and in the publication cited [12], are known to undergo several developmental stages. Their development may be envisaged as an analogue of a multicellular organism's ontogeny [13], and a microbial culture can be described as "young," "mature," or "aging."

In this context, the data of work [12] were hypothetically interpreted in terms of the suggestion that acetylcholine and histamine "rejuvenate" the microalgal culture, i.e., prolong the earlier cultivation stages characterized by rapid cell division and expansion of chloroplast membranes harboring lipids rich in

Table 6. Influence of dopamine on the carotenoid and chlorophyll content in *H. lacustris* BM-1* cells

Photosynthetic pigments	Content, mg/g of biomass								
	upon inoculation	control		DA, 0.1 μM		DA, 1 μM		DA, 10 μM	
		7	14	7	14	7	14	7	14
Chlorophyll *a*	2.34 ± 0.20	1.20 ± 0.20	1.23 ± 0.15	1.59 ± 0.15	1.46 ± 0.15	1.04 ± 0.10	1.42 ± 0.10	1.28 ± 0.10	1.52 ± 0.15
Chlorophyll *b*	1.23 ± 0.15	0.55 ± 0.15	0.67 ± 0.15	0.74 ± 0.10	0.77 ± 0.10	0.43 ± 0.10	0.77 ± 0.15	0.57 ± 0.10	0.78 ± 0.15
Chlorophyll *a* + *b*	3.57 ± 0.20	1.75 ± 0.20	1.90 ± 0.20	2.34 ± 0.20	2.23 ± 0.20	1.47 ± 0.15	2.19 ± 0.15	1.85 ± 0.20	2.30 ± 0.20
Carotenoids	0.59 ± 0.10	1.91 ± 0.20	4.44 ± 0.20	2.21 ± 0.20	4.44 ± 0.20	1.70 ± 0.15	5.07 ± 0.20	1.96 ± 0.15	4.07 ± 0.20

* Averaged results of three repeats.

Table 7. Influence of norepinephrine on the carotenoid and chlorophyll content in *H. lacustris* IPPAS H-239* cells

Photosynthetic pigments	Content, mg/g of biomass								
	upon inoculation	control		NE, 0.1 μM		NE, 1 μM		NE, 10 μM	
		7	14	7	14	7	14	7	14
Chlorophyll *a*	1.91 ± 0.15	1.33 ± 0.15	1.76 ± 0.15	1.33 ± 0.15	1.22 ± 0.10	1.26 ± 0.10	1.30 ± 0.15	1.26 ± 0.15	1.26 ± 0.10
Chlorophyll *b*	0.85 ± 0.10	0.55 ± 0.10	0.68 ± 0.15	0.62 ± 0.10	0.22 ± 0.10	0.44 ± 0.10	0.30 ± 0.10	0.51 ± 0.10	0.48 ± 0.15
Chlorophyll *a* + *b*	2.76 ± 0.20	1.88 ± 0.15	2.44 ± 0.20	1.95 ± 0.15	1.44 ± 0.15	1.70 ± 0.15	1.60 ± 0.15	1.78 ± 0.15	1.74 ± 0.15
Carotenoids	0.73 ± 0.10	2.85 ± 0.20	3.26 ± 0.20	3.09 ± 0.25	2.04 ± 0.20	2.66 ± 0.20	2.52 ± 0.20	2.86 ± 0.20	2.28 ± 0.20

* Averaged results of three repeats.

Table 8. Influence of norepinephrine on the carotenoid and chlorophyll content in *H. lacustris* BM-1* cells

Photosynthetic pigments	Content, mg/g of biomass								
	upon inoculation	control		NE, 0.1 μM		NE, 1 μM		NE, 10 μM	
		7	14	7	14	7	14	7	14
Chlorophyll *a*	2.58 ± 0.20	1.58 ± 0.15	1.74 ± 0.15	1.75 ± 0.15	2.06 ± 0.20	1.75 ± 0.15	1.98 ± 0.15	1.65 ± 0.15	2.10 ± 0.20
Chlorophyll *b*	1.05 ± 0.10	0.67 ± 0.10	0.63 ± 0.10	0.78 ± 0.10	0.72 ± 0.10	0.71 ± 0.10	0.81 ± 0.10	0.71 ± 0.10	0.83 ± 0.10
Chlorophyll *a* + *b*	3.63 ± 0.20	2.26 ± 0.20	2.37 ± 0.20	2.54 ± 0.20	2.78 ± 0.25	2.46 ± 0.20	2.79 ± 0.25	2.36 ± 0.20	2.93 ± 0.25
Carotenoids	0.79 ± 0.10	1.99 ± 0.15	3.03 ± 0.20	2.16 ± 0.20	3.42 ± 0.20	2.04 ± 0.15	3.47 ± 0.20	1.91 ± 0.15	3.81 ± 0.25

* Averaged results of three repeats.

PUFAs. Conversely, dopamine can be envisaged as an "aging-promoting agent" that augments the degree of saturation of membrane lipids and reduces the photosynthetic pigment content [12].

As for *H. lacustris*, it should be re-emphasized that its culture is characterized by a specific quasi-aging process involving the transition from the "green" vegetative (chlorophyll-rich) through the "brown" palmelloid (combining chlorophylls and carotenoids) to the "reddish" encysted (carotenoid-accumulating) form.

Among the neurotransmitters tested in the present work, norepinephrine and acetylcholine stimulated the synthesis of both chlorophylls and carotenoids in the two strains of *H. lacustris* on days 7 and 14 of cultivation; histamine and dopamine promoted these processes only in strain BM-1. In distinction from BM-1, histamine, serotonin, and dopamine decreased the chlorophyll and carotenoid content of strain IPPAS H-239.

The results presented in this work seem to be somewhat paradoxical in light of the literature data on the competition between (1) the synthesis of chlorophyll forming a part of the photsystems and (2) the formation of secondary carotenoids, especially astaxanthin, in *H. lacustris* (reviewed, [3, 14]). However, are these two process inevitably antagonistic (according to the zero-sum principle)?

The data obtained can be interpreted in terms of recent literature data on the intermediate developmental stage (the "middle-aged" culture) that combines chlorophyll and carotenoid production. Such a culture chiefly contains nonmotile palmelloid cells featuring a sizeable amount of astaxanthin against the background of a still significant chlorophyll content [3].

Table 9. Influence of acetylcholine on the carotenoi and chlorophyll content in *H. lacustris* IPPAS H-239* cells

Photosynthetic pigments	Content, mg/g of biomass								
	upon inoculation	control		ACh, 0.1 μM		ACh, 1 μM		ACh, 10 μM	
		7	14	7	14	7	14	7	14
Chlorophyll *a*	1.87 ± 0.15	1.33 ± 0.15	1.17 ± 0.15	1.93 ± 0.20	1.92 ± 0.20	1.75 ± 0.15	1.83 ± 0.15	1.80 ± 0.15	1.29 ± 0.10
Chlorophyll *b*	0.83 ± 0.10	0.67 ± 0.10	0.56 ± 0.10	0.91 ± 0.15	0.92 ± 0.15	0.85 ± 0.15	0.85 ± 0.15	0.88 ± 0.15	0.63 ± 0.10
Chlorophyll *a* + *b*	2.71 ± 0.20	2.00 ± 0.20	1.74 ± 0.15	2.84 ± 0.20	2.85 ± 0.20	2.61 ± 0.20	2.68 ± 0.20	2.68 ± 0.20	1.91 ± 0.15
Carotenoids	0.53 ± 0.10	2.71 ± 0.20	5.73 ± 0.25	3.97 ± 0.25	8.01 ± 0.25	3.78 ± 0.20	7.91 ± 0.25	3.60 ± 0.20	6.02 ± 0.25

* Averaged results of three repeats.

Table 10. Influence of acetylcholine on the carotenoid and chlorophyll content in *H. lacustris* BM-1* cells

Photosynthetic pigments	Content, mg/g of biomass								
	Upon inoculation	Control		ACh, 0.1 μM		ACh, 1 μM		ACh, 10 μM	
		7	14	7	14	7	14	7	14
Chlorophyll *a*	4.81 ± 0.20	1.27 ± 0.15	1.05 ± 0.15	1.23 ± 0.15	0.71 ± 0.10	1.30 ± 0.15	1.45 ± 0.15	1.12 ± 0.10	1.90 ± 0.15
Chlorophyll *b*	1.27 ± 0.15	0.54 ± 0.10	0.53 ± 0.10	0.54 ± 0.10	0.36 ± 0.10	0.60 ± 0.10	0.65 ± 0.10	0.57 ± 0.10	0.82 ± 0.15
Chlorophyll *a* + *b*	7.08 ± 0.25	1.82 ± 0.15	1.57 ± 0.15	1.77 ± 0.15	1.07 ± 0.15	1.89 ± 0.20	2.11 ± 0.20	1.69 ± 0.15	2.72 ± 0.20
Carotenoids	1.34 ± 0.15	1.85 ± 0.15	2.58 ± 0.20	1.85 ± 0.15	2.02 ± 0.20	1.98 ± 0.20	2.99 ± 0.25	1.71 ± 0.15	4.01 ± 0.3

* Averaged results of three repeats.

Presumably, acetylcholine and norepinephrine in both tested strains as well as histamine and dopamine in strain BM-1 lock the development of the culture at the "middle-aged" palmelloid stage. To re-emphasize, acetylcholine and histamine prolonged the relatively early developmental stage with a high PUFA and chlorophyll content in *Scenedesmus quadricauda* belonging to the same class (Chlorophyceae) as *H. lacustris* [12]. Therefore, the hypothetical mode of action of neurotransmitters is based on regulating the carotenoid and chlorophyll synthesis pathways so as to achieve an equilibrium between them and maintain sufficiently high concentrations of both pigment types.

On the contrary, neurotransmitters such as serotonin in strain IPPAS H-239 presumably impede the onset of the palmelloid stage, which can account for the inhibitory effects of the neurotransmitters on both carotenoid and chlorophyll synthesis.

The data obtained in this work seem to hold no biotechnological value at first glance. The production of astaxanthin with *H. lacustris* is only commercially viable against the background of its chemical synthesis if the astaxanthin content in *H. lacustris* cells exceeds 5% of the dry weight of the biomass (reviewed, [3]). Such a high astaxanthin yield is only possible with the final "reddish" encysted culture stage of *H. lacustris* and not the palmelloid stage. Should neurotransmitters not be included in the list of potential biotechnologically applicable promoters of carotenoid synthesis in *H. lacustris*, even though neurotransmitters are quite inexpensive if applied at very low (submicromolar) concentrations?

Apparently, dismissing neurotransmitters as biotechnologically useless is premature. Accumulation of palmelloid cells in the culture is of biotechnological interest per se since palmelloid cells are much easier to convert to astaxanthin-filled "reddish" cells than vegetative "green" cells [15]. Palmelloid cells require comparatively low doses of supplementary factors (high light, high salinity, etc.) for this purpose.

One of the neurotransmitters, dopamine, was applied to *H. lacustris* against the background of salt stress as a conventional method of increasing the astaxanthin yield (the cultivation medium contained 1 g/L NaCl). It was established that 33 μM dopamine weakly (by 7.63%) stimulated biomass accumulation but significantly (by 41.25%) increased the astaxanthin content in *H. lacustris* cells and their astaxanthin productivity (by 52.04%) in comparison to those grown with only NaCl. In addition, dopamine stimulates lipid synthesis in the cells [4]. This is obviously related to the fact that astaxanthin accumulates in cytoplasmic lipid droplets; moreover, some of the stages of its biosynthesis are carried out in them [3].

In summary, the data obtained in this work concerning the concomitant stimulation of carotenoid and chlorophyll synthesis by some neurotransmitters in *H. lacustris* (strains IPPAS H-239 and BM-1) can potentially be used to boost the astaxanthin yield by combining the neurotransmitters with low doses of other factors that promote astaxanthin production and facilitate the synthesis of additional microalgal products such as PUFA-enriched lipids. They can be isolated from the biomass after extracting the carotenoids [3].

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This work does not contain any studies involving human and animal subjects.

CONFLICT OF INTEREST

The authors of this work declare that they have no conflicts of interest.

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