УДК 574.5
DOI 10.29003/m4988.0514-7468.2025_47_4/550-562
EDN PMKRCV

NEUROCHEMICAL POLLUTANTS IN THE AQUATIC MEDIUM: THE RESULTS OF STUDIES WITH MODEL ORGANISMS (MICROALGAE)

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The constantly extending list of humankind-produced environmentally toxic compounds currently includes pharmacological preparations. Among them, of potential relevance are neurotransmitters including such biogenic amines as norepinephrine, dopamine, serotonin, and histamine, as well as acetylcholine. These neurotransmitters were tested in the present work using such model organisms as the green microalgae Chlorella vulgaris Beijer, Scenedesmus quadricauda (Turp.) Breb. K-1149, and Haematococcus lacustris (= pluvialis) strains IPPAS H-239 and BM-1, as well as the cyanobacterium Limnospira platensis IPPAS B-256. It was established that all tested neurotransmitters significantly stimulate the growth of the cultures of microalgae at sufficiently low (micromolar) concentrations. In light of the results of this work, uncontrollable microalgal growth seems to be possible under the influence of trace amounts of neurotransmitters in natural and artificial water bodies, which might cause their eutrophication. All tested substances influenced the photosynthetic pigment content at micromolar (or submicromolar) concentrations, acetylcholine being a quasi-universal promoter of their biosynthesis that presumably stimulates the photosynthetic activity of the microalgae. The effects of the other tested substances varied depending on the microalgal species involved but predominantly resulted in promoting photosynthetic pigment biosynthesis. A biotechnological project aimed at stimulating the microalgal biomass yield by supplementing microalgal cultures with neurotransmitters seems to hold promise for producing drugs, food additives, or biofuel.

Key words: *ecotoxicants, pharmaceuticals, neurotransmitters, serotonin, histamine, norepinephrine, dopamine, acetylcholine, microalgae, eutrophication.*

Abbreviations: *5-HT, serotonin; ACh, acetylcholine; BA, biogenic amine; DA, dopamine; NE, norepinephrine; PPCP, pharmaceuticals and health care products; QS, quorum sensing; WTP, wastewater treatment plant.*

For citation: Cao, Boyang, Oleskin, A.V., "Neurochemical pollutants in the aquatic medium: the results of studies with model organisms (microalgae)", *Zhizn Zemli* [Life of the Earth] **47**, no 4, 550–562 (2025) (in Engl., abstr. in Russ.). DOI: 10.29003/m4988.0514-7468.2025_47_4/550-562.

НЕЙРОХИМИЧЕСКИЕ ПОЛЛЮТАНТЫ В ВОДНОЙ СРЕДЕ: РЕЗУЛЬТАТЫ ИССЛЕДОВАНИЙ НА МОДЕЛЬНЫХ ОБЪЕКТАХ (МИКРОВОДОРОСЛЯХ)

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Список антропогенных экологически токсичных соединений пополняется в последние десятилетия, наряду с другими «подарками» человека биосфере, лекарственными препаратами. Среди последних немаловажное значение имеют нейротрансмиттеры, в т. ч. биогенные амины норадреналин, дофамин, серотонин,

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гистамин, а также ацетилхолин. Эти нейротрансмиттеры испытаны в настоящей работе на модельных тест-объектах: зелёных микроводорослях Chlorella vulgaris Beijer, Scenedesmus quadricauda (Turp.) Breb. K-1149, Haematococcus lacustris (= pluvialis) штаммы IPPAS H-239 и BM-1 и цианобактерии Limnospira platensis IPPAS B-256. Установлено, что все тестированные нейротрансмиттеры значимо стимулируют рост культур исследованных микроводорослей в достаточно низких (микромолярных) концентрациях. В свете полученных в настоящей работе результатов реальным представляется перспектива неконтролируемого роста микроводорослей под воздействием даже «следовых» количеств нейротрансмиттеров в естественных и искусственных водоёмах с перспективой их эвтрофикации.

Все испытанные вещества также влияли в микромолярных (или субмикромолярных) концентрациях на содержание фотосинтетических пигментов, причём ацетилхолин выступал как почти универсальный стимулятор их биосинтеза, и предположительно должен стимулировать фотосинтетическую активность микроводорослей. Воздействие других тестированных веществ носило видоспецифический характер, однако во многих случаях они также оказывали стимуляторное воздействие на биосинтез фотосинтетических пигментов. Биотехнологический проект, направленный на увеличение выхода биомассы микроводорослей путём добавления нейротрансмиттеров в их культуры, имеет перспективы в плане стимулирования производства лекарственных препаратов, пищевых добавок или биотоплива из микроводорослей.

Ключевые слова: *экотоксиканты, фармацевтические препараты, нейротрансмиттеры, серотонин, гистамин, норадреналин, дофамин, ацетилхолин, микроводоросли, эвтрофикация.*

Ссылка для цитирования: *Цао Боян , Олескин А.В.* Нейрохимические поллютанты в водной среде: результаты исследований на модельных объектах (микроводорослях) // Жизнь Земли. 2025. Т. 47, № 4. С. 550–562. DOI: 10.29003/m4988.0514-7468.2025_47_4/550-562.

Поступила 05.10.2025 / Принята к публикации 26.11.2025

Introduction: pharmaceuticals as ecotoxicants. The present work is concerned with a new type of environmental pollutants, *neuroactive compounds*. It focuses on their effects on the growth and biochemical characteristics of model organisms such as green microalgae (Chlorophyta) and cyanobacteria. This work is of direct relevance to an actively developing subfield of modern environmental science referred to as environmental toxicology that deals with the harmful effects of chemical, physical, and biological factors on living organisms and their populations and ecosystems [5].

The number of humankind-produced environmentally toxic compounds has been constantly increasing over the course of recent decades. A global threat for the Earth's ecosystems is currently posed not only by pesticide and industrial waste products. Of increasing importance in this context are pharmaceuticals and personal care products (PPCPs). These substances are released into the environment with the wastewater of health care institutions and the facilities of pharmaceutical, cosmetic, and food industry; they also form a part of municipal waste. Importantly, "*pharmaceuticals are routinely present in semi-rural and urban rivers and require management alongside more traditional pollutants*" [20]. It has been estimated between 30 and 90% of the orally administered doses of pharmaceuticals are excreted with the urine of patients utilizing them [22]. Significant amounts of pharmaceuticals are used in veterinary medicine and enter the soil or water via the animal organism. Pharmaceuticals are also released into the environment by wastewater treatment plants (WTPs), and they frequently pass through their filters. They are present in WTP sludge and landfill leachate [15].

In spite of the relative instability of some pharmaceuticals (including the neurotransmitters considered below) in the environment, their environmental toxicity depends on their capacity to affect living organisms and whole ecosystems at very low concentrations. If nanograms or micrograms of pharmaceuticals per liter are chronically released into the soil, water, or other media, they would supplement the effects produced by the human-produced harmful cocktail and synergistically interact with them. In particular, this results in disrupting reproduction processes in amphibians, fish, mollusks, etc. [16]. For instance, hormones of the estradiol group cause feminization and ovary development in male fish; similar effects are exerted on frogs, alligators, or mussels [16]. Levonorgestrel, the active component of hormone-based prophylactics, accumulates in the rainbow trout organism that has been in contact with the wastewater of Swedish cities and reaches concentrations of 8.5–12 ng/mL, which is close to the levonorgestrel level in the blood of its human consumers [18].

Generally, at least 9 types of pharmaceuticals are classified as dangerous ecotoxicants. These are hormones, antibiotics, lipid metabolism regulators, beta-blockers, anticonvulsants, antineoplastics, and diagnostic contrast substances. A serious risk is posed by personal care products such as fragrances, preservatives, disinfectants, and sunscreen agents [32].

The effects of very low concentrations of some pharmaceuticals clearly manifest themselves in aquatic ecosystems because they are identical with or homologous to the signals produced by various hydrobionts. Many preparations exert a specific influence on the nervous cells of zooplankton or nekton representatives. A wide spectrum of aquatic organisms including bacteria, algae, invertebrates, and fishes, have receptors for such neuroactive pollutants, which accounts for their sensitivity to them. For instance, such widely used psychopharmacological preparations as Prozac (an antidepressant) and amphetamines (cognitive activity promoters) cause major changes in bacterial and algal associations within aquatic ecosystems [7].

Neurotransmitters as potentially important ecotoxicants. The pharmaceutical ecotoxicants of the new generation include *neurotransmitters,* i.e., substances that transmit impulses between nervous cells (neurons) or between a neuron and a muscular or glandular cell. An important subtype of neurotransmitters are biogenic amines such as catecholamines (dopamine, norepinephrine, and epinephrine), serotonin, histamine, etc. Importantly, the term "neurotransmitter" is somewhat arbitrary since such compounds also function in organisms that lack a nervous system, such as primitive invertebrates [3], plants [9], fungi [1, 2], protozoans [1, 2], and bacteria (reviewed, [8]), in which they operate as signals or regulatory molecules [8-11]. For instance, norepinephrine and epinephrine substantially stimulate blooming in a component of aquatic ecosystems, the duckweed *Lemna paucicostata*; the adrenoreceptors that are present in the duckweed and other plants regulate cytoplasm movement and pollen and seed germination [26]. Neurotransmitters are actively involved in plant responses to stress. For instance, damaging potato leaves results in an increase in dopamine, norepinephrine, and epinephrine concentrations in them. The dopamine concentration also increases in the tissues of the cactus *Portulacca callus* upon injury [7].

These compounds are not included in the official lists of globally dangerous ecotoxins and they relatively rapidly decompose in the aquatic environment. However, they are likely to be constantly released into the environment with the wastewater of pharmaceutical factories, healthcare institutions, and food-producing plants. Dopamine, norepinephrine, and serotonin are known to be produced by pharmaceutical enterprises in Russia and other countries. For instance, dopamine as a cardiotonic and hypertensive preparation is supplied by the Promomed company in Russia and Admed Arzneimittel in Germany. Acetylcholine (Brain

Food™) is utilized as a food additive. Food industry wastewater inevitably contains neurotransmitters that are present in the blood and other biological liquids of animals (notably, 40 to 80 μg/L serotonin is contained in the human blood serum [4]). Histamine accumulates in food items during their storage, due to the bacterial conversion of histidine to histamine (see: [8]). In addition, neurotransmitters are secondarily produced and accumulated in natural ecosystems under the influence of other humankind-produced ecotoxicants. For instance, the release of cocaine and other neuroactive pollutants into rivers, e.g., the River Thames in London [21] results in increasing the dopamine concentrations in the organism of eels and other fishes that release dopamine into the environment under stress or after an injury.

Apart from neurotransmitters *per se*, of ecotoxicological interest are substances that interact with them, their agonists, antagonists (blockers), re-uptake inhibitors, etc. For instance, it was revealed that propranolol, a β-adrenoreceptor blocker, is released into the water and reduces the capacity of fish to spawn. Serotonin re-uptake inhibitors citalopram and fluoxetine are used as antidepressants; however, they also affect locomotive behaviour in aquatic vertebrates and invertebrates [30].

In this work, such neurotransmitters as acetylcholine (ACh), serotonin (5-HT), histamine, norepinephrine (NE), and dopamine (DA) were tested for ecotoxic effects on microalgae and cyanobacteria as model organisms.

Of environmental importance are both (i) the inhibitory effects of neurotransmitters on the growth, photosynthetic activity, and other characteristics of microalgae that pose the threat of disrupting phytoplankton-dependent trophic chain in ecosystems, and (ii) their stimulatory effects that can cause uncontrollable microalgae proliferation ("blooming") and eventually the eutrophication of water bodies.

In the literature, studies on the effects of neurotransmitters on other types of model organisms are described. It was demonstrated that dopamine addition changed the response of the water flea *Daphnia magna* to a lack of food (microalgae) in the medium: with dopamine, the water fleas grow and maturate as if food were plentiful, even though the food deficiency decreases the growth rate and slows down maturation without dopamine [19]. These findings can be explained in terms of the regulatory effects of neurotransmitters in water inhabitants that are exemplified by zooplankton representatives. In addition, our data obtained using high-performance liquid chromatography with amperometric detection indicate that dopamine is produced by *D. magna per se* at a concentration of 0.255±0.05 μM. Besides, it will be pointed out below that dopamine (like the other tested neurotransmitters) promotes the growth of the microalga *Chlorella vulgaris* that is consumed by water fleas. Presumably, the predator *D. magna* releases a substance that stimulates the growth of its prey. Dopamine also promotes cell aggregation in *C. vulgaris* (unpublished data obtained in collaboration with the student Jia Hui). Plausibly, it is advantageous for the water flea to consume compact microalgal pellets rather than individual cells [6].

The above data additionally emphasize the reason why even very low concentrations (trace amounts) of neurotransmitters are of interest in ecotoxicological terms: neurotransmitters are "erroneously" perceived by natural ecosystem components as their own endogenous signals or regulatory agents (or their homologs) and, therefore, they exert a specific influence on those components.

It is the "molecular mimicry" of human-produced neuroactive pollutants that resemble endogenous signals and regulators that is a prerequisite for their sufficiently strong ecotoxic effects even at very low concentrations. Such effects were demonstrated in the Experimental section of the present work which green microalgae and cyanobacteria were utilized in.

Neurotransmitter effects on model organisms. The following main test subjects were used in this work: the cyanobacterium *Limnospira platensis* IPPAS B-256 and the eukaryotic green microalgae *Chlorella vulgaris* Beijer, *Scenedesmus quadricauda* (Turp.) Breb. K-1149, and *Haematococcus lacustris* (= *pluvialis*) (strains IPPAS H-239 and BM-1). In the following, the data obtained in the published work [12, 13, 23, 24] are summarized and generalized from the ecotoxicological viewpoint.

Neurotransmitter impact on the growth of the model organisms. Microalgal cultures were grown under photoautotrophic conditions. 0.1, 1, 10, or 100 μM acetylcholine, dopamine, histamine, norepinephrine, and serotonin hydrochlorides were added to the cultures upon inoculation; the control cultures were supplemented with an equal volume of water. The growth of the cultures with and without neurotransmitters was compared by directly counting their cells in a Goryaev chamber or measuring their dry weight. The data presented herein are arithmetic means. 4–5 independent replicas of each experiment were conducted, and the cell numbers were estimated at least three times in each replicate. Student's *t*-test was applied to the data obtained using Microsoft Excel software at $p < 0.05$.

Growth dynamics of C. vulgaris with serotonin (5-HT), histamine, dopamine (DA), norepinephrine (NE), acetylcholine (ACh) and without additions (the control system) is demonstrated in **Figs 1–3**, the data are summed up in Table 1 below. DA and NE increased the cell numbers on days 1 and 2 but not on day 4 of cultivation, i.e., they mainly brought about growth acceleration without a significant increase in plateau level on day 4. In contrast, 5-HT, ACh, and histamine exerted a true stimulatory effect with an increase in cell number that the *C. vulgaris* culture ultimately produced. These effects were produced with 1 and/or 10 μM neurotransmitters and not at their maximum (100 μM) concentrations.

Impact of neurotransmitters on the growth of S. quadricauda. All tested neurotransmitters at concentrations of 1 and 10 μM brought about an increase in cell number in the *S. quadricauda* culture, and this effect persisted until the end of the cultivation period when the growth plateau was reached (on day 7).

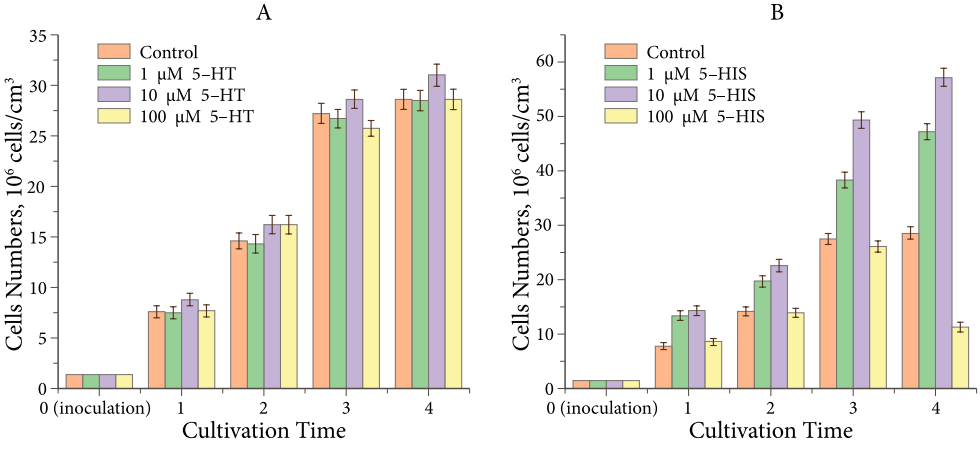


Fig. 1. Effect of serotonin (5-HT, A) and histamine (His, B) on *C. vulgaris* growth. All data obtained are statistically significant, according to Student's *t* test at p =0.05.

Рис. 1. Действие серотонина (5-HT, A) и гистамина (His, B) на рост *C. vulgaris*. Все данные достоверны при $p = 0.05$ по *t*-критерию Стьюдента.

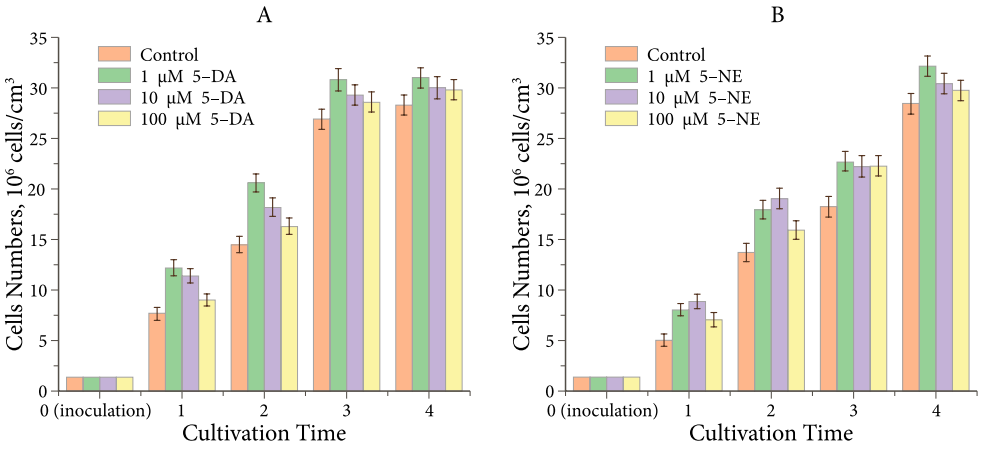


Fig. 2. Effect of dopamine (DA, A) and norepinephrine (NE, B) on *C. vulgaris* growth. All data obtained are statistically significant, according to Student's *t* test at p =0.05.

Рис. 2. Действие дофамина (DA, A) и норадреналина (NE, B) на рост *C. vulgaris*. Все данные достоверны при p = 0.05 по *t*-критерию Стьюдента

Impact of neurotransmitters on the growth and cell differentiation of H. lacustris. This microalga transitions from the vegetative (green-colored because of the chlorophyll) to the resting (red-colored, accumulating carotenoids) stage via an intermediate palmelloid stage that first loses its flagella and acquires a rounded shape (vegetative palmella, **Fig. 4**, left) and thereupon starts producing secondary carotenoid-containing lipid droplets in its cytoplasm until it is almost completely filled with the red pigment (**Fig. 4**, right).

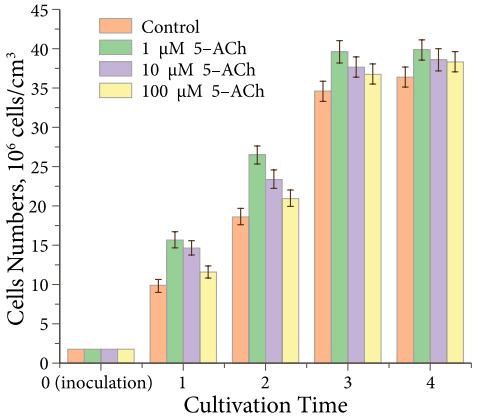
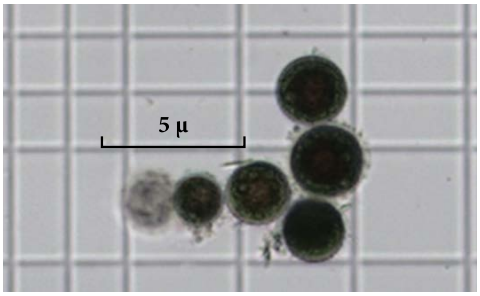


Fig. 3. Effect of acetylcholine (ACh) on *C. vulgaris* growth. All data obtained are statistically significant, according to Student's *t* test at p =0.05.

Рис. 3. Действие ацетилхолина (A) на рост *C. vulgaris*. Все данные достоверны при p = 0.05 по *t*-критерию Стьюдента.

From **Table 1** below it is evident that an increase in the cell numbers in the cultures of the tested *H. lacustris* strains was detected in the presence of histamine, ACh, DA, and 5-HT (in strain BM-1 only). NE and 5-HT (in strain IPPAS B-239) failed to produce any significant effects. A manifest increase in encysted cell percentage was only revealed with 5-HT (in strain BM-1) and DA (in strain IPPAS B-239). ACh (in both strains) and NE (in strain IPPAS B-239 only) increased the palmelloid cell percentage while not affecting or even decreasing the encysted cell number.

Impact of neurotransmitters on the growth of L. platensis. The batch culture of *L. platensis* without additions reached the maximum number of trichomes (hair-like structures composed of several cells) by day 7 of cultivation. Subsequently, the trichome number somewhat decreased. After day 7, the biomass dry weight per 1 cm^3 of culture volume continued increasing (gradually tapering off) and reached its maximum level on day 14 of cultivation.



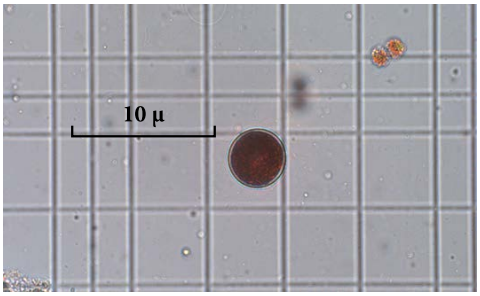


Fig. 4. Vegetative palmelloid (left) and encysted (with astaxanthin-filled lipid droplets in the cytoplasm) (right) *H. lacustris* cells.

Рис. 4. Вегетативные пальмеллоидные (слева) и покоящиеся (капли липидов с астаксантином в цитоплазме) (справа) клетки *H. Lacustris.*

Table 1. Summarized data on the impact of BAs on the growth characteristics of the tested microalgae. Designations: ↗. upward trends; ↘. downward trends; —. insignificant or ambiguous effects. IPPAS H-239 and BM-1, *H. lacustris* strains. The trends are based on data verified using Student's *t* test.

Таблица 1. Обобщённые данные по влиянию БА на ростовые параметры микроводорослей; тенденции: ↗, увеличение параметра; ↘, уменьшение параметра; —, эффект незначительный или неоднозначный. IPPAS H-239 и BM-1, штаммы *H. lacustris*. Данные в основе тенденций достоверны при p = 0.05 по t-критерию Стьюдента.

Microalgal species/strain	Characteristics	Biogenic amines				
		5-HT	His	DA	NE	ACh
C. vulgaris	Cell number per 1 cm^3	↗	↗	↗*	↗*	↗
S. quadricauda	Cell number per 1 cm^3	↗	↗	↗	↗	↗
IPPAS H-239	Cell number per 1 cm^3	—	↗	↗	—	↗
	Vegetative cell number per 1 cm^3	↘	↗	↘	↘	↗
	Palmelloid number per 1 cm^3	—	↗	↘	↗	↗
	Resting cell number per 1 cm^3	↗***	↗		—	—
BM-1	Cell number per 1 cm^3	↗	↗	↗	—	↗
	Vegetative cell number per 1 cm^3	↘	↗	↗	↗	↗
	Palmelloid number per 1 cm^3	↘	↗	↘	↘	↗
	Resting cell number per 1 cm^3	↗	↗	—	—	↘
L. platensis	Trichome number per 1 cm^3	↘	↘	↘	—	↘
	Dry weight of biomass, mg/mL	↗*	↗*	↘**	—	↗*

* Growth-accelerating effect without increasing call number at the end of cultivation; ** Growth-decelerating effect; *** Unverifiable effect

Apparently, the trichome number decrease was outweighed by an increase in trichome size, so that the biomass content could further increase. ACh, histamine, and 5-HT increased and DA decreased the biomass content of *L. platensis* on day 7 of cultivation, but these effects became insinificsnt by day 14. All tested neurotransmitters except NE reduced the trichome number on day 7; all these substances but NE prevented the decrease in trichome number that was observed in the control culture on day 14 of cultivation.

Neurotransmitter impact on the photosynthetic pigment content of microalgae. Chlorophyll *a* and *b* as well as total carotenoids were analyzed spectrophotometrically using their extinction coefficients in chloroform.

Effects of neurotransmitters on the photosynthetic pigment content of C. vulgaris.. All tested neurotransmitters increased, to some extent, the chlorophyll *a* and *b* content; 5-HT, ACh, and NE (to a limited extent) also elevated the carotenoid content. These data are summed up in Table 2 below. By increasing the photosynthetic pigment content, the neurotransmitters presumably promote the photosynthetic activity of *C. vulgaris* cells.

Effects of neurotransmitters on the photosynthetic pigment content of S. quadricauda. It is shown in **Table 2** that ACh and NE increased the total chlorophyll and carotenoid contents. which were decreased by DA. In contrast to *C. vulgaris*, 5-HT and histamine in *S. quadricauda* were without effect on the total photosystem component content. However, with histamine, the chlorophyll *a/b* ratio was shifted in favor of chlorophyll *a* and the chlorophyll:carotenoid ratio in favor of carotenoids suggestive of a stressor-type influence of this neurotransmitter.

Table 2. Summarized data on the influence of BA on photosynthetic pigment content in the tested microalgae. Designations: ↗, upward trends; ↘, downward trends; — insignificant or ambiguous effects. IPPAS H-239 and BM-1, *H. lacustris* strains. The trends are based on data verified with the Kruskal-Wallis test.

Таблица 2. Обобщённые данные по влиянию БА на содержание фотосинтетических пигментов в тестированных микроводорослях, тенденции: ↗, увеличение параметра; ↘, уменьшение параметра; —, эффект незначительный или неоднозначный. IPPAS H-239 и BM-1, штаммы *H. lacustris.* Данные в основе тенденций достоверны по H-критерию Крускала-Уоллеса.

Characteristics	Species/strains of microalgae	Biogenic amines				
		5-HT	His	DA	NE	Ach
Chlorophyll *a* content	*C. vulgaris*	↗	↗	—	↗	↗
	S.quadricauda	—	↗	↘	↗	↗
	IPPAS H-239	↘	↘	↗	↗	↗
	BM-1	—	↗	↗	↗	↗
	L. platensis	↗	↘	↗	—	↘
Chlorophyll *b* content	*C. vulgaris*	↗	↗	—	↗	—
	S.quadricauda	—	↘	↘	↗	↗
	IPPAS H-239	↘	↘	↗	↗	↗
	BM-1	—	↗	↗	↗	↗
	L. platensis	Chlorophyll *b* lacking				
Carotenoid content	*C. vulga ris*	↗	—	—	↗	↗
	S.quadricauda	—	↗	↘	↗	↗
	IPPAS H-239	↘	↘	↘	↗	↗
	BM-1	—	↗	↗	↗	↗
	L. platensis	↗	↗	↗	—	↗

Effects of BAs on the photosynthetic pigment content of H. lacustris. *H. lacustris* transitions from the vegetative stage with green chlorophyll-containing cells to the resting carotenoid-accumulating reddish stage via the intermediate palmelloid stage with flagella-lacking rounded brown cells. The chlorophyll *a* and *b* content is reduced with a concomitant increase in carotenoid content. 5-HT and histamine decrease and ACh, NE, and DA increase the chlorophyll content of *H. lacustris* IPPAS H-238 cells (on day 7 and 14 of cultivation). In strain BM-1 5-HT did not affect the chlorophyll content whereas the rest of BAs increased it. The concentration of carotenoids is decreased in strain IPPAS B-239 under the influence of histamine, DA, and 5-HT and elevated in the presence of NE and ACh. In strain BM-1, 5-HT does not influence the carotenoid content whereas the rest of the BAs increase it.

Evaluating the potential role of neurotransmitters as ecotoxicants in light of the data obtained. The present work deals with the impact of neurotransmitters, potentially important human-produced exotoxicants, on the biomass yield and the photosynthetic pigment content of some eukaryotic microalgae and cyanobacteria. The tested neurotransmitters such as DA, NE, 5-HT, histamine, and ACh significantly stimulate the growth of cultures of the microalgae under study at sufficiently low (micromolar or submicromolar) concentrations that are close to their physiological concentrations in the plant or animal organism.

In light of the results of this work, it seems plausible that microalgae can start uncontrollably growing even in the presence of trace amounts of neurotransmitters in the parts of water bodies that are relatively distant from the points at which neurotransmitter-containing wastewater is discharged into them by food- or drug-producing plants. Due to the very low concentrations involved, neurotransmitters can exert their effects even though they are naturally degraded in abiotic (e.g, photooxidation) and biotic (enzyme-dependent) processes. The data obtained give grounds for the suggestion that "neuroactive" wastewater should be still better purified in order to prevent water blooming and eutrophication

All tested neurotransmitters also influenced (at micromiolar concentrations) the photosynthetic pigment contents, acetylcholine behaving as a quasi-universal biosynthesis promoter with the tested microalgae, although it only raised the carotenoid content in the cyanobacterium *L. platensis* and even reduced the chlorophyll level on day 7 of cultivation (Table 2). The impact of the other tested substances was species-specific but it predominantly resulted in promoting the biosynthesis of photosynthetic pigments. For instance, serotonin, histamine, and norepinephrine increased the total chlorophyll and carotenoid content in *C. vulgaris*.

The data on the impact of BAs on FA and pigment contents in microalgae including a cyanobacterium at low (micromolar) concentrations can hypothetically be explained by suggesting that these organisms possess an analog of population density-gauging (quorum sensing, QS) systems that are widely spread in the microbial realm. Over the course of the last decades, the main classes of quorum sensing signals were characterized, including aromatic signal molecules (exemplified by AI-3) that are structurally similar (homologous) to dopamine and norepinephrine (reviewed, [8]).

Of special interest is research on the effects of neurotransmitters on genomic systems that control the synthesis and metabolism of photosynthetic pigments, similar to studies on the mechanism of action of phytohormones on the microalgal genome [14, 25, 33]. A promising area of research is based on using published databases for screening for the reference genomic sequences of the receptors, signal transmission pathway components, biosynthetic enzymes, and transporters of neurotransmitters in model organisms and for the quest for homologous sequences in published microalgal genomes.

In environmental terms, a promising idea is to edit microalgal genomes, supplementing them with operons for enzymatic neurotransmitter degradation in order to prevent their possible eutrophicating effects on water bodies.

The data obtained on the stimulatory effects of micromolar neurotransmitter concentrations on biomass accumulation and photosynthetic pigment content is of potential relevance to biotechnology, forasmuch as such neurotransmitter amounts are relatively inexpensive. A project aimed at boosting the biomass yield by adding neurotransmitters to microalgal cultures, hold some promise in terms of promoting the production of drug preparations, food additives, or biofuel from microalgae.

From the ecological and hydrobiological viewpoint, the neurotransmitter effects on the growth-related and biochemical characteristics of *C. vulgaris, S. quadricauda, H. lacustris,* and *L. platensis* as widespread inhabitants of freshwater and brackish water bodies are of much interest. To reiterate, neurotransmitters are implicated in multidirectional interactions among the components of natural or artificial aquatic ecosystems. Importantly, our previously published work is concerned with such neurotransmitter producers as zooplanktonic invertebrates exemplified by *D. magna* (that was established to produce dopamine) and coastal plants in which endogenous neurotransmitters were detected, in agreement with similar studies conducted by other researchers [9, 10, 27-29, 31].

Funding. This research was partly funded by the Development Program of the Interdisciplinary Scientific and Educational School of Lomonosov Moscow State University *The Future of the Planet and Global Environmental Change* as well as by the Shenzhen Municipal Government and Shenzhen MSU-BIT University.

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