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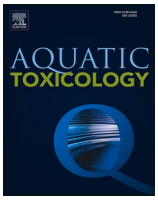

Bioactive compounds from *Schisandra chinensis* – Risk for aquatic plants?

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ABSTRACT

Schisandra chinensis is a potential plant for production of nutrient supplements due to adaptogens content. The dominant bioactive substance, lignan schisandrin, has positive effects on human health, but it can cause possible allelopathic effects in relation to other plants. *S. chinensis* is not native to European ecosystems, and its ecotoxicological properties have not been verified yet. *Lemna minor* was selected as a model aquatic plant to test its potential impact on the aquatic environment. Crude water extract from *S. chinensis* fruits, simulating the natural soaking of active substances in a surface water body, was used in treatments from 0.045 to 45 mg/L (according to the content of schisandrin as the dominating lignan). During seven days of cultivation, the growth (number of plants, leaf area, fresh weight) and photosynthetic activity of L. *minor* fronds were assessed. In low treatments (0.045 and 0.09 mg/L), the extract of *S. chinensis* did not cause any changes in duckweed growth parameters or photosynthetic performance. Higher treatments (0.45 and 0.9 mg/L) caused significant limitations in plants' number, total leaf area, and fresh weight. The photosynthetic parameters (basal chlorophyll fluorescence, quantum yields) were affected only by 0.9 mg/L. The highest treatment, 45 mg/L, exhibited extreme toxicity to duckweed plants causing their death during the first five days of cultivation. Schisandrin and other bioactive substances extractable from *S. chinensis* fruits can negatively impact water biota in the case of massive contamination of surface water.

1. Introduction

Schisandra chinensis (Turcz.) Baill (*Schisandraceae*) grows wild in the most Eastern parts of Russia (Primorsk and Chabarowsk regions), the Kuril Islands, southern Sakhalin and also north-eastern China, Korea and Japan (Hancke et al., 1999). Plants of the *Schisandraceae* family contain a variety of pharmacologically active lignans like schisandrin, deoxyschisandrin, deangeloylgomisin B, gomisin A, gomisin O, gamma-schisandrin and isogomisin O (Smejkal et al., 2010). Many studies and scientific papers address the positive effects of *S. chinensis* extracts on human health, and therefore the plant is classified as an adaptogen.

As a result of their high potential for enhancing physical endurance and stress resistance, plant adaptogens became popular in professional sports about 50 years ago. Even though plant adaptogens are now commonly used, there are only few clinical trials on humans. Several benefits were demonstrated by the meta-analysis for treating chronic fatigue, cognitive impairment, and immune dysfunction (Todorova et al., 2021). The positive effect of bioactive substances from *Schisandra* on the most common civilisation diseases such as cancer (Jung et al., 2019), diabetes (An et al., al.,2015; Pi et al., 2015), obesity (Liu et al., 2015), and others has also been proven. Moreover, the bioactive substances can have protective and regenerative role e.g. on skeletal muscles (Leis et al., 2020). In general, lignans can decrease triglycerides and total cholesterol levels, leading to body mass reduction, they are hypoglycaemic and can have nephroprotective activity. Schisandrins also influence the endocrine system, decreasing cortisol and slightly increasing testosterone levels (Leis et al., 2020).

Many studies have looked at the positive effects of the active substances of *S. chinensis* on the human body and health. There is a growing demand for food supplements containing bioactive substances from this plant. However, with the increasing consumption of such food supplements by humans, there is a risk that these substances will enter the wastewater and the surrounding environment. In addition, *S. chinensis* is

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increasingly being grown in gardens as an ornamental plant near garden ponds. Fruits falling into the surface water bodies like garden ponds could disrupt the aquatic ecosystem by affecting aquatic plants and animals. Due to the current lack of ecotoxicological data on the effects of active substances from *S. chinensis* on the surrounding environment, this issue needs to be addressed and possible disturbance of sensitive ecosystems should be assessed. Currently, the ecotoxicological data on plant lignans in a water environment are scarce, and schisandrin was not evaluated at all. In a few studies the representatives of lignans are presented as allelochemicals and potential alternative herbicides. Scavo et al. (2019a; 2019b) identified a group of biological compounds, including lignans, in extracts from cardoon leaves. The extracts had inhibitory effects on six weed species (*Amaranthus retroflexus L.*, *Portulaca oleracea* L., *Stellaria media* L., *Anagallis arvensis* (L.) *Vil.*, *Echinochloa crus-galli* L. and *Lolium perenne* L.) in which the germination rate was limited by 31% and the root and shoot length nearly 90%. The potential phytotoxic effect of allelochemicals can be connected with cytotoxic and anti-mitotic activity, as proved for podophyllotoxin in *Arabidopsis* roots (Costas-Gil et al., 2018).

Real content of schisandrin and other lignans in *S. chinensis* fruits is highly variable according to the way and place of cultivation, the ripening stage of the fruits and other factors. According to the literature sources the content of schisandrin can be from 2.1 mg/g (Kohda et al., 2012) to 5.0 mg/g of fruit dry weight (Slanina et al., 1997). There are many ways how to isolate lignans from *S. chinensis* fruits. Ma et al. (2011) published ionic liquid-based ultrasonic extraction (ILUAE) which has been successfully used to extract four biphenyl cyclooctene lignans from *S. chinensis* fruits. Also, Brezinova et al. (2010) described a simple and rapid method for the determination of six lignans found in *S. chinensis* plant cell cultures where lignans were extracted from plant samples with methanol and the extracts were efficiently purified by solid phase extraction followed by chromatographic separation.

Plants from genus *Schisandra* are spread mainly in south-eastern Asia, but few species can be found even in USA, Mexico and other regions including Europe. *S. chinensis* is not the original species in the Czech Republic and is currently grown in arboretums and as ornamental plant in gardens. However, Teodoridis (2005) confirmed the assignment of fossil seeds of *S. moravica* (MAI) GREGOR from Šafov and additionally seeds of the same species from the Cheb, Sokolov and Most Basins (Czech Republic) to the genus *Schisandra* MICH. At present, the possible introduction of this plant and its farm cultivation in the Czech Republic and in Europe is expected as a source of quality fruits for the production of food supplements. Therefore, it is important to deal with the possible impact on the local environment.

In this paper we describe the results of our ecotoxicological research with aqueous extract of *S. chinensis* fruits and its impact on the environment in Europe. Duckweed (*Lemna minor)*, which is used for standard ecotoxicological tests, was selected as the experimental organism (OECD, 2006). Phytotoxicity tests, where the duckweed is used as a test organism, usually assess growth parameters such as the number of plants, leaf area and biomass (OECD, 2006), or the content of photosynthetic pigments (Paczkowska et al., 2007). Growth responses are preceded by changes in biochemical and physiological processes at the cellular and tissue levels, which can be widely used as biomarkers to provide an early warning of potential hazards (Kummerova et al., 2016). The aim of this study was to describe and evaluate the growth and photosynthetic activity of duckweed exposed for 7 days to various concentrations of aqueous extract from *S. chinensis* fruits.

2. Materials and methods

2.1. S. chinensis plant materials and extraction

The ripe fruits of *S. chinensis* were obtained from a plant originating in Russia, but grown in the Czech Republic in the Vracov area. After harvesting, the fruits were separated from the stems and cleaned of impurities. They were then dried naturally in air, the average dry mass was determined to be 20% of the fresh weight.

A Soxhlet extractor was chosen to extract the active lignans from the *S. chinensis* fruit. Distilled water was used as an extractant in the Soxhlet extractor to mimic the natural environment in which *S. chinensis* fruits fall to the ground and water in rivers by natural fall and the lignans are released and leached to the water. The extracted amount of dry fruits was 15 g, the extraction volume was 300 mL and the extraction lasted 8 h.

High performance liquid chromatography HPLC (Agilent 1100 Series, Agilent Technologies, USA) was used to analyse the active ingredient content of the aqueous extract obtained. Aqueous extract from *S. chinensis* fruits (SCE) was analysed on the presence of the usual dominating compound schisandrin and its content was determined 45 mg/L.

2.2. Duckweed (Lemna minor) cultivation

In accordance with the ISO standard (ISO-20079, 2007), duckweed (L. *minor* L.) was grown in the laboratory in Steinberg nutrient solution under controlled conditions with temperature 22 ± 2 °C, relative air humidity 60%, photoperiod 12/12, irradiance 150 μmol/m^2.s provided by white fluorescent tubes (Osram, Germany). SCE was diluted with Steinberg solution to the concentration series of 0.9 mg/L, 0.45 mg/L, 0.09 mg/L, and 0.045 mg/L.

For each SCE concentration, 5 black plastic cups were used (diameter 5 cm, 40 mL of testing solution). Furthermore, one series of 5 cups of pure Steinberg solution was used as a control, and a series of 5 cups was used for undiluted SCE (45 mg/L). Duckweed plants were transferred to each cup (12 plants per cup).

2.3. Measured parameters

At the beginning of testing (day 0) and after 1, 3, 5 and 7 days of the cultivation the number of plants per each testing cup, their total leaf area size, and selected parameters of chlorophyll fluorescence of plants per cup were measured in each treatment. On the last day of the experiment (day 7) the plants were gently dried and weighed to assess differences in fresh weight.

2.4. Chlorophyll fluorescence measurements

After 10 min of plant dark adaptation, a set of chlorophyll fluorescence parameters (F_0 – basal chlorophyll fluorescence, QY max– potential yield of photochemical reactions in photosystem II (F_V/F_M), QY Lss – effective quantum yield of photosystem II (Φ_{II})) was determined from an analysis of slow kinetics supplemented with saturation pulses (recorded by a fluorescence imaging system FluorCam MF700, PSI, Czech Republic). This tool enabled to analyse whole surface area of a cup from each treatment in the only one step. Measuring setup and calculation of selected parameters were adopted from Kummerova et al. (2007). The ambient temperature during the measurement was of 21 ± 2 °C.

2.5. Statistics

The software STATISTICA (StatSoft Inc.®) was used for statistical evaluation of the obtained results. The results are considered to be the average of five repetitions of all assessed parameters. The significance of the differences of the average values between the treatments was evaluated by the one-way analysis of variance after verification of normality and homogeneity of data variance (ANOVA, $P < 0.05$).

3. Results

3.1. Leaf area, number and fresh weight of duckweed plants

In accordance with the ISO standard (ISO-20079, 2007), the following parameters were assessed in duckweed phytotoxicity tests: the number of plants and at least one other biometric variable, such as the total leaf area. Fig. 1A shows that the duckweed in the treatment 45 mg/L SCE had the same number of plants throughout the whole testing period. In the treatments 0.9 and 0.45 mg/L, the number of duckweed plants increased only minimally. However, in the concentrations of 0.09 and 0.045 mg/L representing highly diluted SCE, duckweed increased the number of plants during the entire testing period, similarly to the control. Total leaf area (Fig. 1B) correlates with the increase in the number of plants on each measurement day. Duckweed in the highest treatment 45 mg/L SCE did not show any increase in leaf area compared to the control series throughout the 7-day test. The duckweed treated with 0.9 and 0.45 mg/L SCE had a minimal increase in leaf area. The plants exposed to 0.09 and 0.045 mg/L SCE treatments were only minimally affected and their leaf area increased in a similar trend as the control series during the 7-day test (Fig. 1B).

The fresh weight of individual plants after seven days of cultivation (Fig. 1C) did not vary considerably in different SCE treatments. At 0.9 mg/L SCE treatment, the fresh weight per plant was the lowest as compared to control due to the small size of newly formed plants.

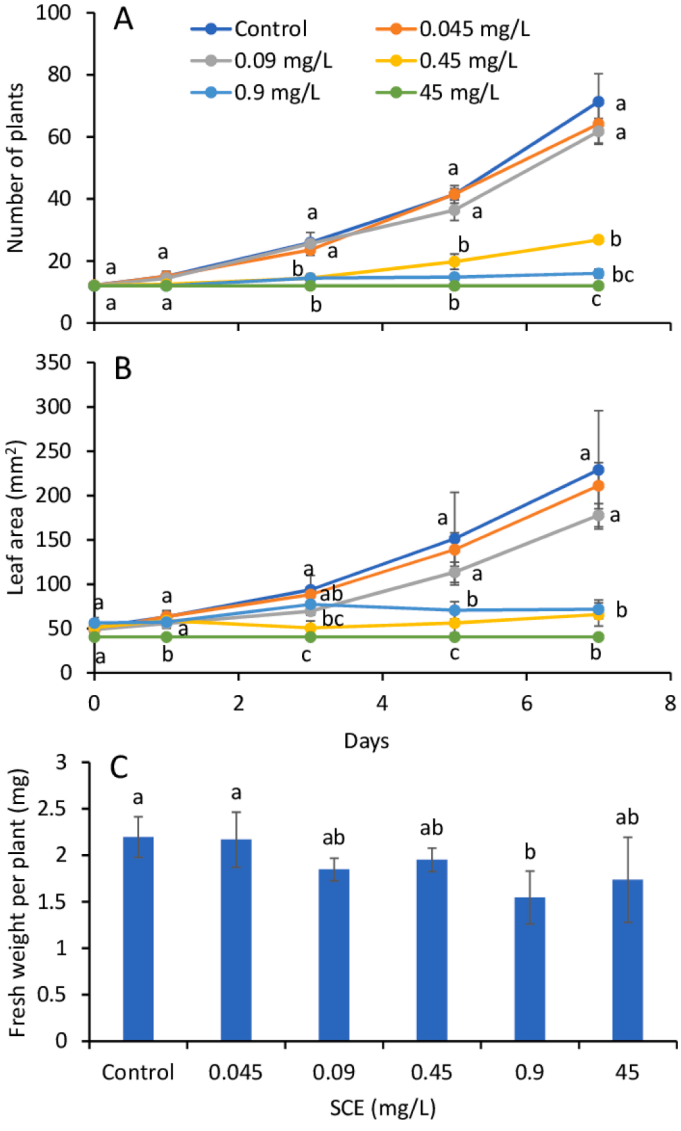

Fig. 1. Number of plants (A), their total leaf area (B; mm^2) and fresh weight per plant (C; mg) of duckweed cultivated in Steinberg medium without (control) or with SCE (from 0.045 to 45 mg/L) for seven days. Data points represent mean over five replicates, standard deviations are indicated by error bars. Different letters mark significant differences between treatments within the time point (ANOVA, Tukey HSD test, $P<0.05$).

3.2. Photosynthetic activity

3.2.1. Basal chlorophyll fluorescence - F_0

Stress-induced changes in photosynthetic apparatus usually result in the reversible inactivation of photosystem II (PSII) connected with an increase in basal chlorophyll fluorescence (F_0). The most considerable change in F_0 values was recorded in 45 mg/L SCE treatment (Fig. 2A). Immediately after application (up to one hour) the F_0 reached nearly two times higher value than the control and other SCE treatments. After one day of cultivation, the F_0 value of this treatment decreased under the values of other treatments and continued with a decrease in the

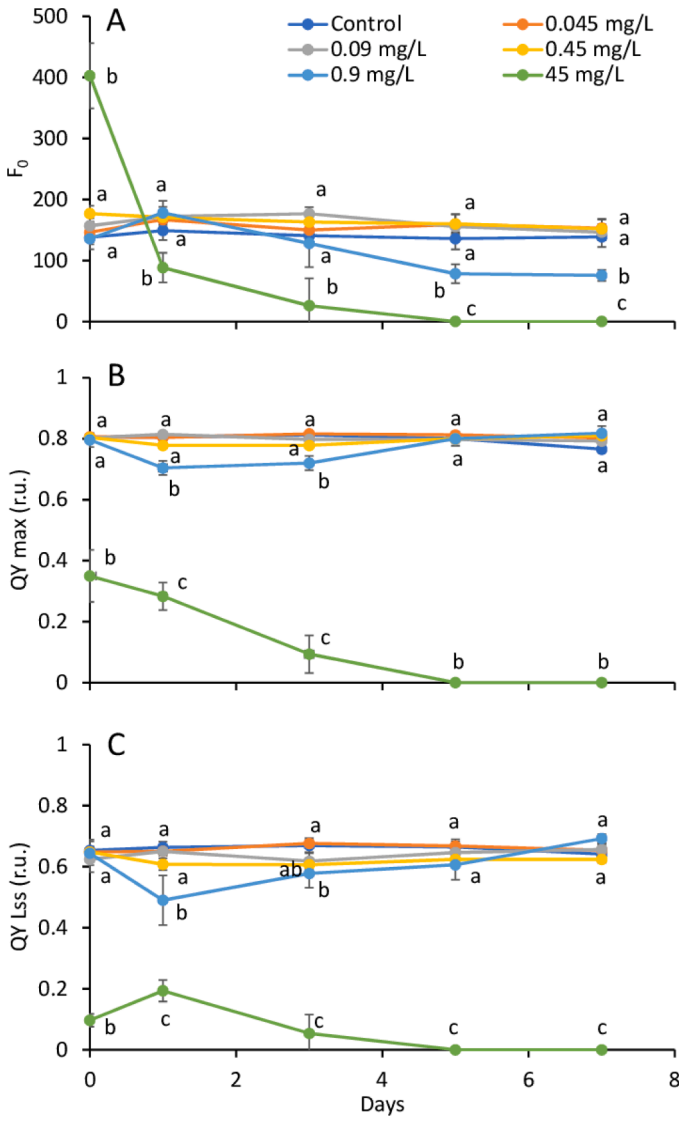

Fig. 2. Basal chlorophyll fluorescence (F_0; A), maximal quantum yield of photosystem II (QY max; B) and effective quantum yield of PSII photochemistry (QY Lss; C) recorded on duckweed cultivated in Steinberg medium without (control) or with SCE (from 0.045 to 45 mg/L) for seven days. Statistical evaluation as given in Fig. 1.

following days of cultivation. On day 5 it reached the value of 0 showing the photosynthetic activity of plants in this treatment was completely knocked out.

Plants treated with 0.9 mg/L SCE exhibited no significant changes in the F_0 value during the first three days of cultivation, but the decrease of the F_0 value on day 5 is probably connected with a low number of new plants and the small size of their fronds. The F_0 value in the control and other SCE treatments remained at similar values throughout the whole 7-day test, without any deviation which indicates that at these concentrations the duckweed plants were already able to adapt to the SCE occurrence.

3.2.2. *Potential yield of photochemical reactions in photosystem II - QY max*

The QY max value of plants exposed to 45 mg/L SCE was significantly lower immediately after SCE application in comparison with control and other SCE treatments (Fig. 2B). The QY max value during the whole 7-day test decreased and on day 5 it reached a value 0. This phenomenon indicates that the aqueous extract of *S. chinensis* at the concentration of 45 mg/L has a strong inhibitory effect on duckweed plants.

Duckweed plants growing in the 0.9 mg/L SCE showed lower QY max value on the first and third day compared to the control and other treatments. After that, the value recovered and on day 5 it reached a value similar to that of the control and other treatments.

3.2.3. *Effective quantum yield of photosystem II - QY Lss*

Similarly, as in QY max, the effective quantum yield QY Lss of duckweed plants exposed to 45 mg/L SCE showed significantly lower values than other treatments throughout the 7-day testing. From the fifth day, the QY Lss value dropped to 0 (Fig. 2C).

Duckweed plants treated with the 0.9 mg/L SCE exhibited a decrease in QY Lss on day 1 and an increase in QY Lss in the following days. On day 7, this treatment showed even the highest QY Lss value of all plants; however, the differences were insignificant. QY Lss in the other treatments showed similar values and did not vary significantly.

4. Discussion

Plants produce many biologically active substances that can be beneficial for human health and well-being. Nevertheless, a lot of these compounds can be allelopathic on other organisms in the ecosystems, including other plants. In the case of *Schisandra chinensis,* the extract of their fruits contains pharmacologically active lignans with schisandrin as the dominating compound. This study aimed to simulate natural conditions when the extraction of compounds contained in *S. chinensis* fruits occurs accidentally in a surface water body.

The ecotoxicological data on the effects of plant lignans in a water environment are scarce, and schisandrin was not evaluated at all. Lignans are presented as allelochemicals and potential alternative herbicides as described by Scavo et al. (2019a; 2019b) for compounds extracted from cardoon leaves. The extract caused an inhibition of seed germination rate by 31% and the root and shoot length nearly 90% in six weed species. The potential phytotoxic effect of allelochemicals can be connected with cytotoxic and anti-mitotic activity (Costas-Gil et al., 2018). In our case, SCE limited the growth of duckweed plants. The number of newly formed plants was considerably lowered by 75% in 0.45 mg/L and by up to 93% in 0.9 mg/L treatment. Similarly, the total leaf size was limited in these treatments. Nevertheless, the fresh weight of a single plant was lowered only in 0.9 mg/L treatment where only a few new plants with smaller size were recorded as compared to 0.45 mg/L. The undiluted SCE (45 mg/L) caused the death of duckweed plants. With the decreasing concentration, the inhibitory effect of SCE diminished.

Besides the growth parameters, the photosynthetic response of duckweed plants treated with SCE was assessed. Allelochemicals can potentially impair the performance of all processes of photosynthesis, including chlorophyll content, the thylakoid electron transport - light reaction, and carbon reduction cycle - dark reaction (Zhou and Yu, 2006) but the detailed mechanisms remain largely unclear. Photosynthesis represents a central anabolic pathway in plants, which results in the production of oxygen and energy-rich organic compounds necessary for growth. It is well known that photosynthetic parameters such as the content of photosynthetic pigments, efficiency of primary processes (Gonzalez-Naranjo et al., 2015), and carbon fixation are recognized as reliable indicators of stress in plants. An inhibition of photosynthetic processes is very often a key mechanism of toxic effects of many noxious substances. Chlorophyll fluorescence parameters (F_0, QY max, QY Lss, and others) might be used as indicators of stress affecting the photochemical pathway that utilizes the absorbed light energy (Krause and Weis, 1991; Mallakin et al., 2002). Duckweed leaves treated with 0.9 and 45 mg/L SCE bleached during the first two days of cultivation, showing a radical loss of chlorophylls (data not shown). This phenomenon can be connected with the inhibition of chlorophyll synthesis, stimulation of their degradation, or both.

Disturbance in primary photosynthetic processes is typically characterised as a change in chlorophyll ***a*** fluorescence and a reduction in quantum yields of photosystem II photochemistry. The most noticeable changes were recorded in duckweed plants exposed to 0.9 and 45 mg/L – an increase in F_0 signal followed by a drop and a decrease in quantum yield values. When comparing the highest treatments, SCE 45 mg/L caused the death of duckweed plants. But even though the considerable growth inhibition, SCE 0.9 mg/L limited the photosynthetic response only partially as can be seen on quantum yields recovery and this phenomenon indicates that the plants were able to cope with the effect of SCE.

Literature sources (Zhou and Yu, 2006) described that allelochemicals could affect photosystem II function, Hill reaction, electron transport and even the CO_2 assimilation, but the mechanism of action is still unclear. Nevertheless, as in green algae, due to the tight contact of duckweed plants with contaminated water, it can be supposed the direct effect of SCE on its cells and chloroplasts.

5. Conclusion

Schisandrin and other substances utilisable from *S. chinensis* fruits have a potentially positive effect on human health. But as plant allelochemicals, they can represent a threat to the environment in relatively low concentrations. The duckweed plant is not only a bioindicator but also an integral part of water biota as a primary producer in the food chain. The negative effect of the extract from *S. chinensis* fruits on its growth and photosynthesis under potentially environmentally-relevant concentrations shows its potential to harm the autotrophic part of the aquatic ecosystem.

CRediT authorship contribution statement

Jana Valíčková: Conceptualization, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Štěpán Zezulka:** Data curation, Formal analysis, Writing – review & editing. **Eliška Maršálková:** Conceptualization, Methodology, Supervision, Writing – review & editing. **Josef Kotlík:** Supervision, Writing – review & editing. **Blahoslav Maršálek:** Supervision, Writing – review & editing. **Radka Opatřilová:** Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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