ASSESSMENT OF POTENTIAL GENOTOXICITY OF THE PHLOROTANNIN PREPARATIONS DEMONSTRATING HIGH ANTIBIOTIC AND ANTIFUNGAL ACTIVITIES

Renata Islamova[1], Elizaveta Zamyatkina[1], Sofia Ilinykh[2], Elena Stepchenkova[1,3], Elena Tarakhovskaya[1,3]

[1] *Saint Petersburg State University, Saint Petersburg, Russia;*

[2] *Saint-Petersburg State Chemical and Pharmaceutical University, Saint Petersburg, Russia;*

[3] *Vavilov Institute of General Genetics, Saint Petersburg Branch, Saint Petersburg, Russia*

E-mail: renata.tag.isl@gmail.com

Introduction:
Among the bioactive metabolites produced by marine organism, phlorotannins currently attract special attention due to their high antibiotic, antifungal, and cytotoxic capacities. Phlorotannins are unique phenolic metabolites of brown algae – oligomers and polymers of phloroglucinol (1,3,5-trihydroxybenzene). Brown algae contain from 0.5 to 30% phlorotannins per dry weight. Different phlorotannin preparations are currently extensively studied from the perspective of their use in clinical pharmacy. However, these biologically active compounds are still not tested for their possible deleterious side effects, such as mutagenic activity.

Aim of study:
In this study we tested antibiotic, antifungal, and mutagenic activity of three phlorotannin preparations in order to assess their perspectives for applied relevance in medicine.

Materials and methods:
Phlorotannins were isolated from thalli of three brown algae (*Fucus serratus*, *Ectocarpus siliculosus*, and *Desmarestia aculeata*) (Figure 1). Antibacterial and antifungal effects were estimated as minimum inhibitory concentrations (MIC) of phlorotannin preparations against two model objects: Gram-negative bacteria *Escherichia coli* strain KA796 and ascomycete yeast *Saccharomyces cerevisiae* haploid strain LAN201-ura3Δ. Mutagenic activity of the extracts was assessed in the Ames test using three tester strains of *Salmonella typhimurium* (TA97, TA98, and TA100). Rat liver extract was used for the metabolic activation of the potential promutagens.

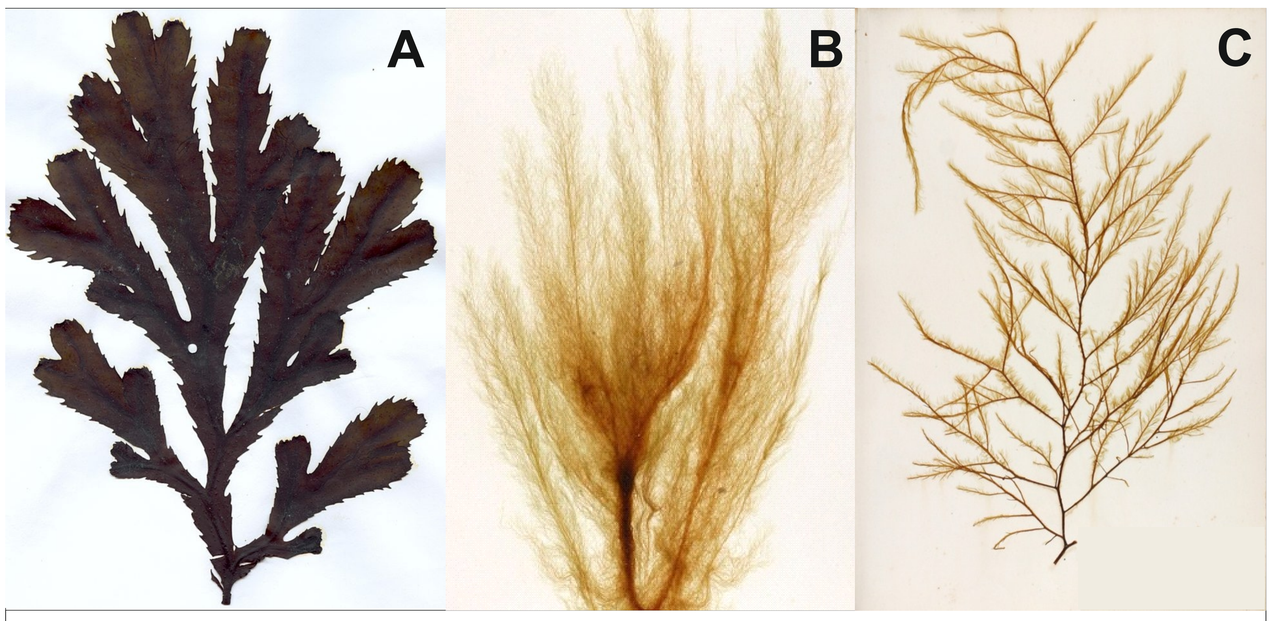

Figure 1. Brown algae used in the present study, as phlorotannin sources: A - *Fucus serratus*; B - *Ectocarpus siliculosus*; C - *Desmarestia aculeata*

Results and discussion:
All three tested phlorotannin preparations showed considerable antibacterial and antifungal activity. Phlorotannins of *D. aculeata* were the most toxic with MIC values 5 and 4 µg/ml for *E. coli* and *S. cerevisiae*, correspondingly. MIC values of *F. serratus* extracts were 20 µg/ml for *E. coli* and 10 µg/ml for *S. cerevisiae*. Phlorotannin preparations isolated from *E. siliculosus* showed MIC 25 µg/ml for both test-objects (Table 1). These MIC values are similar to those of widely used antibiotics and fungicides, such as tetracycline, ampicillin, fluconazole and amphotericin B.
Phlorotannins of *D. aculeata* showed no mutagenic effects in the both variants of the Ames test (with and without metabolic activation). Meanwhile the phlorotannin preparations of *E. siliculosus* and *F. serratus* demonstrated slight mutagenic activity (fold change 1.3-1.4, $P<0.05$) compared to the negative control after metabolic activation for TA100 strain (base pair substitutions), and preparations of *F. serratus* also showed considerable mutagenic activity (fold change 2.3, $P<0.05$) without metabolic activation for TA97 strain (frameshift mutations) (Table 1).

Algae (phlorothannin sourses)	MIC µg/ml		The Ames test	
	Escherihia coli	*Saccharomyces cerevisiae*	MA+	MA–
Fucus serratus	**20**	**10**	**TA 100**	**TA 97**
Ectocarpus siliculosus	**25**	**25**	**TA 100**	—
Desmarestia aculeata	**5**	**4**	—	—

Table 1. MIC values (µg/ml) of phlorothannins extracts isolated from brown algae against *E. coli* and *S. cerevisiae.* Tester strains of *S. typhimurium* showing enhanced mutation frequency after phlorotannins treatment in the Ames test with metabolic activation (MA+) and without metabolic activation (MA–).

Conclusions:
Phlorotannin preparations of *D. aculeata* featured the maximal antibacterial and antifungal activities and did not demonstrate significant genotoxicity in the Ames test. Thus, these preparations may be regarded as the most perspective for further use in clinical pharmacy.

This study was funded by the Russian Science Foundation (grant № 22-24-20039) and St. Petersburg Science Foundation (grant № 35/2022)

24th International Congress PHYTOPHARM 2023
Saint-Petersburg, Russia, 25-27 May, 2023

SPCPU
on service of science and health of the nation since1919

Saint-Petersburg State Chemical Pharmaceutical University

XXIV International Congress "Phytofarm 2023"

May 25 – 27, 2023
Saint Petersburg

www.spcpu.ru/phytopharm

List of poster presentations at «Phytopharm 2023»:

Poster number	Author	Poster title
1	Ivanova R. Kasyan I. Brinza J.	Degradation kinetics of a dye obtained from lakonos berries
2	Pavlova A. Khasanova S. Kudashkina N. Nizamutdinov T. Fazlyakhmetova S.	Qualitative determination of flavonoids in shoots of Crataegus pennsylvanica Ashe
3	Markov A. Agaev M. Basevich A.	Optimization of the technology for obtaining essential oil of oregano herb
4	Repkin N. Murza S. Voronin V. Kazina N.	Fatty acid profile of yellow and oriental mustard seeds after growing on a substrate with excess zinc
5	Bolgov A. Buzlam A. Gudkova A.	Adaptogens: problems of classification, safety and selection
6	Andreeva I. Miksina P.	Characteristics of the polysaccharide composition of chlorella biomass

7	Prikhodko V. Orlyakhina D. Petrova V. Semivelychenko E. Plisko G. Ivkin D. Wrapped S.	Procognitive effect of Cistus salviifolius L. in experimental steatohepatitis
8	Danilova A. Danilov L. Pivovarova N.	Statistical Optimization of Biomass Extraction Parameters of Scutellaria Baikal Cells to Increase the Yield of Polyphenolic Compounds
9	Dilenova E. Zhigzhitsapova S. Goncharova D. Emelyanova E. Tikhoev Z.	Essential oils of rare species of wormwood plants of the Buryat flora
10	Polonova A. Taraskin, W.	The content of coumarins and tannins in Halophyllum dauricum (L.) G. DON
11	Islamova R. Zamyatkina E.. Ilinykh S. Stepchenkova E. Tarakhovskaya E.	Evaluation of the potential genotoxicity of phlorotannins with high antibiotic and antifungal activity
12	Orazov A. Nadtochii L. Maksot A.	Comparative analysis of milk of various types of farm animals for the production of high-protein ice cream