

Ref. Your Submission JAPH-D-22-00144R1

Dear Dr. Meinita,

We have received the reports from our advisors on your manuscript, "A concise review of the bioactivity and pharmacological properties of the genus *Codium* (Bryopsidales, Chlorophyta)", which you submitted to Journal of Applied Phycology.

Based on the advice received, I feel that your manuscript could be reconsidered for publication should you be prepared to incorporate major revisions.

When preparing your revised manuscript, you are asked to carefully consider the reviewer comments which are attached.

FOR POSSIBLE REVIEWER ATTACHMENTS PLEASE VISIT THE WEBSITE

Your username is: *****

If you forgot your password, you can click the 'Send Login Details' link on the EM Login page at <https://www.editorialmanager.com/japh/>.

We look forward to receiving your revised manuscript within eight weeks.

Please make sure to submit your editable source files (i. e. Word, TeX).

With kind regards,
Michael A. Borowitzka, PhD
Editor in Chief

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Editor in Chief
Journal of Applied Phycology

Dear Editor:

We would like to re-submit the manuscript titled “**A concise review of the bioactivity and pharmacological properties of the genus *Codium* (Bryopsidales, Chlorophyta)**”. The manuscript ID is JAPH-D-22-00144

We thank you and the reviewers for your thoughtful suggestions and insights. The manuscript has benefited from these insightful suggestions. I look forward to working with you and the reviewers to move this manuscript closer to publication in the *Journal of Applied Phycology*.

The author's revisions are indicated and highlighted using red color font. The responses to all comments have been prepared and attached herewith/given below. Please check the attachment below.

Thank you for your consideration. Looking forward to hearing from you.

Sincerely yours,
Dr. Maria Dyah Nur Meinita

COMMENTS FOR THE AUTHOR:

Please read carefully all of the constructive comments made by three referees. According to their advice your article need major revision.

Reviewer #1: The manuscript entitled "A concise review of the bioactivity and pharmacological properties of the genus *Codium* (Bryopsidales, Chlorophyta)" addresses a relevant and appropriate topic for this journal.

The authors have prepared a concise review of the genus *Codium* and, of course, it would not be easy to include all species of this genus in a concise review. However, I think that the authors could have written less about *Codium fragile* (nearly half of the entire article) and thus would have had more space to write more about other species of the genus *Codium*, which are equally important.

Some corrections have to be introduced before being accepted for publication
Correction suggestions can be found in the "doc" attached to this revision.

Response to reviewer:

Thank you for your insightful suggestion. We have revised the manuscript thoroughly and added some other *Codium* species.

Reviewer #2: The reviewer had attached the details of comments. Please see the PDF copy.

Response to reviewer:

Thank you for your insightful suggestion. We have revised the manuscript thoroughly

Reviewer #3: The subject of this review is interesting, but the current manuscript should be greatly improved before publication.

First, the literature was not revised exhaustively. For example, the paper by Dembitsky et al. published in *Biochemical Systematics and Ecology*, Volume 31, Issue 10, October 2003, 1125-1145, was not considered, however it appears immediately when the words "*Codium*" and "Fatty acid" are used. This paper should have been revised to write about "Lipids" in page 6 lines 17-41. This means that the key words were not properly chosen.

Response to reviewer:

Thank you for your insightful comments and suggestion. We have added some references including Dembitsky et al. (2003) and also other references. We have revised the lipid section thoroughly (line 141-164).

Third, this manuscript is very poorly written with lots of repetitions, for example, in the abstract (I tried to correct the style a little, avoiding repetitions):

The genus *Codium* is one of the most important genera of marine green macroalgae. Its distribution of this genus is widespread worldwide. It comprises highly diverse species a high degree of diversity in species with different characteristics. This genus plays an important ecological role in marine ecosystems, as it is a primary producer of marine organisms. However, some species in the genus *Codium* are invasive species and may disturb the functioning of the ecosystem. Economically, *Codium* has promising potential as a source of diverse nutritional and pharmacological compounds.

Codium is edible, has a high nutrient value, and is rich in bioactive compounds. Hence, some species in the genus *Codium* have been consumed as food and used as herbal medicines in some Asian countries.

In recent decades, studies of the bioactivity and pharmacological properties of the genus several compounds obtained from *Codium* have attracted the attention of scientists.

This study aims to identify the gap in studies analyzing about *Codium* that have been conducted in the past three decades by collecting, compiling, and reviewing published research articles on its bioactivity and pharmacological properties of the genus *Codium*.

Compounds obtained from *Codium* have demonstrated significant biological activities, such as immunostimulatory, anticoagulant, anticancer, anti-inflammatory, antioxidant, antiviral, antibacterial, antifungal, antitumor, anti-angiogenic, osteoprotective, and anti-obesity activities. This review provides information that can be used as a future guideline for sustainably utilizing the genus *Codium*.

Response to reviewer:

Thank you for your help. We have revised the abstract based on your suggestion.

The title should also be improved. "A concise review of the bioactivity and pharmacological properties of the genus *Codium* (Bryopsidales, Chlorophyta)"
For both the title and abstract, as well as the whole Manuscript: Is it *Codium* in general, or certain compounds from this seaweed that have biological properties? In the latter case, I think a better title could be:
"A concise review about the bioactivity and pharmacological properties of compounds extracted/obtained from species of genus *Codium* (Bryopsidales, Chlorophyta)"

Response to reviewer:

Thank you for your suggestion. We decided to use the first title.

Fourth, a review has a style different to that of a paper. It should not have Methods and Results and Discussion.

Response to reviewer:

We have removed the methods, result and discussion

Some further comments:

Page 5. Regarding sulfated polysaccharides, the paragraph is chaotic, the literature is not exhaustive at all, and the nomenclature is wrong. Fig 2. What is the meaning of R?

Response to reviewer:

Thank you for your suggestion. We have revised the sulphated polysaccharide part and corrected the nomenclature. In Figure 2, R refers to carbon compounds, while O refers to oxygen.

Page 7. Flavonoids, coumarins, tocopherols, and nitrogen-containing compounds, including alkaloids, chlorophyll derivatives, amino acids, and amines are not proteins, so, please correct the title.

Response to reviewer:

Thank you for your correction. We have revised and moved it to bioactivity section.

Lines 31-35. In which sense are these lectins unique?

Response to reviewer:

Two new lectins from the green alga *Codium isthmocladum* (CiL-1 and CiL-2) were isolated. The uniqueness of these lectins are

- a. CiL-2 was identified by amino acid sequencing. The CiL-2 N-terminal sequence 1FQIGQGSMGNKTITGVS17 showed no similarity to any known protein.
- b. CiL-1 showed no similarity with any lectin, but moderate similarity was found between CiL-1 and hypothetical proteins from several aquatic pathogenic microorganisms.

Line 44. What kind of mineral can reach 40% of the dry weight of seaweed?

Response to reviewer:

Thank you for the correction. We did a mistake. Ruperez et al. (2002) found that ash content of some macroalgae ranged from 21.1–39.3%. We have revised the sentence.

Michael A. Borowitzka
Editor in Chief
Journal of Applied Phycology

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Thank you for your consideration. Looking forward to hearing from you.

Maria Dyah Nur Meinita

Comments to the author (if any):

Reviewer #1: line 1057 - Figure 3. Structure of tocots found in *Codium* species (Note "*Codium*" in italics)

Author’s response: Thank you for the correction. We have revised it

Reviewer #2: Based from the revisions made by the authors, this reviewer has no further comments and recommends for its possible publication.

Author’s response: Thank you for reviewing and giving insightful comment, correction and suggestion.

Editors comments: Figure 4 - the figures lack tick marks on the axes. Figure 4b could also be deleted as it repeats information shown in Fig 6. There is also something wrong with the figure legend for Fig 6 [there is no a and b in this figure nor any data on year. The figure is also hard to interpret as we do not know how many citations each circle represents - they are all the same size, but this is probably misleading.

Author’s response: Thank you for the correction. We have revised Figure 4 based on your suggestion.

In the references, please do not use et al, but list all authors.

Author's response: Thank you for the correction. We have revised the references. However, we are still not sure how to write the authors of the reference below. If we include all of the DAISIE partners, it would be too many authors

Vilà M, Basnou C, Pyšek P, Josefsson M, Genovesi P, Gollasch S, Nentwig W, Olenin S, Roques A, Roy D, Hulme PE, DAISIE partners (2010) How well do we understand the impacts of alien species on ecosystem services? A pan-European, cross-taxa assessment. *Front Ecol Environ* 8:135–144. <https://doi.org/10.1890/080083>