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Florine Wang
Special Issue Editor
Marine Drugs

Dear Editor:

We would like to re-submit the manuscript titled "**Fucoesterol of Marine Macroalgae: Bioactivity, Safety and Toxicity on Organism**". The manuscript ID is **marinedrugs-1396074**

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 *Marine drugs*.

The author's revisions are indicated with track changes 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,

Maria Dyah Nur Meinita

E-mail: maria.meinita@unsoed.ac.id (M.D.N.M)

A. RESPONSE TO THE COMMENTS OF REVIEWER#1

Reviewer 1

Comments and Suggestions for Authors

The manuscript (review) entitled "Fucosterol of Marine Macroalgae: Bioactivity, Safety and Toxicity on Organism" addresses a current and relevant topic about one of the main compounds produced by brown algae and about its numerous bioactivities. This manuscript is well written and well structured. However, the authors should make the corrections suggested below, especially in terms of algae taxonomy.

Response: We thank to the reviewer for the appreciation, comments and suggestions on our manuscript. Thank you for the detailed correction on algae taxonomy. We have carefully addressed all the concerns raised by the reviewer, and made the necessary changes following reviewer's comment, correction and suggestions. Please note that we revised the manuscript using track changes and the revision are written in red font.

Corrections needed:

line 47 - reported to be dominant in *Stephanocystis hakodatensis* (formerly *Cytoseira hakodatensis*) ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 52 - and *Sargassum* (formerly *Hizikia*) are widely ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 93 - Among the 16 marine algae, *Sargassum fusiforme* (formerly *Hizikia fusiformis*) has ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 96 - ... of *S. fusiforme* have ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 95/96 - ... bioactivity of *S. fusiforme* have ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 99 - ... of fucosterol in *S. fusiforme* has ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 101 - ... *Ecklonia cava* subsp. *stolonifera* (formerly *Ecklonia stolonifera*) is ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 107 - ... from *Ecklonia cava* subsp. *stolonifera* were ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

Figure 3 - Note: Correct the names of the algae listed below
Anthophyscus longifolius (formerly *Sargassum longifolium*)
Padina sanctae-crucis
Silvetia siliquosa (formerly *Pelvetia siliquosa*)
Ecklonia cava subsp. *stolonifera* (formerly *Ecklonia stolonifera*)
Sargassum aquifolium (formerly *Sargassum binderi*)
Eisenia bicyclis
Sargassum fusiforme (formerly *Hizikia fusiformis*)

Response: We thank the reviewer for correcting the Figure 3. We have revised it thoroughly

line 138 - ... *Ecklonia cava* subsp. *stolonifera* ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 145 - ... *Sargassum fusiforme* ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 150/151 - ... These findings illustrate that fucosterol extracts from *Eisenia bicyclis*, *Ecklonia cava* subsp. *stolonifera*, *Sargassum fusiforme* and *Silvetia siliquosa* have ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 163 - ... *Ecklonia cava* subsp. *stolonifera* ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 164 - ... *Ecklonia cava* subsp. *stolonifera* ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 169 - ... *Sargassum fusiforme*-derived fucosterol ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 172 - ... *Sargassum fusiforme* ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 182 - reported by Park et al. [35] *in vitro* and *in vivo*; fucosterol from *Sargassum fusiforme* can ... (Note: "*in vitro*" and "*in vivo*" in italicas)

Response: We thank the reviewer for correcting these words. We have revised it.

line 189 - *Padina sanctae-crucis* ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 191 - ..., fucosterol from *Sargassum fusiforme* ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 220 - *Sargassum aquifolium* (formerly *Sargassum binderi*) inhibited ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 229 - ... *Sargassum fusiforme* ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 232 - ... *Sargassum fusiforme* ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 235 - ... *Sargassum fusiforme* ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 251 - ... *Ecklonia cava* subsp. *stolonifera* ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 252/258 - ... *Ecklonia cava* subsp. *stolonifera* ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 274 - ... *Sargassum fusiforme* ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 279 - *Caenorhabditis elegans* (Nematoda).

Response: We thank the reviewer for correcting the Nematoda species name. We have revised it.

line 287/288 - ... *Fusarium culmorum* (Fungi, Ascomycota).

Response: We thank the reviewer for correcting the Fungi species name. We have revised it

line 290 - ... *Pyricularia oryzae* (Fungi, Ascomycota) mycelia... (Note: the word "mycelia" is not in italics)

Response: We thank the reviewer for correcting the Fungi species name. We have revised it

Table 1 - *Turbinaria conoides* (not "Conoides") 6x

Response: We thank the reviewer for correcting Table 1. We have revised it thoroughly.

line 320 - ..., only genera *Turbinaria* and *Sargassum* have been studied (the word "and" is not in italics)

Response: We thank the reviewer for the correction. We have revised it

Table 2 - *Sargassum aquifolium* (formerly *Sargassum binderi*)
Sargassum fusiforme (formerly *Hizikia fusiformis*)
Ecklonia cava subsp. *stolonifera* (formerly *Ecklonia stolonifera*)
Padina sanctae-crucis

Response: We thank the reviewer for correcting Table 2. We have revised it thoroughly

line 341 - ... with fucosterol of *Sargassum aquifolium* at a ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 343 - ... *Sargassum aquifolium*

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 345 - ... *Sargassum fusiforme* ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 365 - ... *Ecklonia cava* subsp. *stolonifera* ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 368 - ... *Ecklonia cava* subsp. *stolonifera* ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 393 - ... *Ecklonia cava* subsp. *stolonifera* ...

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

Table 3 - *Ecklonia cava* subsp. *stolonifera*

Sargassum fusiforme

Sargassum fusiforme

Sargassum fusiforme

Ecklonia cava* subsp. *stolonifera

Response: We thank the reviewer for correcting Table 3. We have revised it thoroughly

line 403 - *Sargassum fusiforme*

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 411/412 - *Sargassum fusiforme*

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 414 - *Sargassum fusiforme*

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 418 - *Ecklonia cava* subsp. *stolonifera*

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 473/474 - *Hizikia fusiformis*/*Sargassum fusiforme* and *Ecklonia cava* subsp. *stolonifera* are the two species with the highest

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

line 478 - *in vitro*, *in vivo*, ... (in italics, please)

Response: We thank the reviewer for the correction. We have revised it.

line 540 - *Pelvetia siliquosa* (in italics, please)

Response: We thank the reviewer for correcting the macroalgae species name according to the newest taxonomy. We have revised it.

B. RESPONSE TO THE COMMENTS OF REVIEWER#2

Reviewer 2

This review is comprehensively described recent reports of fucosterol on the physiological functionality and safety. I think this is a well-organized report for promoting the use of fucosterol derived from marine products. However, there are some places where the units may not be accurate. Please check the cited references.

Response: We thank to the reviewer for the appreciation, comments and suggestions on our manuscript. Thank you for the accurate correction on the units that we used in the manuscript. We have carefully addressed all the concerns raised by the reviewer, and made the necessary changes following reviewer's comment, correction and suggestions. Please note that we revised the manuscript using track changes and the revision are written in red font.

- Probably μ is missing. Please confirm.

Page1 line43; 312.0 g/g, 378.1 g/g

Response: We thank the Reviewer for accurate correction. Yes, the μ is missing. It should be 312.0 $\mu\text{g/g}$, 378.1 $\mu\text{g/g}$. We have revised them

Page6 line196; 7.8 g/mL,

Response: Yes, the μ is missing. It should be 7.8 $\mu\text{g/mL}$. We have revised it.

line198; 100 g/mL,

Response: Yes, the μ is missing. It should be 100 $\mu\text{g/mL}$. We have revised it.

line199; 100 g/ml, 1000 g/mL

Response: Yes, the μ is missing. It should be 1000 $\mu\text{g/mL}$. We have revised it.

Page7 line203; 20 g/mL

Response: Yes, the μ is missing. It should be 20 $\mu\text{g/mL}$. We have revised it.

Page8 line254; 2.51 M

Response: Yes, the μ is missing. It should be 2.51 μM . We have revised it.

line263; 100 M,

Response: Yes, the μ is missing. It should be 100 μM . We have revised it.

line294; 2 to 16 g/mL

Response: Yes, the μ is missing. It should be 2 to 16 $\mu\text{g/mL}$. We have revised it.

Page9 line310; 8 to 16 mg/mL

Response: Yes, the μ is missing. It should be 8 to 16 $\mu\text{g/mL}$. We have revised it.

line312; 8 mg/mL

Response: Yes, the μ is missing. It should be 8 $\mu\text{g/mL}$. We have revised it.

Page 11 line339; 100 g/mL etc. (There are many points in doubt in the section 2.4.)

Response: Yes, the μ are missing. We have revised them section 2.4 thoroughly.

• **Other points**

Page9 Table 1; concentration unit mg/m \rightarrow mg/mL

Response: Thank you for the accurate correction. We have checked and found that the concentration unit must be in $\mu\text{g/mL}$, not mg/mL. Hence we have corrected the unit in Table 1 thoroughly.

Page6 line 174; *Undaria pinnatifida* \rightarrow Italic type

Response: Thank you for the accurate correction. We have revised it