#### Decision on submission to Heliyon (External) Inbox x

Heliyon <em@editorialmanager.com> to me ▼ Thu, Jul 29, 2021, 4:38 PM 🔥 🕤 🚦

🖶 🖸

Manuscript Number: HELIYON-D-21-03815R3

Title: Optimization of Betaine-Sorbitol Natural Deep Eutectic Solvent-Based Ultrasound-Assisted Extraction and Pancreatic Lipase Inhibitory Activity of Chlorogenic Acid and Caffeine Content from Robusta Green Coffee Beans

Journal: Heliyon

Dear Dr. Ahmad,

Thank you for submitting your manuscript to Heliyon.

I am pleased to inform you that your manuscript has been accepted for publication.

Your accepted manuscript will now be transferred to our production department. We will create a proof which you will be asked to check, and you will also be asked to complete a number of online forms required for publication. If we need additional information from you during the production process, we will contact you directly.

We appreciate and value your contribution to Heliyon. We regularly invite authors of recently published manuscript to participate in the peer review process. If you were not already part of the journal's reviewer pool, you have now been added to it. We look forward to your continued participation in our journal, and we hope you will consider us again for future submissions.

Kind regards, Harry Patrick McGee, MSc. Editorial Assistant Heliyon

Date: To: From:	Jul 29, 2021 "Islamudin Ahmad" islamudinahmad@farmasi.unmul.ac.id "Helivon" info@helivon.com
Subject:	Decision on submission to Heliyon
Manuscript Number: HELIYON-D-21-03815R3 Title: Optimization of Betaine-Sorbitol Natural Deep Eutectic Solvent-Based Ultrasound-Assisted Extraction and Pancreatic Lipase Inhibitory Activity of Chlorogenic Acid and Caffeine Content from Robusta Green Coffee Beans Journal: Heliyon	
Dear Dr. Ahmad,	
Thank you for submitting your manuscript to Heliyon.	
I am pleased to inform you that your manuscript has been accepted for publication.	
Your accepted manuscript will now be transferred to our production department. We will create a proof which you will be asked to check, and you will also be asked to complete a number of online forms required for publication. If we need additional information from you during the production process, we will contact you directly.	
We apprecia review proce participation	te and value your contribution to Heliyon. We regularly invite authors of recently published manuscript to participate in the peer iss. If you were not already part of the journal's reviewer pool, you have now been added to it. We look forward to your continued in our journal, and we hope you will consider us again for future submissions.
Kind regards Harry Patricl Editorial Ass Heliyon	;, McGee, MSc. istant
Embargo Embargos ar embargo an soon as poss	re not automatically set for papers published in Heliyon. Papers appear online a few days after acceptance. To request a media d/or publication on a specific date to assist an institutional press release, please reach out to the Heliyon team (info@heliyon.com) as sible and we will do our best to accommodate your request.
More inform	ation and support
FAQ: When a https://servi	and how will I receive the proofs of my article? ce.elsevier.com/app/answers/detail/a_id/6007/p/10592/supporthub/publishing/related/
You will find	information relevant for you as an author on Elsevier's Author Hub: https://www.elsevier.com/authors
FAQ: How ca https://servi For further a Here you ca interactive to	in I reset a forgotten password? ce.elsevier.com/app/answers/detail/a_id/28452/supporthub/publishing/ ssistance, please visit our customer service site: https://service.elsevier.com/app/home/supporthub/publishing/ n search for solutions on a range of topics, find answers to frequently asked questions, and learn more about Editorial Manager via itorials. You can also talk 24/7 to our customer support team by phone and 24/7 by live chat and email
In compliand URL: https:/	e with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following /www.editorialmanager.com/heliyon/login.asp?a=r). Please contact the publication office if you have any questions.

# A point-by-point reply to Reviewer Comments:

## **Reviewer #1:**

#### **Comments:**

## Dear author,

I carefully read the manusctipt HELIYON-D-21-02618, and it fits with the aim of the journal.

I suggest same changes to improve the quality of the work. My main concern is that the methodology part is not well prepared and the discussion of data is difficult. In particular, please add how you perform the extraction with conventional reflux, (solvent, time of extraction and ratio coffee and solvent). Please add more information about of nades production, as example the amount of material that you use, time of heating. You should describe the experimental past in that way that other researchers can repeat you experiment. Furthermore, please specify how long you sonicate samples and add reference to table 1. "filtred liquid portion " how much material do you filtered? How you dilute the obtaine nades? Which solvent do you use? Please add in table 2 the data that refers to reflux extraction for comparison. Please add a quantification of caffeine and chlorogenic acid of coffee material to consider the efficacy of extraction compared to the total content of this two metabolites in the starting material.

## Author's Replay:

Thank you for your suggestions and comment to improve the quality of our research articles.

As suggested, we have made improvements to the parts in question and we have marked them in red writing.

The extraction/sonication time was carried out in a variety of conditions, which is one of the variable factors in this study.

Table 2, we didn't change it because the table was the result of the RSM experimental design, but we added a narrative about the comparison between reflux results and NADES-UAE in the results section.

While some of the other comments we have revised and was included in our revision.

# **Comments:**

Please specify how you prepare the samples for in vitro activity assay. I suppose the you do dilution of nades and pure compound. But if you perform a dilution you made a solution with betaine, sorbitol, caffeine, chlorogenic acid and the other metabolites extracted from coffee, but not NADES. I suggest to calculate the concentration of each compound in the tested solution. So in my opinion, I think that you should express this concept, empathize that probably there are other compound in the extract that can affect the in vitro results. Relatively to the in silico results I suggest to add sorbitol and betaine capability to bind lipase enzyme.

# Author's Replay:

Basically, this study does not test pure compounds, we only focus on testing extracts obtained both conventionally and non-conventionally. The pure compounds CGA and caffeine are only used as a standard as well as a comparison and it can be used as a reference that both standards have activity against pancreatic lipase according to the studies that have been reported.

We assume that we already know the levels of CGA and caffeine compounds in each of the extracts obtained which have been calculated using HPLC analysis. in this study we only focus on these two compounds. related to the presence of other compounds, it will be more interesting if investigated more deeply in further research.

As suggested, we have made improvements to the parts in question and we have marked them in red writing.

## **Comments:**

In the discussion part, some paragraphs are not appropriated and I suggest to move in the introduction part. Considering the result obtained from RSM, some sentences are too much detailed and some they are reported in tables. Please empathize the main results, how this type of elaboration can be useful. "increasing of Nades: sample comparison...etc etc.. "please improve the discussion. Is any research paper using RSM for investigate nades extraction? Please discuss in the appropriate section.

## Author's Replay:

We have made revisions according to the suggestions by reviewers which we marked with red highlights. in our manuscript we make it separately between the results and discussion. in addition, we have also added literature related to previous research results that support our findings.

# **Comments:**

I suggest to improve the clarity of the manuscript and change the conclusion part. I don't agree with your conclusion sentences. Data that you report are prelimary results of the activity on lipase of some compound. We are far away from obesity therapy. I think that your speculation is not appropriated. I attach PDF file with others comments. In this version, manuscript is not suitable for publication.

# Author's Replay:

We have made revisions according to the suggestions by reviewers which we marked with red highlights.

**Reviewer #2:** 

Methods: In general, the explanation of methods employed in this work have to be completed.

Manuscript Number: HELIYON-D-21-02618

Title: Optimization Simultaneous Extraction of Chlorogenic Acid and Caffeine from Robusta Green Coffee by Betaine-Sorbitol Based NADES and Its Inhibitory Activity on Pancreatic Lipase Authors: Islamudin Ahmad, M.Si., Apt; Adisya Miftah Syakfanaya; Azminah Azminah; Fadlina Chany Saputri; Abdul Mun'im

Overall, the paper is well-written, well-structured and richly illustrated. Additionally, this study represents an interesting contribution to the field. However, the manuscript should be revised. To the authors I have the following questions:

- Section 2.1.: "The sample used and preparation was similar to ..." - to give more details.

- Section 2.2.: "The conventional reflux and Natural Deep Eutectic Solvent-based Ultrasonic-Assisted Extraction (NADES-UAE) process followed our previous study..." - to give mucho more details (extraction conditions...)

- Why was "betaine - sorbitol" NADES employed, and no other? Please, to clarify.

- Section 2.3.: - please, to complete showing the whole HPLC conditions employed.

- Section 2.3. should appear as subsection at the end of materials and methods section, being included in a analytical methods section together with others methods employed.

- Table 1: why these factors were chosen? The temperature, for example, it is also a very important factor in this context.

- Section 3.1.: include in 2.2 Extraction Process section.

- Section 3.2.: to remove.

- Section 3.3.2: the information contained in this section should be included in the introduction section, as section 3 is for results and discussion. In this section (3.3.2.) should be explained the results obtained (shown on Table 2), regarding the variables studied (Y1, Y2), without considering the whole design yet, as this is explained in other section (3.4.).

- Section 3.4.: to include the equations quadratic for each variable (Y1, Y2), and to explain its behavior depend on the factors studied.

- Conclusion section: please, to enhance including the most important results achieved in the work, between others.

# Author's Replay:

Thank you for your suggestion and comment to improve our manuscript quality. Basically we totally agree with reviewers, here is our response:

- Section 2.1 to 2.3 have been changed
- "betaine sorbitol" NADES was employed
- In fact, in our research as a whole, we have not only selected betaine-sorbitol as the composition of NADES, most of which we have published in various journals. However, in this manuscript we focus on betaine-sorbitol, given that the verification results of the optimum conditions were obtained for this composition. so that the optimum conditions can be used sustainably, especially to obtain extracts rich in CGA and caffeine based on NADES. This result is supported by several studies that have been previously reported, especially research conducted by Duan et al., 2016). In addition, the NADES-based extract that we obtained is more stable in various pharmaceutical dosage forms compared to other compositions (we have not published it), where betaine-sorbitol can simultaneously function as a pharmaceutical exipient.
- Table 1: These factors were selected based on our previous studies (Syakfanaya et al., 2019).

We do not make temperature a factor, because we are still using ordinary sonicators, where the temperature and strength are automatically and constant are set on the tool. we can only set the extraction time.

Overall, we can still get the optimum conditions even though we only use a few factors as independent variables in this study. However, if we use a different tool, of course, it must be optimized further.

- Section 3.1 to 3.4 have been changed and revised
- Conclusion has been revised