DOKUMEN KORESPONDENSI

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Judul	**:**	**Formulation, Optimization, and In Vitro Studies of Roasted Agung Banana var. Semeru Peel Effervescent Antidepressant Tablet**
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Penulis Pertama	**:**	Lannie Hadisoewignyo
Penulis Korespondensi	**:**	Lannie Hadisoewignyo

Tahapan dan Lampiran

No.	Tahapan	Waktu
1.	**Submitted to the journal (Journal of Pharmaceutical Innovation)**	**06-03-2025**
2.	**First revision: Accepted with major revision**	**04-04-2025**
3.	**Revised version submitted**	**14-04-2025**
4.	**Second revision**	**28-06-2025**
5.	**Revised version submitted**	**03-07-2025**
6.	**Paper Accepted**	**07-07-2025**
7.	**Galley Proof**	**09-07-2025**
8.	**Journal publishing agreement**	**10-07-2025**

1. **Submitted to the journal (Food research) - Mar 6, 2025**

Journal of Pharmaceutical Innovation - Receipt of Manuscript 'Formulation, Optimization, and...' External Inbox ×

Journal of Pharmaceutical Innovation <JedJoseph.Adel@springernature.com> Thu, Mar 6, 10:18 PM

to me

Ref: Submission ID 5d98429c-57d7-4337-b4b8-1ba9dca7598d

Dear Dr Hadisoewignyo,

Thank you for submitting your manuscript to Journal of Pharmaceutical Innovation.

Your manuscript is now at our initial Technical Check stage, where we look for adherence to the journal's submission guidelines, including any relevant editorial and publishing policies. If there are any points that need to be addressed prior to progressing we will send you a detailed email. Otherwise, your manuscript will proceed into peer review.

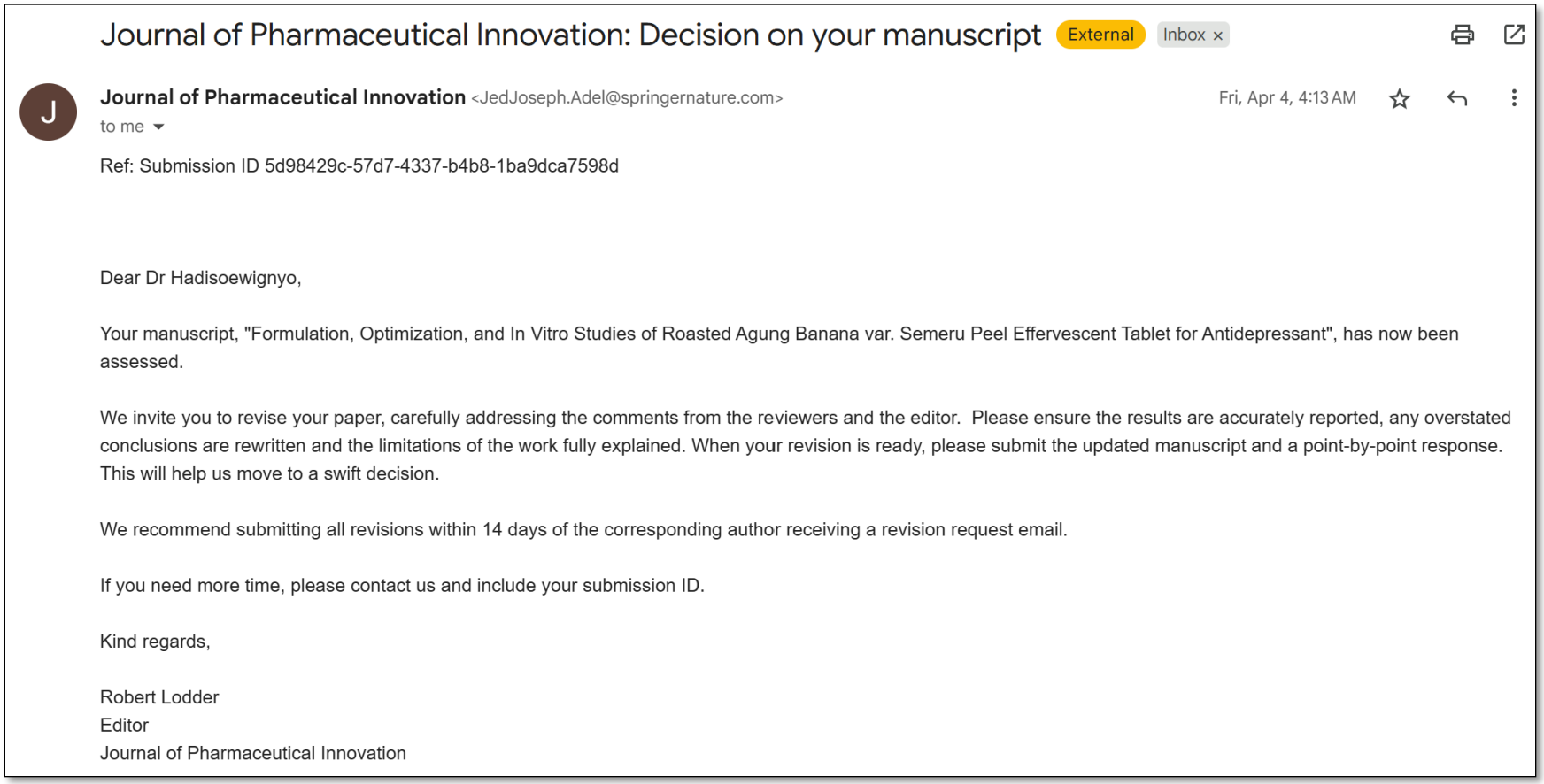
You can check on the status of your submission at any time by using the link below and logging in with the account you created for this submission:

https://submission.springernature.com/submission-details/5d98429c-57d7-4337-b4b8-1ba9dca7598d?utm_source=submissions&utm_medium=email&utm_campaign=confirmation-email&journal_id=12247

Kind regards,

Editorial Assistant
Journal of Pharmaceutical Innovation

2. **First revision: Apr 4, 2025**



Journal of Pharmaceutical Innovation: Decision on your manuscript External Inbox ×

Journal of Pharmaceutical Innovation <JedJoseph.Adel@springernature.com> Fri, Apr 4, 4:13 AM

to me

Ref: Submission ID 5d98429c-57d7-4337-b4b8-1ba9dca7598d

Dear Dr Hadisoewignyo,

Your manuscript, "Formulation, Optimization, and In Vitro Studies of Roasted Agung Banana var. Semeru Peel Effervescent Tablet for Antidepressant", has now been assessed.

We invite you to revise your paper, carefully addressing the comments from the reviewers and the editor. Please ensure the results are accurately reported, any overstated conclusions are rewritten and the limitations of the work fully explained. When your revision is ready, please submit the updated manuscript and a point-by-point response. This will help us move to a swift decision.

We recommend submitting all revisions within 14 days of the corresponding author receiving a revision request email.

If you need more time, please contact us and include your submission ID.

Kind regards,

Robert Lodder
Editor
Journal of Pharmaceutical Innovation

Reviewer Comments:

Reviewer 1

- Title seems incomplete for antidepressant ??
- The claim in the purpose of study (hot melt extrusion simplifies the manufacturing of process of tablet) is not true
- Author's claim about the use of HME for this study is very confusing at the start of this manuscript. At one place it states that HME simplifies the manufacturing of process of tablet, whereas on other places it is written that tablet's effervescent component is made using a melt extrusion while table by direct compression. In introduction the use of HME was introduced as a granule formation method.
- The research does not clearly state the purpose of using HME or banana peel extract. Is that to achieve tablet with optimum (physical) properties or for pharmacological (antidepressant activity). The background poorly supports the purpose of this study.
- Therefore I reject this manuscript.

Attachments:

• https://reviewer-feedback.springernature.com/download/attachment/eb1968eb-fbe0-455a-9445-1b97192b3b9f

Reviewer 2

Attachments:

• https://reviewer-feedback.springernature.com/download/attachment/11507a51-d344-4c05-8249-b3a553e10908
• https://reviewer-feedback.springernature.com/download/attachment/33920153-3704-488f-ae3c-c89d3e934af8

Reviewer 3

The article was having good scientific data and well written.

The following few queries should be raised

1. The roasting temperature and time of banana peels were not mentioned in the manuscript as Morin is the active constituents. Is it stable at 200 0C temp?
2. The author mentioned the hot melt extrusion for the preparation of material ready for the tablet. Then which hot melt extrusion equipment was used.
3. The phytochemical constituents were determining by TLC. The Figure 4 doesn't show the distinguished presence of component. Few plates are not showing Rf value.
4. Author prepared 1000mg tablet, but it will be difficult compression and to sallow.

Attachments:

• https://reviewer-feedback.springernature.com/download/attachment/e7b76943-1920-4661-a4c8-5a028ea50e29

Reviewer 4

Review Comments

The manuscript refers to hot melt extrusion (HME) as a processing technology used in the pharmaceutical, polymer, and food industries. However, there is no detailed explanation or demonstration of this process within the manuscript. The authors should revise the manuscript and ensure that the described process aligns with the actual methodology used for tablet preparation. If HME was not employed, the terminology should be corrected accordingly.

The manuscript lacks details regarding the optimum formulation. The authors should provide a comprehensive description of the formula, including the composition and specific quantities of each component.

The rationale for developing an effervescent tablet is unclear. The authors should clearly justify the need for such a formulation, particularly considering that RBPE alone has demonstrated superior results compared to the developed optimum formulation.

A more detailed and well-reasoned discussion is necessary to enhance the overall quality of the manuscript. A thorough explanation of the results, their significance, and any supporting evidence should be included to strengthen the manuscript's scientific contribution.

Conclusion

The manuscript requires substantial revisions before it can be considered for publication. The authors should address the concerns outlined above to improve the clarity, accuracy, and scientific rigor of the study.

Reviewer 1

- Title seems incomplete for antidepressant ??
- The claim in the purpose of study (hot melt extrusion simplifies the manufacturing of process of tablet) is not true
- Author's claim about the use of HME for this study is very confusing at the start of this manuscript. At one place it states that HME simplifies the manufacturing of process of tablet, whereas on other places it is written that tablet's effervescent component is made using a melt extrusion while table by direct compression. In introduction the use of HME was introduced as a granule formation method.
- The research does not clearly state the purpose of using HME or banana peel extract. Is that to achieve tablet with optimum (physical) properties or for pharmacological (antidepressant activity). The background poorly supports the purpose of this study.
- Therefore I reject this manuscript.

Reviewer 2

The article is about the optimization of effervescent tablet formulas that contain Agung banana peel extract. The goal is mainly to determine the best formulation that showed the optimal antidepressant effect on tested animals.

The test methods were well described, and the materials used were presented properly.

However, there are points that need to be addressed:

Part 1:

Although the article is well presented, I suggest to the author to submit the manuscript for an English proofreading to enhance its clarity.

Part 2: The study is based on the factorial design 2^2. The effervescent component used was 50% (-1) – 55% (+1), and the crospovidone concentration used was 8% (-1) – 10% (+1).

Comment: The factor values range considered in this study is too small. The nonlinearity effect of the factor variation on the response can be missed with this range. If possible, the author might consider increasing the value range of the factors and adding a central point (central composite design).

Part 3:

The article's purpose and novelty are not highlighted through the literature review:

What is the novelty of this work? Why is this work needed? And is there any work done elsewhere before to optimize the RBPE formula? Was the Agung banana peel extract used in effervescent tablets before?

I suggest the author enrich the literature review and give more insight about the problem that is being solved.

Part 3:

Line 93: Please clarify to which formula the MgSt was added.

Rephrase or correct the highlighted phrases/words in red in the manuscript at lines 42, 53, 86, 109, 111, 122, 124, 140, 147, and 152.

Line 144: Replace the phrase with 'A cylinder container with 50 cm in height and 20 cm in diameter is used during this test.'

Line 150: A tail suspension box with 55x15x11.5 dimensions and a 12 cm tape is used during this test.

Line 159: Table 2 content must be described and explained at the beginning. Then the results can be interpreted and discussed.

Line 164: The author says, "This is due to Aerosil and maltodextrin used as a dry extract filler with an extract-to-filler ratio of 30:70. Aerosil contains high amounts of silica and silicates, which have a melting point of 1600ºC [14-15].

Question : How does this ratio affect the total RBPE ash content? An explication is needed.

Line 165: The author says, "This parameter does not have a significant impact on the tablet manufacturing process."

Question: Which parameter? Give some clarifications.

Line 168: The author says, "Figure 1 shows the extract contains an alkaloid, which is indicated by red nodes with Rf scores of 0.4 and 0.71 (1A)."

Suggestion: Before the results discussion, please explain the figure so the reader can also follow the reasoning.

Line 179: The table must be described before the results interpretation and discussion. Please adopt this method for all figures and tables. What does FO stand for? Is it O (for original) or 0?

Line 189: The text format changes. Please revise the format.

Line 212: "Crospovidone has a small size that increases cohesion between particles, which increases tablet friability." Please reformulate.

Suggestion: Crospovidone particles increase the cohesion between

How does the small size of Crospovidone increase the cohesion between particles?

Lines 186–248: In this section, the statistical analysis results are presented, but no actual discussion of the results is presented. Since the statistical results only show the effects, the author might consider discussing the cause of the factors effects.

Line 197: Is it kp or kPa?

Line 200: The author says, "Crospovidone has a small size, and the right amount of fines is needed to fill the space between particles of the tablet mass. Therefore, the resulting tablet becomes more compact and increases the tablet hardness [20]."

Suggestion: The small-sized particles increase the total surface area of the powder bed, which increases the interaction forces between the particles. Hence, the tablet becomes more compact, and its hardness increases. DOI: 10.1016/j.ijpharm.2007.01.035 ; https://doi.org/10.1016/j.jddst.2019.05.049

Line 212: The author says, "Crospovidone has a small size that increases cohesion between particles, which increases tablet friability [21]." Please explain this statement.

Comment: The increase of cohesion between particles usually decreases its friability because the tablet becomes harder.

Line 227: The author says, "As the crospovidone and effervescent component increase, the tablet dissolving time will increase."

Question: Why this observation?

Line 247: "and theoretical test. Therefore, the polynomial equation is valid."

What theoretical test?

Line 273: "Based on the test, both the RBPE group and the tablet optimum formula group give a significant decrease in immobility time results compared to the control."

Why is this result obtained? How can you explain it?

Line 281: "The pathophysiological mechanism of stress induced by TST and FST caused the different immobility time results between TST and FST [23]."

How? Explain.

Line 294: "the optimum formula."

Describe the optimum formula.

Reviewer 3

The article was having good scientific data and well written

The following few queries should be raised

1. The roasting temperature and time of banana peels were not mentioned in the manuscript as Morin is the active constituents. Is it stable at 200 ^{0}C temp?
2. The author mentioned the hot melt extrusion for the preparation of material ready for the tablet. Then which hot melt extrusion equipment was used.
3. The phytochemical constituents were determining by TLC. The Figure 4 doesn't show the distinguished presence of component. Few plates are not showing Rf value.
4. Author prepared 1000mg tablet, but it will be difficult compression and to sallow.

3. Revised version submitted - Apr 14, 2025

Reply to comments

Reviewer 1

1. Title seems incomplete for antidepressant ??

   Reply: This study aims to check the antidepressant effect of RBPE tablet optimum formula

2. The claim in the purpose of study (hot melt extrusion simplifies the manufacturing of process of tablet) is not true

   Reply: We have revised the claim in the manuscript

   (As an approved concept, in this study, RBPE effervescent tablets were manufactured with the direct compression method, where the effervescent component is made by hot melt extrusion (HME) method, and the formula was optimized. Furthermore, the optimum formula was made, and an antidepressant test was carried out to see the antidepressant effect of the extract after being formulated into tablets.)

   The purpose of this research is to find the optimum formula for effervescent tablets made from roasted banana peel extract, where the effervescent component is made using the HME method. The optimum formula obtained was tested for antidepressant effects.

3. Author's claim about the use of HME for this study is very confusing at the start of this manuscript. At one place it states that HME simplifies the manufacturing of process of tablet, whereas on other places it is written that tablet's effervescent component is made using a melt extrusion while table by direct compression. In introduction the use of HME was introduced as a granule formation method.

   Reply: We have revised this statement.

4. The research does not clearly state the purpose of using HME or banana peel extract. Is that to achieve tablet with optimum (physical) properties or for pharmacological (antidepressant activity). The background poorly supports the purpose of this study.

   Reply: HME is only used to make effervescent components consisting of citric acid, tartaric acid, and sodium bicarbonate. After the effervescent component granules are formed through the HME method, they are mixed with extract and other materials. Furthermore, tablets are manufactured using the direct compression method.

5. Therefore I reject this manuscript.

Reviewer 2

Part 1:

1. The article is about the optimization of effervescent tablet formulas that contain Agung banana peel extract. The goal is mainly to determine the best formulation that showed the optimal antidepressant effect on tested animals. The test methods were well described, and the materials used were presented properly. However, there are points that need to be addressed:

   Part 1: Although the article is well presented, I suggest to the author to submit the manuscript for an English proofreading to enhance its clarity.

   Reply: We will pay more attention for improving the English

   Part 2: The study is based on the factorial design 2^2. The effervescent component used was 50% (-1) – 55% (+1), and the crospovidone concentration used was 8% (-1) – 10% (+1). Comment: The factor values range considered in this study is too small. The nonlinearity effect of the factor variation on the response can be missed with this range. If possible, the author might consider increasing the value range of the factors and adding a central point (central composite design).

   Reply: Previously, we have conducted orientation research with a higher range of effervescent component and crospovidone concentration. But apparently the physical quality of tablet doesn't meet the specification. When the effervescent component is under 50% (40%), the dissolving time of the tablets won't meet the specification. On the other hand, the effervescent component over 55% (60%) will made the tablet friability higher than 1%. If the concentration of crospovidone is below than 6%, the dissolving time of the tablets won't meet the specification. Therefore, we used the concentration range of 50-55 for effervescent component and 8-10% for crospovidone.

   Part 3: The article's purpose and novelty are not highlighted through the literature review: What is the novelty of this work? Why is this work needed? And is there any work done elsewhere before to optimize the RBPE formula? Was the Agung banana peel extract used in effervescent tablets before? I suggest the author enrich the literature review and give more insight about the problem that is being solved.

   Reply: The previous studies have tested the antidepressant effects of banana peel extract, and the results show a significant antidepressant effect at a dose of 400 mg/kg BW in mice. Therefore, we do this research to see if the antidepressant effect of the peel extract is still present after it made into tablets. As far as we know, the banana peel extract has not used in effervescent tablet before.

1. Line 93: Please clarify to which formula the MgSt was added.

   Reply: We have clarified in which mixture the MgSt was added.

2. Rephrase or correct the highlighted phrases/words in red in the manuscript at lines 42, 53, 86, 109, 111, 122, 124, 140, 147, and 152.

   Reply: We have rephrased the words

3. Line 144: Replace the phrase with 'A cylinder container with 50 cm in height and 20 cm in diameter is used during this test.

   Reply: We have revised it

4. Line 150: A tail suspension box with 55x15x11.5 dimensions and a 12 cm tape is used during this test.

   Reply: We have revised it

5. Line 159: Table 2 content must be described and explained at the beginning. Then the results can be interpreted and discussed.

   Reply: We have revised it

6. Line 164: The author says, "This is due to Aerosil and maltodextrin used as a dry extract filler with an extract-to-filler ratio of 30:70. Aerosil contains high amounts of silica and silicates, which have a melting point of 1600°C [14-15]. Question : How does this ratio affect the total RBPE ash content? An explication is needed.

   Reply: The dry extract is made by RBPE concentrated extract that are dried with aerosil and maltodextrin mixture. Therefore, the filler affects the RBPE ash content

7. Line 165: The author says, "This parameter does not have a significant impact on the tablet manufacturing process." Question: Which parameter? Give some clarifications.

Reply: This parameter refers to total ash content. We have revised the sentences into 'Although the total ash content isn't meet the specification, it does not have a significant impact on the tablet manufacturing process.'

8. Line 168: The author says, "Figure 1 shows the extract contains an alkaloid, which is indicated by red nodes with Rf scores of 0.4 and 0.71 (1A)." Suggestion: Before the results discussion, please explain the figure so the reader can also follow the reasoning.

   Reply: Thank you, we have added an explain for the figure

9. Line 179: The table must be described before the results interpretation and discussion. Please adopt this method for all figures and tables. What does FO stand for? Is it O (for original) or 0?

   Reply: We have revised it. The O stand for optimum, we have added the change FO to OF and added abbreviation for OF (Optimum Formula)

10. Line 189: The text format changes. Please revise the format.

    Reply: We have revised it

11. Line 212: "Crospovidone has a small size that increases cohesion between particles, which increases tablet friability." Please reformulate.

    Suggestion: Crospovidone particles increase the cohesion between. How does the small size of Crospovidone increase the cohesion between particles?

    Reply: We have reformulated it

12. Lines 186–248: In this section, the statistical analysis results are presented, but no actual discussion of the results is presented. Since the statistical results only show the effects, the author might consider discussing the cause of the factors effects.

    Reply: The reasoning is written in the manuscript with the green highlight

13. Line 197: Is it kp or kPa?

    Reply: It is kp. kp is an international unit of tablet hardness

14. Line 200: The author says, "Crospovidone has a small size, and the right amount of fines is needed to fill the space between particles of the tablet mass. Therefore, the resulting tablet becomes more compact and increases the tablet hardness [20]."

    Suggestion: The small-sized particles increase the total surface area of the powder bed, which increases the interaction forces between the particles. Hence, the tablet becomesmore compact, and its hardness increases. DOI: 10.1016/j.ijpharm.2007.01.035 ; https://doi.org/10.1016/j.jddst.2019.05.049

    Reply: Thank you, I'd like to say sorry before because there is a mistake in interpretating the result. Based on the polynomial equation, the crospovidone is decreasing the tablet hardness. But it is non significantly decreased it.

15. Line 212: The author says, "Crospovidone has a small size that increases cohesion between particles, which increases tablet friability [21]." Please explain this statement. Comment: The increase of cohesion between particles usually decreases its friability because the tablet becomes harder.

    Reply: Thank you for the correction, there are a mistake in writing the manuscript, the polynomial equation shows that crospovidone decreases the tablet friability.

16. Line 227: The author says, "As the crospovidone and effervescent component increase, the tablet dissolving time will increase." Question: Why this observation?

    Reply:

17. Line 247: "and theoretical test. Therefore, the polynomial equation is valid." What theoretical test?

    Reply: Theoretical test refers to tablet physical quality test conducted after the optimum formula is made

18. Line 273: "Based on the test, both the RBPE group and the tablet optimum formula group give a significant decrease in immobility time results compared to the control." Why is this result obtained? How can you explain it?

    Reply: Both RBPE group and the tablet optimum formula could decrease the immobility time is due to its antidepressant effect.

19. Line 281: "The pathophysiological mechanism of stress induced by TST and FST caused the different immobility time results between TST and FST [23]." How? Explain.

    Reply: The treatment of each method gives a different stress effect in animals. Therefore, the immobility time between TST and FST is different. TST induced a higher stress effect than FST because the inhibits neurotransmitter is Serotonin and Dopamin. On the other hand, the FST only inhibits serotonin.

20. Line 294: "the optimum formula." Describe the optimum formula.

    Reply: We have described the optimum formula

Reviewer 3

The article was having good scientific data and well written. The following few queries should be raised

1. The roasting temperature and time of banana peels were not mentioned in the manuscript as Morin is the active constituents. Is it stable at 200 ^{0}C temp?

   Reply: The roasting temperature of 200 ^{0}C causes maillard reaction, and before the reaction is formed, no morin is found in the banana peel extract. Maillard reaction can form new compounds that have antioxidant activity.

2. The author mentioned the hot melt extrusion for the preparation of material ready for the tablet. Then which hot melt extrusion equipment was used.

   Reply: The equipment used for the hot melt extrusion for effervescent component materials is only oven and sieve.

   HME is only used to make effervescent components consisting of citric acid, tartaric acid, and sodium bicarbonate. After the effervescent component granules are formed through the HME method, they are mixed with extract and other materials. Furthermore, tablets are manufactured using the direct compression method.

3. The phytochemical constituents were determining by TLC. The Figure 4 doesn't show the distinguished presence of component. Few plates are not showing Rf value.

   Reply: We have revised the manusctipt

4. Author prepared 1000mg tablet, but it will be difficult compression and to sallow.

Reply: The compression of this research is still have a good compressibility. On the other hand, the tablet is prepared as effervescent tablet that are diluted in water before used.

Reviewer 4

1. Review Comments The manuscript refers to hot melt extrusion (HME) as a processing technology used in the pharmaceutical, polymer, and food industries. However, there is no detailed explanation or demonstration of this process within the manuscript. The authors should revise the manuscript and ensure that the described process aligns with the actual methodology used for tablet preparation. If HME was not employed, the terminology should be corrected accordingly.
   The manuscript lacks details regarding the optimum formulation. The authors should provide a comprehensive description of the formula, including the composition and specific quantities of each component.
   The rationale for developing an effervescent tablet is unclear. The authors should clearly justify the need for such a formulation, particularly considering that RBPE alone has demonstrated superior results compared to the developed optimum formulation.

   Reply:

   HME is only used to make effervescent components consisting of citric acid, tartaric acid, and sodium bicarbonate. After the effervescent component granules are formed through the HME method, they are mixed with extract and other materials. Furthermore, tablets are manufactured using the direct compression method.

   The extract dosage for used in human is a high. Therefore, the authors develop an effervescent tablet because effervescent tablet is not to be swallowed directly but diluted in water first. Even if RBPE is a superior, we can't directly eat the extract alone.

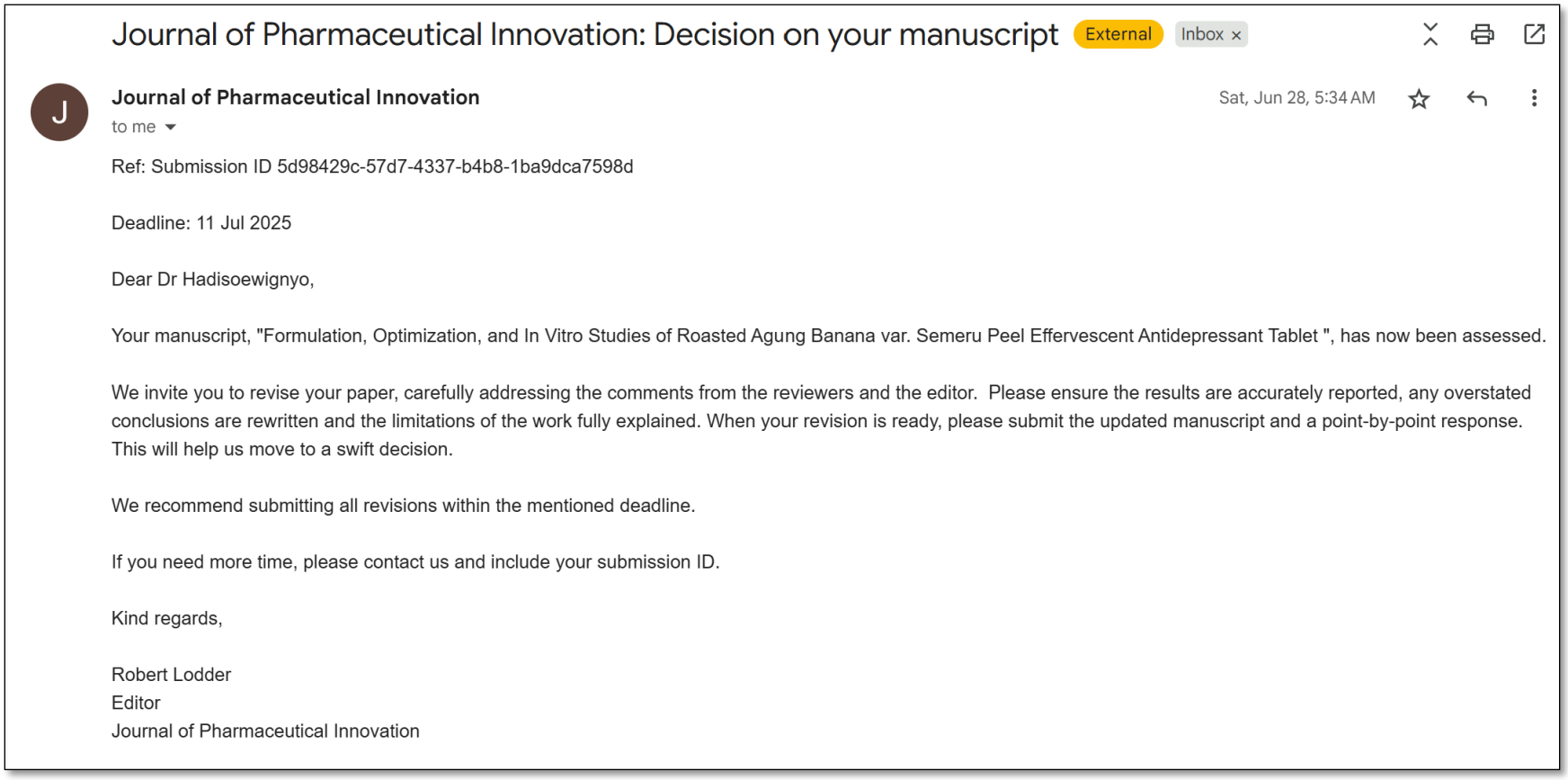
2. A more detailed and well-reasoned discussion is necessary to enhance the overall quality of the manuscript. A thorough explanation of the results, their significance, and any supporting evidence should be included to strengthen the manuscript's scientific contribution.

   Reply: We have added more detail discussion in the manuscript

3. Conclusion
   The manuscript requires substantial revisions before it can be considered for publication. The authors should address the concerns outlined above to improve the clarity, accuracy, and scientific rigor of the study.

   Reply: thank you for your suggestion

4. **Second revision: Accepted with major revision - Jun 28, 2025**



Journal of Pharmaceutical Innovation: Decision on your manuscript External Inbox ×

Journal of Pharmaceutical Innovation Sat, Jun 28, 5:34 AM

to me

Ref: Submission ID 5d98429c-57d7-4337-b4b8-1ba9dca7598d

Deadline: 11 Jul 2025

Dear Dr Hadisoewignyo,

Your manuscript, "Formulation, Optimization, and In Vitro Studies of Roasted Agung Banana var. Semeru Peel Effervescent Antidepressant Tablet ", has now been assessed.

We invite you to revise your paper, carefully addressing the comments from the reviewers and the editor. Please ensure the results are accurately reported, any overstated conclusions are rewritten and the limitations of the work fully explained. When your revision is ready, please submit the updated manuscript and a point-by-point response. This will help us move to a swift decision.

We recommend submitting all revisions within the mentioned deadline.

If you need more time, please contact us and include your submission ID.

Kind regards,

Robert Lodder
Editor
Journal of Pharmaceutical Innovation

Reviewer Comments:

Reviewer 2

All my comments are in the review file!

Attachments:

- https://reviewer-feedback.springernature.com/download/attachment/499c6b8b-c20c-4356-91a5-bca36dcc5b08
- https://reviewer-feedback.springernature.com/download/attachment/3969642f-905c-4b4b-bbf0-424d78616527

The article is about the optimization of effervescent tablet formulas that contain Agung banana peel extract. The goal is mainly to determine the best formulation that showed the optimal antidepressant effect on tested animals. The test methods were well described, and the materials used were presented properly.

The author has improved the clarity of the article, and the results are more organized. However, there are points that need to be addressed:

Introduction: The author needs to develop a state of art about the subject. At this point, we don't know if this work was done before or if the author is the only one that is doing it.

The author only shows the method used in the current article in the introduction. The state of art is neglected. This must be addressed.

From the introduction, the lecturer must have a notion about what the novelty of this work is? Why is this work needed? And is there any work done elsewhere before to optimize the RBPE formula? Was the Agung banana peel extract used in effervescent tablets before?

Which is not the case in the present article.

General observation: The study is based on the factorial design 2^2. The effervescent component used was 50% (-1) – 55% (+1), and the crospovidone concentration used was 8% (-1) – 10% (+1). The factors values ranges considered in this study are too small. These results must be taken cautiously.

The author must include in the conclusion that wider range of the factors values must be considered in further study.

Line 99: rounds

Line 154: Author should present the results in this manner.

Table 2 dispalys the RBPE standardization and specification results. The obtained RBPE ash content was found to be equal to 19.27±0.13%, which does not meet the required specification (total ash content must be < 10%)…

Line 157: Sentence suggestion

Although the total ash content does not meet the specification, it has no effect on the tablet manufacturing process.

Line 158: Delete "the result of RBPE standardization can be seen in table 2".

Line 162 to 166: Change (1A) to (Figure 1A)… Apply this change to the rest also.

Line 166: Suggestion to the author.

Based on this result, it can be concluded that the RBPE used in this study does not contain a tannin compound, which would be displayed by a (precise a specific colour)

Line 176: Change "All the formulas pass the specification for moisture content" with "Table 3 shows the RBPE tablet mass physical quality test results. The measured moisture content of all the formula (from F1 to OF) meets the required specification."

Line 184: It meant to be "which" or "with "? after randomly.

Line 186: Present the table that contains the results before discussing the results. I suggest the author to do this in the rest of the entire article.

The author must explain how the weight uniformity between tablets ensures the active ingredient (API) specification?

A tablet contains API and excipients, so the tablet weight is a total mass. Unless the API mass represents more than 50% of the tablet total mass, which is not the case in this article, the author might explain the declaration.

Line 188: Replace "FvalueF1 2.393" by "$F1_{Fvalue} = 2.393$" and "F(0.05)(2,57) 3.160" by "$F_{0.05;2,57} = 3.160$". Apply this change in the article.

Line 200: Phrase suggestion to the author

The contour plot shows that the variation of the effervescent component and the crospovidone concentration will always increase the tablet hardness.

Line 184 – 226: For a scientific purpose, how do the crospovidone and the effervescent component interact? The response to this question can bring other insight to the obtained results. This is a facultative question.

Line 205: Small-size particles such as Crospovidone, increase the total surface area of the powder particle blend, which allows more surface interaction and therefore increases the tablet cohesion. This can explain the decrease of the tablet friability. https://doi.org/10.1016/j.ijpharm.2021.120424

Line 226: The author meant "decrease"?

5. Revised version submitted - Jul 3, 2025

Reply to commeny

Reviewer: 1

Comments to the Author

Tab S1. The authors should carefully check the separation rationale in class of compounds. e.g. xanthones cannot be indicated as a flavonoid but a xanthonoid.

Alkaloids: Although they may have chemical characteristics compatible with the definition of alkaloid, amino acids, peptides, nucleosides, amino sugars and antibiotics are not considered alkaloids. (IUPAC - alkaloids (A00220), goldbook.iupac.org.)

"7-Hydroxy-1-methoxy-2-methoxyxanthone" this form to report the chemical name is unusual. the two methoxy substituents should be indicated by the prefix "di": 7-Hydroxy-1,2-dimethoxyxanthone

"Coumarin &

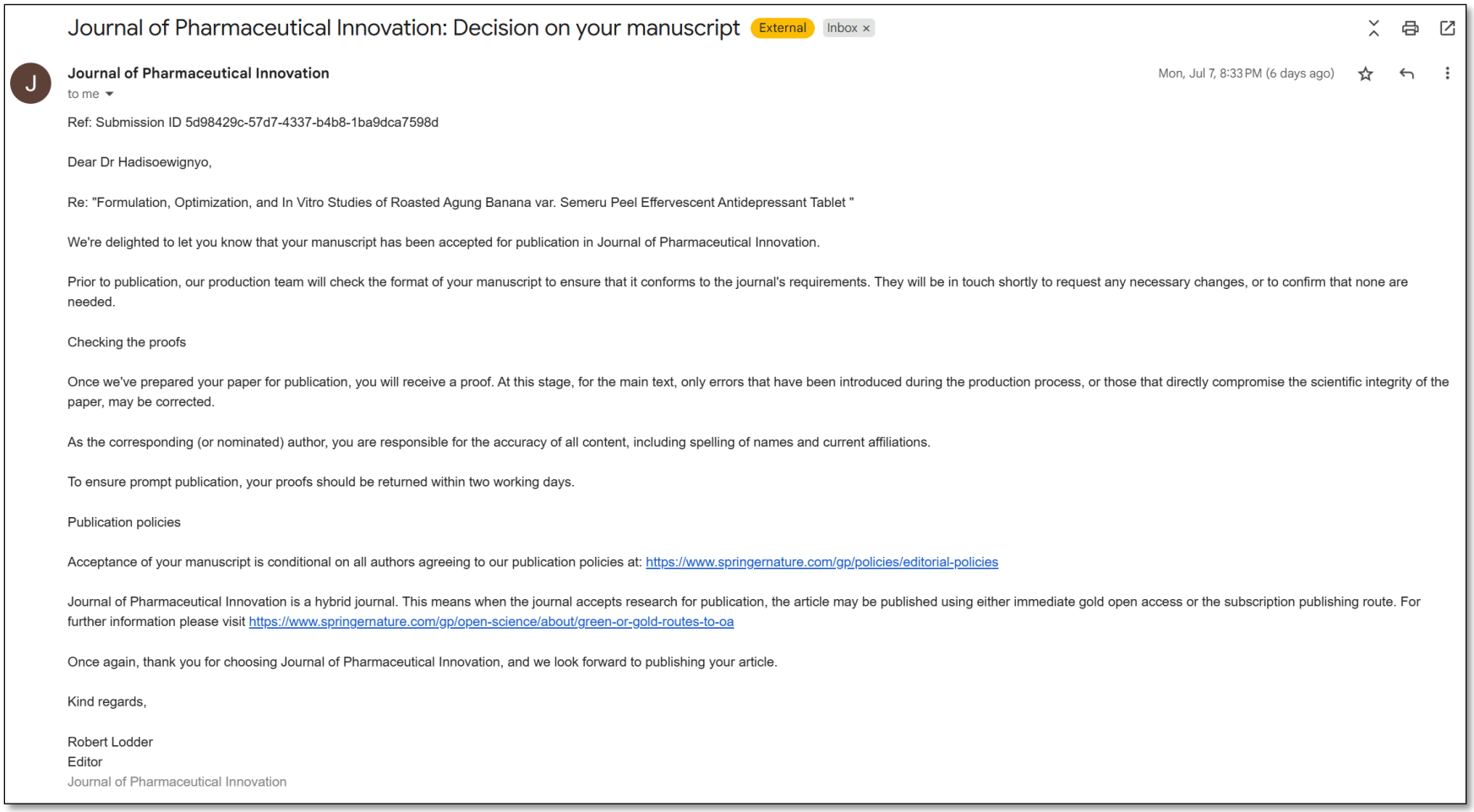
Liganoid"

Check the spelling. Maybe it should be "Lignanoid"

"2,4,5-Trihydeoxybenzaldehyde" check the spelling.

Reply : Thank you for your comment. We have revised all of it.

6. Paper accepted - Jul 7, 2025



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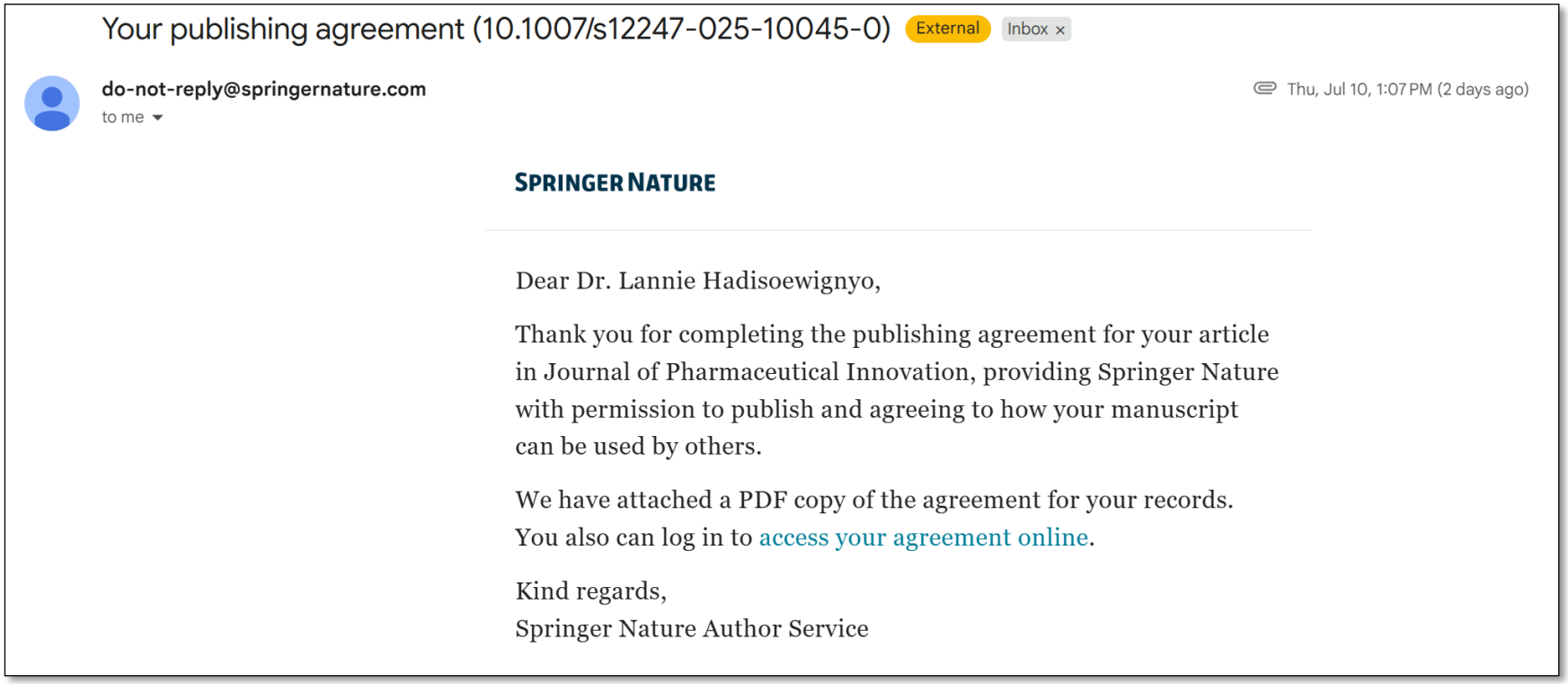

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