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**Subject:** Author New Submission Acknowledgement letter: RPS_209_21
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**CC:**
**Recieved:** Saturday, November 27, 2021

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Dear Dr Dr. Epy Luqman,
Research in Pharmaceutical Sciences has received your manuscript entitled "Potency of Kebar grass (Biophytum petersianum Klotzsch) extract to increase motor reflex and memory in mice offspring (Mus musculus) from lactating mothers exposed to carbofuran " for consideration for publication. The reference number for this manuscript is "RPS_209_21". Kindly quote this in future correspondences related to this manuscript.
The manuscript is being reviewed for possible publication with the understanding that it is being submitted to ONE journal at a time and has NOT been published, simultaneously submitted, or already accepted for publication elsewhere either as a whole or in a part.
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We thank you for submitting your valuable work to the Research in Pharmaceutical Sciences.
Yours sincerely,
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**From:** editor@rpsjournal.net
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**Recieved:** Friday, December 3, 2021

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Dear Dr Luqman,
Research in Pharmaceutical Sciences has received your manuscript entitled Potency of Kebar grass (Biophytum petersianum Klotzsch) extract to increase motor reflex and memory in mice offspring (Mus musculus) from lactating mothers exposed to carbofuran for consideration for publication.
However, the manuscript is not submitted in accordance with journal instructions and requires further technical modifications. Detailed remarks on this are available on the manuscript management site https://review.jow.medknow.com/rps.
You are requested to make the necessary changes in the manuscript in 7 days. Kindly log in as Author.
We thank you for submitting your valuable research work to the Research in Pharmaceutical Sciences.
Yours sincerely,
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**Recieved:** Wednesday, December 8, 2021

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Dear Dr  Luqman,

Research in Pharmaceutical Sciences has received your revised manuscript “RPS_209_21” entitled "Potency of Kebar grass (Biophytum petersianum Klotzsch) extract to increase motor reflex and memory in mice offspring (Mus musculus) from lactating mothers exposed to carbofuran ” the consideration for publication, which was sent for technical modification.

We thank you for submitting your valuable research work to the Research in Pharmaceutical Sciences.

Yours sincerely,

Editorial Team
Research in Pharmaceutical Sciences

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**Subject:** Manuscript for revision: RPS_209_21
**To:** epy-m-l@fkh.unair.ac.id
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**CC:**
**Recieved:** Saturday, January 1, 2022

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Dear Dr  Luqman,
With reference to your manuscript RPS_209_21 entitled Potency of Kebar grass (Biophytum petersianum Klotzsch) extract to increase motor reflex and memory in mice offspring (Mus musculus) from lactating mothers exposed to carbofuran , please review the comments of the referees from our site https://review.jow.medknow.com/rps. The manuscript would be reconsidered after requisite modifications as per the comments and instructions provided by the journal.
If you wish to continue with the publication process, kindly make the changes according to the comments and upload the revised manuscript along with clarifications for all the comments clearly indicating the areas where the changes have been made.
Do check the FAQ regarding replying to the comments and uploading a file. The template of point-by-point comments files for the reviewers, is available in your dashboard under the 'Downloads' menu option.
The journal allows three weeks for the revision of the manuscript. If we do not hear from you within this period, we will consider it as your decision to withdraw your article from publication. Please also note that the submission of the revised article does not guarantee its final acceptance by the journal.
We thank you for submitting your valuable research work to Research in Pharmaceutical Sciences.
With warm personal regards,
Editorial Team
Research in Pharmaceutical Sciences

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**Subject:** Manuscript for revision: RPS_209_21

**To:** epy-m-l@fkh.unair.ac.id

**From:** editor@rpsjournal.net

**CC:**

**Recieved:** Sunday, January 2, 2022

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Dear Dr Luqman,

With reference to your manuscript RPS_209_21 entitled Potency of Kebar grass (Biophytum petersianum Klotzsch) extract to increase motor reflex and memory in mice offspring (Mus musculus) from lactating mothers exposed to carbofuran , please review the comments of the referees from our site https://review.jow.medknow.com/rps. The manuscript would be reconsidered after requisite modifications as per the comments and instructions provided by the journal.

If you wish to continue with the publication process, kindly make the changes according to the comments and upload the revised manuscript along with clarifications for all the comments clearly indicating the areas where the changes have been made.

Do check the FAQ regarding replying to the comments and uploading a file. The template of point-by-point comments files for the reviewers, is available in your dashboard under the 'Downloads' menu option.

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We thank you for submitting your valuable research work to Research in Pharmaceutical Sciences.

With warm personal regards,

Editorial Team

Research in Pharmaceutical Sciences

Dear Author
Greetings
Reviewers have now commented on your paper. You can find them below.

**Reviewer 1**

1. -The manuscript must be corrected due to typographical errors, and must be edited by a native English speaker.
2. -In the abstract, the conclusion needs to improve. It only repeated the results.
3. -Select MeSH words for the keywords.
4. -Define the abbreviations in first appearance.
5. -The introduction needs to be written in a purposeful and constructive way.
6. -What is the innovation of this research according to similar studies?
7. -The method should be summarized and unnecessary items should be removed.
8. -Explain the criteria and method of selecting the dose of the extract and the different compounds used and give references.
9. -Have the final tests been performed on children or on mothers? This is ambiguous in most parts of the text.
10. -If these tests were performed on children, was their age appropriate for behavioral tests? Have they evolved enough to do this type of behavioral study? Reference is required for that.

11. -Reference is required for all chemical and behavioral assessment methods.
12. -Statistical issues in the results should be explained more prominently and interpreted in the discussion of the article.
13. -Using charts can help to better express the results.
14. -In the table, legends and significant values and signs related to between group differences should be explained.
15. -In the discussion, the results are interpreted in detail. However, the text is very long and it is necessary to analyze and confirm the behavioral and histological results by biochemical results obtained in this study and confirm it with previous studies.
16. -The final conclusion only refers to the results and needs to be corrected and written conclusively.

**Reviewer 2**

1. In the abstract, In the part of Experimental approach, please convert "40" from numerical form to "letters" form.
2. English grammar must be corrected in the manuscript.
3. For first time, please write complete form of phrase and then put "," and then write the abbreviation form of it.
4. In the "materials part" please eliminate "laboratory".
5. In the Method section, the author wrote that " on the 15th day of lactation, neuronal cell necrosis in the brain of mice were counted…. and behavioral test were performed on 10-day old mice and memory test were performed on mice. Please write, how did you carry out this protocol from time line view?
6. The author in lines 122 and 123 mentioned "the aim of study was to provide a reference on the potency of kebar grass extract to reduce free radicals by an increase in SOD and GSH…., and in results mentioned "carbofuran increase MDA, GSH and …. Also, in line 287 of discussion mentioned "antioxidant GSH" and in lines 310 and 311 mentioned "the increase GSH is a mechanism of antioxidant defense to protect the body from oxidative stress by ROS. The carbofuran increased GSH and kebar grass decreased GSH". It seems they are paradox.Please, the author, explain it.
7. Please, explain "a, b, c, d" in the table.
8. Please explain the difference between this submission and reference 3 of this manuscript?

**Reviewer 3**

1. The main title is not clear and complete. For example, it is not mentioned whether the aqueous extract is used or hydro-alcoholic extract. It is suggested instead of the word "Potential" write "beneficial effects of" ...
2. The type of memory should be written in the title and in the Materials and Methods section. It seems that spatial memory is examined in this study.
3. Please indicate the P values in each significant case in the abstract section.
4. In the introduction, the reason for selecting Kebar grass for the purpose of the study is not properly stated. It needs to be more explained.
5. The author should explain how they choose these doses of doses of kebar grass or carbofuran.
6. H&E histochemical image quality is not good.
7. It is suggested that related molecular tests be added to the study to evaluate the apoptosis in brain tissue.
8. The values of p should be listed in the tables of the result section.
9. Please check carefully for the typo and grammatical mistakes in all parts of manuscript.

[EDITORIAL COMMENTS]:

Thank you for submitting your valuable work to Research in Pharmaceutical Sciences journal. For further process of your manuscript please consider the following comments.

1. The number of references should be decreased to a maximum of 30.
2. Please provide all the references according to RPS format. The acceptable format is:
   -Rezazadeh M, Jafari N, Akbari V, Amirian M, Tabbakhian M, Minaiyan M, et al. A mucoadhesive thermosensitive hydrogel containing erythropoietin as a potential treatment in oral mucositis: in vitro and in vivo studies. Drug Deliv Transl Res. 2018;8(5):1226-1237. DOI: 10.1007/s13346-018-0566-9.
3. Please provide the **Acknowledgment** section, in the manuscript file.
4. If a figure has different parts including different graphs or images, therefore different Capital/UPPERCASE letters in Times New Roman, solid black or white (depends on background color), and bold must be

assigned to each part at the top left corner of the part and then each Latin characters should be defined in the figure legend.

Thank you in advance for your cooperation
Yours Faithfully
Dr. Shiva Dehghan Khalili
Assistant of Editor
Research in Pharmaceutical Sciences

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**Subject:** RPS Manuscript for revision: RPS_209_21 Completion date is nearing
**To:** epy-m-l@fkh.unair.ac.id
**From:** editor@rpsjournal.net
**CC:**
**Recieved:** Wednesday, January 5, 2022

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Dear Dr Luqman,
This mail is with reference to your manuscript 'RPS_209_21' entitled Potency of Kebar grass (Biophytum petersianum Klotzsch) extract to increase motor reflex and memory in mice offspring (Mus musculus) from lactating mothers exposed to carbofuran , which was sent to you some time back for revision.
We have not received the modified manuscript to date. If we do not hear from you within the due date Jan 12, 2022 12:00:00 AM, we will consider it your non-desire to continue the article with us.
Details are available at the manuscript management site https://review.jow.medknow.com/rps. Kindly log in as Author.

Thanking you
Editorial Team
Research in Pharmaceutical Sciences

**Original article**

# Beneficial effects of Kebar grass (*Biophytum petersianum* Klotzsch) ethanol extract to increase motor reflex and spatial memory in mice offspring (*Mus musculus*) from lactating mothers exposed to carbofuran

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**Running title:** Motor reflex and memory exposed to carbofuran

**Dear The Editor Research in Pharmaceutical Sciences**

I request the publication of the original paper at your reputed journal, which have been not published any where in any language and online or hard print version. I (we) affirm that-

1. The manuscript has been prepared in accordance with the latest “Instruction for authors”.
2. The article is original and has not been published previously, is not under consideration for publication elsewhere, and if accepted, it will not be published elsewhere in the same form, in English or any other language. The submission of the article has the approval of the all the authors and the authorities of the host institute where work had been carried out.
3. All the authors have made substantive and intellectual contributions to the article and assume full responsibility for all opinions, conclusion and statements expressed in the articles.
4. I (we) agree to abide by the comments of referees/editorial board and will modify the article as per their recommendations for publication.

Dear Sir, you need to know that all authors concur with the submission and have seen a draft copy of the manuscript and agree with its publication and there are no conflict of interest. If any things will be found I will be only responsible for the same.
Kindly consider it.

Yours Truly,

Dr. Epy Muhammad Luqman, DVM, MSc

**Original article**

# Beneficial effects of Kebar grass (*Biophytum petersianum* Klotzsch) ethanol extract to increase motor reflex and spatial memory in mice offspring (*Mus musculus*) from lactating mothers exposed to carbofuran


## Abstract

**Background and purpose**: This study aims to determine the potency of Kebar grass (*Biophytum petersianum* Klotzsch) ethanol extract to overcome an increase in cerebellar neuronal cell necrosis, which has an impact on decreasing motor reflex function and spatial memory of mice (*Mus musculus*) from lactating mothers exposed to carbofuran.
**Experimental approach**: Forty lactating mice (*Mus musculus*) used and were divided into four groups, each group consisted of ten. Group C (control), T1 (Carbofuran 0.0125mg/day), T2 (vitamin C 5mg + carbofuran 0.0125mg/day), T3 (Kebar grass extract 3.375mg + carbofuran 0.0125mg/day). Carbofuran, vitamin C and Kebar grass ethanol extract were exposed orally on day 0 to 14 postnatal. On the 15$^{th}$ day, and the brains of the mice were necropsised to measure the levels of malondialdehyde (MDA), superoxide dismutase (SOD), glutathione (GSH), hematoxylin-eosin staining, and motor reflex tests were performed on 10-day-old mice and aged 30 days were tested on their swimming and spatial memory in an eight-arm radial maze.
**Results**: Carbofuran caused a significant increase in MDA, GSH neuronal cell necrosis, surface righting reflex, a significant decrease in SOD, swimming ability, and eight-arm radial maze memory test ($P<0.05$). Kebar grass extract and vitamin C administration could decrease in MDA, GSH, neuron cell necrosis, surface righting reflex, a significant increase in SOD, swimming ability, and eight-arm radial maze memory test ($P<0.05$).
**Conclusion and implications**: Lactating mothers exposed to carbofuran could cause brain oxidative stress, impaired motor reflexes, and spatial memory in mice offspring. Kebar grass ethanol extract and vitamin C administration could prevent brain oxidative stress and inhibit disorders in motor reflexes, and spatial memory in mice offspring. Kebar grass ethanol extract administration was more effective than vitamin C.



**Keywords :** Carbofuran, cerebellum, Kebar grass, lactation, pesticide stress, vitamin C.


## INTRODUCTION

Furadan, with the active ingredient carbofuran, is widely used in agriculture and it is proven that residues are found on soil, surfaces, rainwater and food that can harm organisms that are not the target of insecticides (1). Carbofuran exposure produces motor reflex anomalies in newborns, as well as abnormalities in the development of brain function in children, such as a diminished ability to remember and focus power (2). Contamination by carbofuran in laboratory animals induces oxidative stress and impairs cognitive, memory, and motor functions (3). The cerebral cortex, cerebellum, and brainstem all suffer severe oxidative damage as a result of carbofuran induction (4).

The brain is vulnerable to oxidative damage due to the relatively low enzymatic and non-enzymatic antioxidant systems and the large amounts of free radicals produced due to the high oxygen demand (5). Oral carbofuran administration has been demonstrated to raise MDA and decrease SOD in the brains of mice throughout embryonic and lactation periods, indicating that it stimulates reactive oxygen species (ROS) (6, 7). The cerebellum develops from the middle of the

pregnancy until a few days after the fetus is born (8). The cerebellum is responsible for controlling movement, maintaining balance, regulating position, and coordinating body motions. In the human brain, the cerebellum is thought to play a role in motor function as well as cognitive activities (9). Oxidative damage caused by free radicals also plays a central role in cognitive decline and spatial learning and memory (10). Protective markers of oxidative stress (MDA) and antioxidant (GSH) in the brain have been investigated to observe the relationship between spatial memory and oxidative stress (11). The increase in ROS that induces neuronal cell death due to carbofuran exposure is able to reduce motor reflex function and memory ability.

Antioxidant compounds overcome oxidative damage caused by nutritional imbalances, xenobiotics, and strenuous physical activity. Biosystems include two types of antioxidants, non-enzymatic molecules such as glutathione and vitamins (C, D and E) and enzymatic indicators such as SOD, catalase, and GSH. Kebar grass (*Biophytum petersianum* Klotzsch) is a plant that belongs to the Oxalidaceae family that is found to naturally and widely grow in Kebar District, West Papua, Indonesia (12). Kebar grass contains flavonoids, vitamins E and A as antioxidants to neutralize toxic agents, prevent damage caused by toxic agents and maintain cell health. Flavonoids, which serve as primary antioxidants, are free radical acceptors, so that they can inhibit free radical chain reactions in lipid oxidation, which can prevent membrane damage (13).Vitamin E can inhibit oxidation reactions by binding vitamin E radicals to become free vitamin E which functions again as an antioxidant. Beta carotene works by reacting with free radicals and causing free radicals to become stable (14).

This study aims to find out the potency of Kebar grass (*Biophytum petersianum* Klotzsch) ethanol extract to overcome an increase in free radicals by an increase in MDA and GSH, a decrease in SOD, and cerebellar neuronal cell necrosis, which has an impact on decreasing motor reflex function and spatial memory in mice (*Mus musculus*) from lactating mothers exposed to carbofuran. This study is expected to provide a reference on the potency of Kebar grass extract ethanol to reduce free radicals by a decrease in MDA and GSH, an increase in SOD and a decrease in neuronal cell necrosis, motor reflexes in mice: swimming ability and surface righting reflex (swimming direction and head angle position), as well as a memory test of the eight-arm radial maze. In addition, the data obtained can also be used to provide information to the public about the dangers caused by the careless use of carbofuran, especially in lactating mothers.

## MATERIALS AND METHODS

The research procedure was conducted according to the permit by testing the code of ethics committee of experimental animals with the number 1.KE.107.06.2019 at the Faculty of Veterinary Medicine, Universitas Airlangga.

### *Materials*

This experimental study went through the following stages: synchronization of the oestrus cycle of mice using pregnant mare serum gonadotropin (PMSG) (Holland, Boxmeer, Intervet, Folligon) and human chorionic gonadotropin (hCG) (Holland, Boxmeer, Intervet, Chorulon), examination on mice gestation through vaginal plug observation, and administration of carbofuran by gavage for 14 days in lactating mothers. On the 15$^{th}$ day of lactation, neuronal cell necrosis in the brains of mice was counted, and behavioral tests of mice consisting of: swimming ability, surface righting reflex (direction and position of swimming) were performed on 10-day-old mice, and memory tests of eight-arm radial maze were performed on mice aged 30 days old.

The materials used were 10 week lactating mice (*Mus musculus*) weighing 25-35 grams obtained from the Veterinary Center Farma Surabaya, Kebar grass (*Biophytum petersianum*

Klotzsch) ethanol extract, carboxymethyl cellulose (CMC) Na, 70% ethanol, carbofuran (2,3-Dihydro-2,2-dimethyl-7-benzofuranol N-methylcarbamate 98 %) from Aldrich Chemistry with Bellstain Registry number 1428746, Product of USA. Pellet feed for mice, aquadest as a solvent for carbofuran, vitamin C, drinking water, husks as a base for cages, 10% formalin, alcohol. The tools used were plastic cages and wire mesh for experimental animal cages, drinking containers, sonde needles, test tubes. Microscopic examination was performed by counting neuronal cell necrosis with hematoxylin and eosin staining (HE, Millicell®-HA, Merck, Germany). Under a microscope (Olympus® CX-41), three slices of each sample were observed and examined.

***Method***

***Synchronization of the estrous cycle using PMSG and HCG hormones***

For 7 days, 10 week old female mice (*Mus musculus*) weighing 25-35 grams were adapted to the habitat. On the eighth day, PMSG was given at a dose of 5 IU/head, and hCG was injected at a dose of 5 IU/head on the tenth day. Male mice aged 12 weeks were subsequently mated. After that, the mice were maintained in cages and fed ad libitum.

***Examination on mouse gestation***

A gestation examination was done on the 11th day, and if a vaginal plug was found in the female mice's vulva, that day was regarded as day 0 of gestation. The expecting mothers were then separated into five cages to give birth.

***Preparation of Kebar grass ethanol extract***

This research uses dried Kebar grass. The extract of Kebar grass was made at the Pharmacognosy and Phytochemical Laboratory of the Faculty of Pharmacy, Universitas Airlangga. The dried grass is boiled in distilled water. A total of 350 grams of simplicia of Kebar grass which have been mashed are macerated in a tube for 3x24 hours with 70% ethanol solvent ratio of 1:10, then filtered and the dregs are macerated again 2 times with the same treatment. The maserate is evaporated by a rotary evaporator at a temperature of 30-40$^0$C to form a thick extract. The extract was put in a bottle and stored in the refrigerator.

***Administration of Carbofuran and Kebar Grass***

Mothers who had given birth were divided into four groups: C (control administered with 0.5 ml of aquadest), T1 (administered with Carbofuran 1/4 $LD_{50}$ 0.0125 mg/day), T2 (administered with vitamin C 5 mg + carbofuran 1/4 $LD_{50}$ 0.0125 mg/day), and T3 (administered with Kebar grass extract 3.375 mg + carbofuran 1/4 $LD_{50}$ 0.0125 mg/day). The carbofuran dose used was the ¼ $LD_{50}$ (0.0125 mg/25g mice/day) (15). The determination of the dosage of Kebar grass ethanol extract used in this study refers to research conducted by Labib et al. (16). Kebar grass provides an effective antioxidant effect to prevent oxidative stress by 0.135 mg/gBW/day. Carbofuran, vitamin C, and Kebar grass were exposed orally on days 0 to 14 postnatal (during 14 days of lactation) using a 3 ml syringe. On the 15$^{th}$ day, the brains of the mice were necropsied to measure the levels of MDA, SOD, and GSH, hematoxylin-eosin (HE) staining and motor reflex function tests (neurobehavioral tests): surface righting reflex conducted on 10-day-old mice, swimming and a spatial memory test of eight-arm radial maze were conducted on mice aged 30 days old.

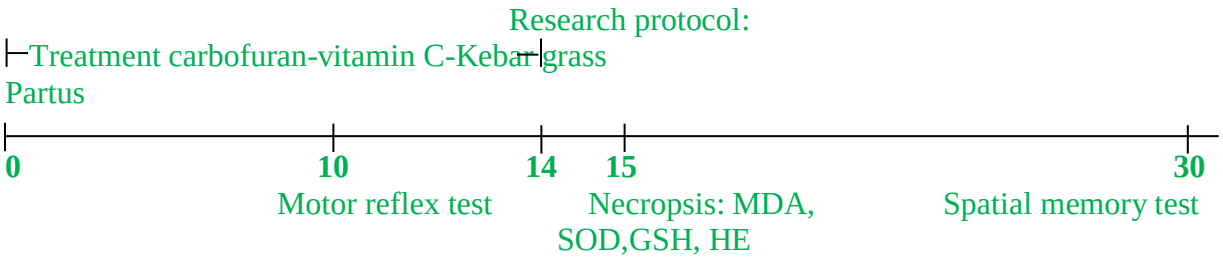
***Measurement of MDA, SOD and GSH levels using the Elisa method (R&D Systems® ELISA Kits)***

The sample was diluted with calibrator diluent RD5-16 (2x dilution). The mixture (75µl sample plus 75µl Callibrator diluent RD5-16) was then homogenized. The standard assay (standard solution stock, 4000 pg/ml) was prepared with calllibrator diluent RD5-16. 50µl of assay diluent RD1-54 was put into the well. A 50 µl sample and standard solution were added

to the well. The well was covered with an adhesive strip, and the solution was gently homogenized in the well. The solution was incubated at room temperature for 2 hours. The solution in the well was taken and washed 5 times with a with 400µl wash buffer. The well was absorbed using a paper towel. 100µl mouse MDA, SOD, and GSH conjugate were added. The well was covered with an adhesive strip and it was incubated for 2 hours at room temperature. The solution in the well was taken and washed 5 times with a with 400µl wash buffer. The well was absorbed using a paper towel. For each well, 100µl of substrate solution was added (by mixing 1:1 color reagent A and reagent B, which were homogenized for 15 minutes in a dark bottle) to each well. It was incubated at room temperature for 30 minutes in the dark. A 100µl stop solution was added to each well and and they were mixed gently. The absorbance was read at a wavelength of 450 nm.

***Staining on mice's brain using hematoxylin and eosin (HE)***

On the 15th day, the mice were sacrificed for taking the brains and making histopathological preparations with HE staining. Observations of the brains of mice were carried out at five microscopic angles, that is, at the four angles and the center of the preparation, with a magnification of 400X (3).




***Motor reflex tests:***

***Surface Righting Reflex***. Mice aged 10 days were used in this experiment. The mice were placed supine on a flat surface to be evaluated. A stopwatch was used to record the amount of time it took the mice to change positions from supine to prone (17).

***Swimming Ability***. Mice aged 30 days were used in the experiment. The mice were placed in a water container filled with warm water (between 27 and 30 $^{o}$Celsius), and their movements were recorded: ***Head angle position****:* Score 0: dive, Score 1: nose above the water surface, Score 2: nose and upper head above the water's surface, Score 3: As in score 2, the eyes are above the water's surface, and a fourth of the earlobe is above it, Score 4: as in score 3, the entire earlobe is above the water surface. ***Swimming direction****:* Score 1: floating, Score 2: swimming in circles, Score 3: swimming straight or nearly straight, Score 4: sinking (18).

***Spatial memory test with an eight arm radial maze memory test***

The tools were made up of eight plastic arms, each measuring 32 cm in length and 5 cm in width, with a diameter of 20 cm in the centre. ***The adaptation phase****:* Mice aged 30 days were used in the experiment. They were adapted for 7 days and fed pellets, and given water every day. ***The initial phase****:* The mice were examined in an eight-arm radial maze on the seventh day of the adaptation phase. ***The training phase****:* Before being taught in an eight-arm radial maze, the mice were fasted for 12 hours. The mice were then placed in the center of the maze and given 10 minutes to investigate it. ***In the test phase***, The five-day test phase begins one day after the training period is completed. The test was deemed complete when the mice had entered all arms or 10 minutes had passed. The number of errors in each session (entering an arm that has already been visited and/or not entering one or more arms in each session were both counted as errors)

and the number of accurate choices in entering each arm in each session were the results of observations to be recorded (entering an arm that has not been visited previously in that session). The memory score formula was used to determine each mouse's memory score (19):

$$\text{Memory score} = \frac{(\text{The correct number of arms}) - (\text{The incorrect number of arms})}{(\text{The correct number of arms}) + (\text{The incorrect number of arms})}$$

One is the maximum memory score that can be achieved. On a scale of -1 to 1, the closer the memory score is to 1, the better the memory of the experimental animals being tested. A score of -1, on the other hand, implies the inverse (all arm entries are incorrect).

***Data analysis***

The average number of neuronal cell necrosis was characterized by pyknosis and karyorexic neuron cells. The data for calculating the levels of MDA, SOD, GSH, and the number of neuronal cell necrosis used the ANOVA test and Duncan's test. The Kruskal-Wallis test was used to assess data on motor reflex ability and memory in mice in the eight-arm radial maze, and if the results were significantly different, the Mann Whitney test was used. To make statistical calculations easier, the Statistical Product and Service Solution (SPSS) version 20.0 was used.

**RESULTS**

In this study, it was shown that the carbofuran group (T1) was able to significantly increase levels of MDA, GSH, neuronal cell necrosis, and surface righting reflex movements. Carbofuran was also able to reduce SOD levels, swimming movements according to head angle position, swimming movements according to swimming directions, and spatial memory abilities through the 8-Arm radial maze test compared to the control group (C) ($P<0.05$) (Table 1).

In the group administered with Kebar grass extract and carbofuran (T3), it was shown that it was able to significantly reduce the levels of MDA, GSH, neuronal cell necrosis, and surface righting reflex movements ($P<0.05$). The Kebar grass extract group (T3) was also able to increase swimming movement according to head angle position, swimming movement according to swimming direction, and spatial memory ability through the eight arm radial maze test compared to the carbofuran group (T1) ($P<0.05$) (Table 1). Except for swimming movements according to swimming directions, decreased levels of MDA, GSH, neuronal cell necrosis, surface righting reflex movements, and increased swimming movements according to head angle position, and spatial memory ability through the 8-Arm radial maze test could not match the control group (C) (Table 1).

The group administered with vitamin C (T2) could not significantly reduce the levels of MDA, GSH, and increase memory ability through the eight arm radial maze test compared to the carbofuran group (T1). However, vitamin C (T2) was able to significantly reduce neuronal cell necrosis and surface righting reflex. Vitamin C was also able to increase swimming movements according to the head angle and swimming movements according to the direction of swimming ($P<0.05$). Similarly, the administration of Kebar grass ethanol extract, vitamin C (T2) also did not increase SOD levels. However, compared to the administration of Kebar grass ethanol extract (T3), vitamin C was still significantly lower in reducing levels of MDA, GSH, neuronal cell necrosis, and surface righting reflex. Vitamin C was also unable to increase swimming movements according to swimming direction and the eight arm radial maze test compared to Kebar grass ethanol extract ($P<0.05$) (Table 1).

The mean neuronal cell necrosis number was characterized by increased pyknosis and

karyorexic neurons in the T1 group. Administration of Kebar grass ethanol extract (T3) and vitamin C (T2) can reduce the number of neuronal cell necrosis even though it has not reached the number of neuron cells in the control group (C) ($P<0.05$). However, administration of kebar grass ethanol extract (T3) is still better than vitamin C (T2), as it is shown in the number of pyknotic and karyorexic neuron cells in Figure 1.

## DISCUSSION

Carbofuran that is a broad-spectrum insecticide, is lipophilic and can enter mothers' breast milk. Carbofuran exposure to lactating mothers is proven to cause increased MDA levels and brain necrosis in mice that were breastfed for 9 days (15). Increased levels of MDA and non-enzymatic antioxidant GSH and decreased SOD are the beginning of oxidative stress in animal body systems exposed to toxic substances. The results of this study showed that a subacute dose of carbofuran for 14 days of lactation also significantly increased MDA and GSH levels ($P<0.05$). It showed that carbofuran was able to cause oxidative stress in the brains of mice that were suckling their mothers for 14 days. In this study, there was a significant decrease in SOD due to exposure to carbofuran ($P<0.05$), which indicated that oxidative stress had arisen in the brains of mice. A decrease in SOD indicates a failure of the antioxidant system and can cause brain toxicity in mice. Similar observations have been made in the brains of fetal mice whose pregnant mothers were exposed to carbofuran (7). Increased GSH is a mechanism of antioxidant defense to protect the body from oxidative stress by ROS. Similar results were found in the hearts of mice exposed to carbofuran for 28 days (20). Oxidative stress in the brains of mice induced by carbofuran in this study increased MDA and GSH levels, and decreased SOD ($P<0.05$).

The levels of MDA and GSH decreased significantly when Kebar grass ethanol extract was administered to the mice ($P<0.05$), and there was no decrease in MDA and GSH found in the administration of vitamin C ($P>0.05$). The results of this study were in accordance with previous studies showing that vitamin C and curcumin could reduce heart and brain GSH but not significantly different (20, 21). Meanwhile, the SOD levels did not increase either with the administration of Kebar grass ethanol extract or vitamin C ($P>0.05$). The decrease in MDA and GSH levels due to the administration of Kebar grass ethanol extract is due to flavonoids, vitamins A and E contained in Kebar grass ethanol extract and is useful in preventing cell damage due to oxidative stress (21).

The content of vitamin A and vitamin E in Kebar grass ethanol extract also functions to react with free radicals and stabilize free radicals. Vitamin A and carotenoids interact with free radicals and prevent cell lipid peroxidation. Vitamin E is a major lipophilic antioxidant that inactivates peroxyl radicals through direct transfer of hydrogen atoms and protects lipid tissues from damage due to free radicals (12). Vitamin C is also a potential antioxidant that has been proven to reduce the free radical load by neutralizing reactive chemical species through oxygen binding, hydroperoxide reduction, and free radical stabilization into neutral and non-toxic materials (14).

The decrease in MDA and GSH levels due to the administration of Kebar grass ethanol extract is better than vitamin C because antioxidants from fruits and vegetables are the best sources compared to conventional antioxidant supplements. Higher doses of antioxidant supplements do not replace the need for a healthy diet. Antioxidant supplements of vitamins C and E, as daily antioxidants can be consumed from fruits and vegetables (22).

In this study, the number of neuronal cell necrosis increased to 59.01 % ($P<0.05$). When exposed to carbofuran during the peak of neurogenesis, the number of neuronal cells necrosis increased by 662.64% when compared to the embryonic phase (days 14-17 of gestation) (14). Meanwhile, carbofuran exposure at the peak of the lactation period (on the days 1-4 of lactation) increased to 287.87% (15). It was discovered that the response to carbofuran-induced neuronal cell necrosis was significantly dependent on the critical phase of organ development. The administration of Kebar grass ethanol extract and vitamin C reduced necrosis by 17.48 and 11.64% compared to the carbofuran group ($P<0.05$) (Table 1).

This showed that the flavonoid contained in Kebar grass ethanol extract was more potent in anticipating excess oxidative stress that caused neuronal cell necrosis than vitamin C administration. It is in line with the study by Noorozi et al. (23) that the protective impact of vitamin C on DNA damage is much lower than that of all flavonoid content except quercetin-3-glucoside, apigenin, and rutin. The greater antioxidant potency of most flavonoids than vitamin C indicates that the strong effect of one of the flavonoids is quercetin.

Oral carbofuran administration has increased MDA and decreased SOD, which has an impact on increasing neuronal cell death throughout the embryonic and lactation periods (6, 7). Oxidative damage caused by free radicals also plays a central role in cognitive decline and spatial learning and memory (10). The oxidative stress (MDA) and antioxidant (GSH) defense markers in brain's spatial memory (11). Contamination by carbofuran in laboratory animals induces oxidative stress and impairs cognitive, spatial memory, and motor functions (3). The increase in free radicals that induce neuronal cell death due to carbofuran exposure is able to reduce motor reflex function and memory ability.

In this study, administration of carbofuran caused a significant increase in surface righting reflex and a significant decrease in swimming ability: swimming direction and head angle position as well as spatial memory ability (eight arm radial maze) ($P<0.05$). Perinatal exposure to carbofuran caused oxidative stress, and oxidative stress that may contribute to the decrease in cerebellar structure and the impairment of motor coordination in hypergravity-exposed rat neonates (24). The swimming endurance test is a pharmacological screening method for determining the effect of toxic substances on movement coordination, including testing for both decreased and increased central nerve control. Table 1 shows that there is a decrease in swimming ability according to swimming direction and head angle position. This indicates that carbofuran can shorten the onset of fatigue or reduce swimming endurance. Maternal high levels of the redox active amino acid homocysteine hyperhomocysteinemia (hHCY) found an increased level of MDA, and decreased SOD in the brain tissues of rats caused impairment of reflex ontogeny, locomotion, muscle strength, and motor coordination (25). Effects of carbofuran exposure on acetylcholinesterase (AChE) in the brain and swimming activity. The lowest carbofuran concentration resulted in a considerable reduction in swimming activity (21%). Exposure to the greatest quantities of carbofuran led in a reduction in locomotor activity (26).

Administration of Kebar grass ethanol extract and vitamin C was able to reduce surface righting reflex time and also increase swimming ability according to head angle position, swimming direction ($P<0.05$). However, the administration of Kebar grass ethanol extract was still better than vitamin C in reducing surface righting reflex time, as well as increasing swimming ability according to swimming direction, and head angle position (Table 1). The antioxidant enhances swimming endurance by elevation of the antioxidant capacity of the skeletal muscles, which has thereby highlighted the potential of this natural product as an antioxidant in the treatment of fatigue (27). The study confirmed numerous motoric

manifestations of cisplatin-induced neurotoxicity in rats and supplementation with N-acetylcysteine (NAC) was successfully prevented decrease motor performance (28).

Carbofuran exposure during lactation (perinatal) significantly decreased learning and memory patterns, as demonstrated by decreased latency time to reach food and time spent on the food arm. The number of mice who made mistakes entering the arm of the eight arm radial maze was used to assess memory function in this study ($P<0.05$) (Table 1). Both the Kruskal-Wallis and Mann-Whitney tests revealed a significant decline, showing that carbofuran exposure may impair memory function in mice. This is in line with a prior study that discovered carbofuran can cause neurobehavioral, neurochemical, and neurophysiological issues. Carbofuran exposure leads to increased expression of caspase 3, and the number of degenerative neurons in the hippocampus, leading to enormous deficits in learning and memory (2). The mechanism of action of carbofuran is compatible with the prevention of memory loss, so the use of antioxidants as neuroprotectives and preventing neuronal death by free radicals is highly recommended (29). Kebar grass ethanol extract administration can improve the memory ability of mice but is not found in the administration of vitamin C. This is in accordance with the research of Barichello et al. (30), which states that the administration of antioxidants can prevent hippocampal oxidative stress as a cause of memory impairment. Antioxidants in Kebar grass ethanol extract were better than vitamin C because antioxidants from fruits and vegetables are the best sources compared to conventional antioxidant supplements, even though high doses of the supplements are administered and it can be dangerous for those who consume them (26).

## Conclusion

Lactating mothers exposed to carbofuran could cause brain oxidative stress, impaired motor reflexes and spatial memory in mice offspring. Kebar grass ethanol extract and vitamin C administration could prevent brain oxidative stress and inhibit disorders in motor reflexes and spatial memory in mice offspring. Kebar grass ethanol extract administration was more effective than vitamin C.

## Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Authors' contribution

Epy Muhammad Luqman: Conceptualization, Methodology, Software, Eka Pramyrtha Hestianah: Data curation, Writing-Original draft preparation. Widjiati Widjiati: Visualization, Investigation, Suryo Kuncorojakti: Supervision, Viski Fitri Hendrawan: Writing-Reviewing and Editing.

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Table 1. Levels of MDA, SOD, GSH, number of neuronal cell necrosis, surface righting reflex, swimming direction and head angle position, eight arm radial maze test mice from mothers exposed to carbofuran, vitamin C and Kebar grass.

| Variable | Control | T1 | T2 | T3 |
|---|---|---|---|---|
| MDA(nmol/mg) (mean±SD) | $0.14^{c} \pm 0.038$ | $1.64^{a} \pm 0.08$ | $1.49^{a} \pm 0.13$ | $0.88^{b} \pm 0.52$ |
| SOD (ng/mL) (mean±SD) | $0.75^{a} \pm 0.62$ | $0.60^{b} \pm 0.01$ | $0.60^{b} \pm 0.01$ | $0.65^{b} \pm 0.04$ |
| GSH (ng/mL) (mean±SD) | $4.90^{c} \pm 1.56$ | $19.10^{a} \pm 2.44$ | $18.69^{a} \pm 2.38$ | $10.12^{b} \pm 2.66$ |
| Nekrosis sel neuron (mean±SD) | $29.28^{a} \pm 2.74$ | $46.56^{d} \pm 7.21$ | $43.15^{c} \pm 1.19$ | $35.44^{b} \pm 6.11$ |
| Surface Righting Reflex (mean±SD) | $0.68^{a} \pm 0.06$ | $1.96^{d} \pm 0.10$ | $1.40^{c} \pm 0.10$ | $0.86^{b} \pm 0.21$ |
| Head angle position (mean±SD) | $3.00^{a} \pm 0.01$ | $2.14^{c} \pm 0.37$ | $2.30^{b} \pm 0.16$ | $2.46^{b} \pm 0.26$ |
| Swimming direction (mean±SD) | $3.00^{a} \pm 0.01$ | $2.04^{b} \pm 0.27$ | $2.76^{a} \pm 0.24$ | $2.89^{a} \pm 0.65$ |
| 8-Arm Radial Maze (mean±SD) | $1.00^{a} \pm 0.07$ | $0.85^{c} \pm 0.11$ | $0.87^{c} \pm 0.15$ | $0.93^{b} \pm 0.15$ |

Mean with different letters (a, b, c, d) within a row are significantly different ($P < 0.05$). Carbofuran group (T1) had increased levels of MDA, GSH, neuronal cell necrosis, and surface righting reflex movements than control group ($^{a,b,d}$ $P<0.05$). Carbofuran group (T1) had decreased SOD levels, swimming movements according to head angle position, swimming directions and spatial memory ($^{b,c}$ $P<0.05$). Kebar grass extract (T3) had decreased the levels of MDA, GSH, neuronal cell necrosis, and surface righting reflex movements ($^{a,b}$ $P<0.05$) and increased swimming movement according to head angle position, swimming direction and spatial than carbofuran group (T1) ($^{a,b}$ $P<0.05$). Vitamin C (T2) had decreased neuronal cell necrosis and surface righting reflex ($^{a,b}$ $P<0.05$) and had increased swimming movements according to the head angle and the direction of swimming carbofuran group (T1) ($^{a,b}$ $P<0.05$). **C** (Control group), T1 (group exposed to Carbofuran 1/4 $LD_{50}$ 0.0125 mg/day), T2 (group exposed to vitamin C 5 mg + Carbofuran 1/4 $LD_{50}$ 0.0125 mg/day), T3 (group exposed to Kebar grass extract 3.375 mg + Carbofuran 1/4 $LD_{50}$ 0.0125 mg/ day).

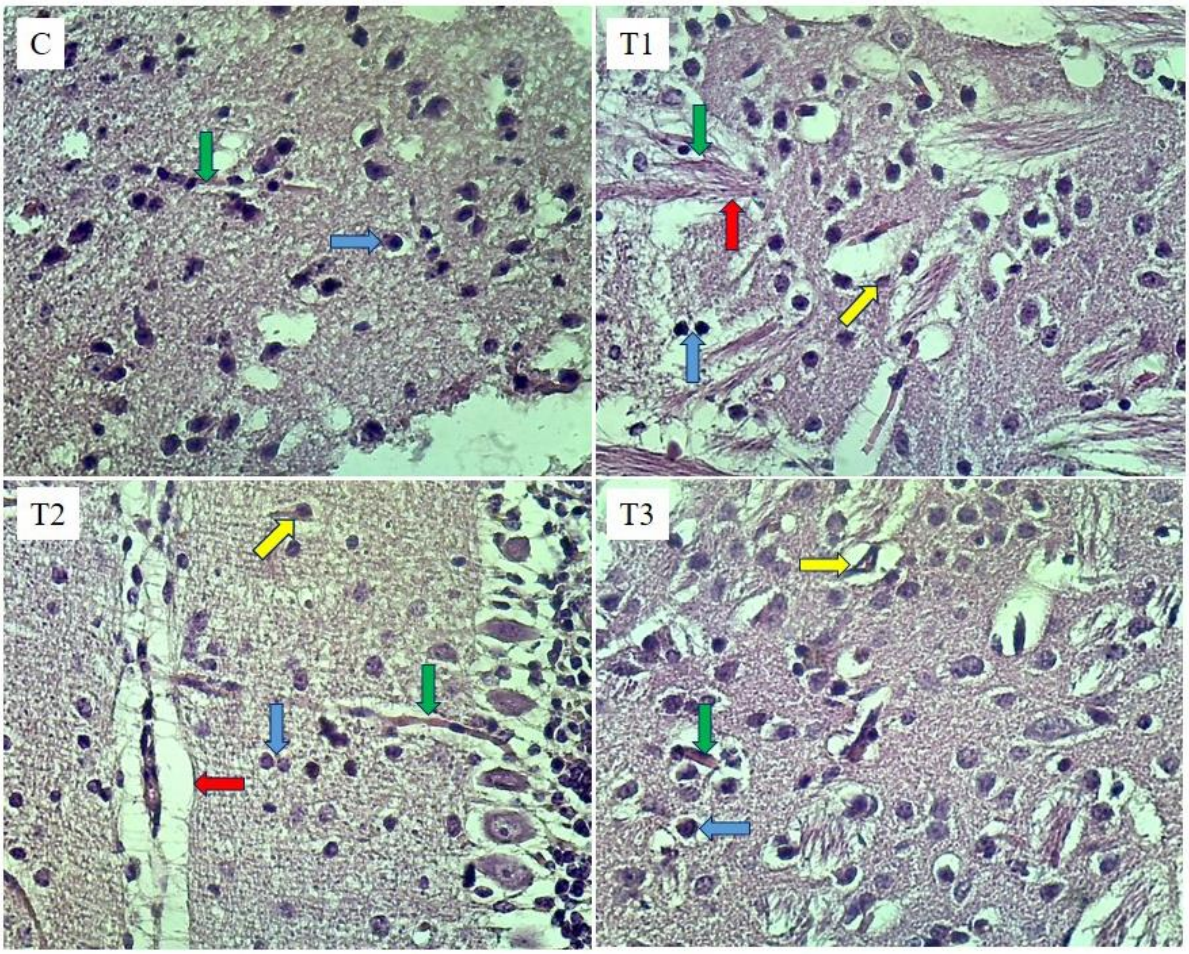


**Figure 1.** Cerebellum images of each group (C, T1, T2 dan T3). Red arrow: Astrocytes, yellow arrow : oligodendrocytes, green arrow : microglia, dan blue arrow: Neuron (400x magnification). **Notes : C** (Control group), T1 (group exposed to Carbofuran 1/4 $LD_{50}$ 0.0125 mg/day), T2 (group exposed to vitamin C 5 mg + Carbofuran 1/4 $LD_{50}$ 0.0125 mg/day), T3 (group exposed to kebar grass extract 3.375 mg + Carbofuran 1/4 $LD_{50}$ 0.0125 mg/ day).

**Rebuttal Letter**
Research in Pharmaceutical Sciences
Editorial Office

I am submitting a revision of manuscript entitled "Beneficial effects of Kebar grass (*Biophytum petersianum* Klotzsch) ethanol extract to increase motor reflex and spatial memory in mice offspring (*Mus musculus*) from lactating mothers exposed to carbofuran" (manuscript number is RPS_209_21). I corrected the manuscript (reviewer 1: red text, reviewer 2: green text, reviewer 3: blue text, editor: violet text):

**Reviewer 1**

1. I have checked carefully for typographical and grammatical mistakes in all parts of the manuscript.
2. In the abstract, I have improved the conclusion, not only repeated the results.
3. I have changed the keywords according to MeSH words.

4. I have changed to writing the complete form of a phrase for the first time and then writing the abbreviated form of it.
5. I have written in a purposeful and constructive way in the introduction section.
6. The innovation of this research is to prove that there is a transmission of carbofuran metabolites through mother's milk to children during 14 days of lactation on brain function in breastfeeding. Another innovation is the administration of Kebar grass extract as an antioxidant to prevent oxidative stress due to the toxic substance carbofuran. Previous studies have proven that the transmission of carbofuran metabolites occurs on brain development during gestation (Luqman et al. 2019. Mouse (*Mus Musculus*) embryonic cerebral cortex cell death caused by carbofuran insecticide exposure) and treatment of kebar grass extract as an antioxidant to prevent oxidative stress due to toxic substances in reproductive system (Rusyawardani et al. 2020. Effect of Kebar Grass (*Biophytum petersianum*) Extract on the Seminiferous Tubules in Male Mice (*Mus musculus*) Treated With 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD).
7. In the method section, I have summarized and unnecessary items have been removed.
8. I will explain how to choose these doses of Kebar grass or carbofuran and give references.
9. I have added that mice aged 10 days were used in the experiment.
10. In this study, using mice aged 30 days (PD 30) while in another study using mice aged 3-4 weeks (PD 21-28) (Chaim G Pick and Joseph Yanai. Eight Arm Maze for Mice. The International journal of neuroscience 1983. 21(1-2):63-6. DOI: 10.3109/00207458308986121. While other researchers used rats that were 40 days old (PD 40) (M. Salami, Z. Aghanouri, M. Noureddini and AA Rashidi, 2008 Early Dark Rearing Influences Spatial Performances in the Radial Arm Maze Journal of Medical Sciences, 8: 699-706 DOI: 10.3923/jms.2008.699.706). So the use of mice aged 30 days (PD 30) is still relevant to be used in this test.
11. The RPS journal limits the number of references so that not all chemical and behavioral assessment methods are required references. Certain chemical and behavioral assessment methods require references.
12. I have explained the statistical issues in the results more prominently and interpreted them in the discussion of the article.
13. I prefer to display data in tables rather than charts. The data in the table can show the main data while the chart only shows the total number or the average number.
14. In the table, I have explained the legends and significant values and signs related to between group differences.
15. I have interpreted the results in the discussion more in depth, analyzed and confirmed the behavioral and histological results by biochemical results obtained in this study, and confirmed them with previous studies.
16. The final conclusion, I have corrected and written conclusively, not only refers to the results.

**Reviewer 2**

1. In the abstract, as part of the experimental approach, I converted "40" from numerical to "letters" form.
2. I have checked carefully for typographical and grammatical mistakes in all parts of the manuscript.

3. I have changed to writing the complete form of a phrase for the first time and then writing the abbreviated form of it.
4. I have eliminated "laboratory" from the "materials part."
5. I have added a research protocol in time line view.
6. In the introduction section, it was written that carbofuran could increase MDA and GSH (The increased level of GSH in cardiac muscles may contribute to improve the antioxidant defense mechanism evolved by the animal system to protect it from the damage caused by free radical-mediated oxidative stress (Jaiswal SK, Sharma A, Gupta VK, Singh RK, Sharma B. Curcumin Mediated Attenuation of Carbofuran Induced Oxidative Stress in Rat Brain. Biochem Res Int. 2016; 7637931.doi: 10.1155/2016/7637931. In the results and discussion section, it was stated that the Kebar grass extract treatment could reduce MDA and GSH.
7. I have explained "a, b, c, and d" in the legends and significant values and signs related to between group differences.
8. The article mentioned in the 3rd reference was exposed for 10 days without any combination of treatment. Meanwhile, articles that are submitted are exposed for 14 days followed by treatment.

**Reviewer 3**

1. I have changed the title clearly, completely and mentioned the type of Kebar grass extract.
2. I have added the type of memory in the title and in the Materials and Methods section.
3. I have added the P values in each significant case in the abstract section.
4. In the introduction section, I have given the reason and explained of selecting Kebar grass for the purpose of the study.
5. I have explained how to choose these doses of kebar grass or carbofuran and give references.
6. H&E histochemical image quality has been replaced.
7. Requests for data related to molecular tests to evaluate the apoptosis in brain tissue will be used in other manuscripts to compare cell death between apoptosis (intrinsic and extrinsic pathway) and autophagy.
8. I have added the values of P in the tables of the result section.
9. I have checked carefully for typographical and grammatical mistakes in all parts of the manuscript.

**Editor**

1. I have decreased the number of references to 30.
2. I have provided all the references according to RPS format.
3. I have provided the acknowledgement section, in the manuscript file.
4. A figure had different Capital/UPPERCASE letters in Times New Roman, solid black or white, and bold to each part at the top left corner.

There are some of the same corrections from the reviewers:

1. The explanation of "a, b, c, d" in the legends and significant values and signs related to between group differences.
2. The checked for typos and grammatical mistakes in all parts of the manuscript.
3. The P values in each significant case in the abstract and result section.

Yours Sincerely,
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## View Notification Detail

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Dr Epy Luqman,
Research in Pharmaceutical Sciences has received your revised manuscript entitled '[ARTICLE_TITLE].'
The manuscript will be re-evaluated by concerned referees for the final decision regarding its suitability for publication. We will get back to you within four weeks.
We thank you for submitting your valuable research work to Research in Pharmaceutical Sciences.
With warm personal regards,
The Editorial Team
Research in Pharmaceutical Sciences

## View Notification Detail

**Subject:** Manuscript for revision: RPS_209_21
**To:** epy-m-l@fkh.unair.ac.id
**From:** editor@rpsjournal.net
**CC:**
**Recieved:** Sunday, January 9, 2022

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Dear Dr Luqman,
With reference to your manuscript RPS_209_21 entitled Beneficial effects of Kebar grass (Biophytum petersianum Klotzsch) ethanol extract to increase motor reflex and spatial memory in mice offspring (Mus musculus) from lactating mothers exposed to carbofuran , please review the comments of the referees from our site https://review.jow.medknow.com/rps. The manuscript would be reconsidered after requisite modifications as per the comments and instructions provided by the journal.
If you wish to continue with the publication process, kindly make the changes according to the comments and upload the revised manuscript along with clarifications for all the comments clearly indicating the areas where the changes have been made.
Do check the FAQ regarding replying to the comments and uploading a file. The template of point-by-point comments files for the reviewers, is available in your dashboard under the 'Downloads' menu option.
The journal allows three weeks for the revision of the manuscript. If we do not hear from you within this period, we will consider it as your decision to withdraw your article from publication. Please also note that the submission of the revised article does not guarantee its final acceptance by the journal.
We thank you for submitting your valuable research work to Research in Pharmaceutical Sciences.
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With warm personal regards,
Editorial Team
Research in Pharmaceutical Sciences

# RPS-209-21 Final editing phase

External

Inbox

R

**RPS <rps@pharm.mui.ac.ir>**

Fri, Feb 25, 2022, 11:34 PM

to me

Dear Dr. Luqman

I hope everything is going well  with you
Your article entitled "**Beneficial effects of kebar grass (*Biophytum petersianum* klotzsch) ethanol extract to increase motor reflex and spatial memory in mice offspring (*Mus musculus*) from lactating mothers exposed to carbofuran**" is in the editing process. However, there are some points and modifications which should be considered carefully before proofing this manuscript. Please see the attachment and do the best changes and modifications according to the comments mentioned in the text. Also please inform that all changes and modifications must be performed. You are kindly requested to perform all your changes via Track change mode and return the modified manuscript within one week.
Thank you in advance for your cooperation.

Sincerely
Bahar Samiee
Assistant Editor of RPS Journal
School of Pharmacy and Pharmaceutical Sciences
Isfahan University of Medical Sciences
Isfahan, Iran

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**Jaber Emami (Pharm.D, Ph.D)**
**Professor of Pharmaceutics and Biopharmaceutics**
**Editor-in-Chief of Research in Pharmaceutical Sciences**
**Department of Pharmaceutics**
**School of Pharmacy and Pharmaceutical Sciences**
**Isfahan University of Medical Sciences**
**Isfahan, I.R. Iran**
**Tel: 0098 - (313) 792-7111**
**Fax: 0098 - (313) 668 – 0011**
**E-Mail:** emami@pharm.mui.ac.ir
rps@pharm.mui.ac.ir

## View Notification Detail

**Subject:** Author-side fee of your manuscript:RPS_209_21
**To:** epy-m-l@fkh.unair.ac.id
**From:** editor@rpsjournal.net
**CC:**
**Recieved:** Tuesday, March 1, 2022

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Dear Dr Luqman,
We are pleased to inform that your manuscript "Beneficial effects of Kebar grass (Biophytum petersianum Klotzsch) ethanol extract to increase motor reflex and spatial memory in mice offspring (Mus musculus) from lactating mothers exposed to carbofuran " is now acceptable after clearing the dues for publication of the manuscript. The details of the same can be found on the journal website under ‘Instructions to the Authors’ page.

The payment can be done using the following link:
https://prepayment.medknow.com/uniprr/index?apicaller=UNIPRR
The following options are available for payment:

- Pay online
- Cheque payment
- Wire transfer

Once the payment is received at our end, the manuscript would be processed further and you would receive an edited version of article in about 2-3 weeks from now for a final check and correction.
We thank you for submitting your valuable research work to Research in Pharmaceutical Sciences.

- With warm personal regards,

Yours sincerely,
Editorial Team
Research in Pharmaceutical Sciences
CLOSE

## View Notification Detail

**Subject:** Author-side fee received...:RPS_209_21
**To:** epy-m-l@fkh.unair.ac.id
**From:** editor@rpsjournal.net

**CC:**
**Recieved:** Thursday, March 31, 2022

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Dear Dr Luqman,
We have received the payment for "Beneficial effects of Kebar grass (Biophytum petersianum Klotzsch) ethanol extract to increase motor reflex and spatial memory in mice offspring (Mus musculus) from lactating mothers exposed to carbofuran " and you would receive an edited version of article in about 2-3 weeks from now for a final check and correction.

Editorial Team
Research in Pharmaceutical Sciences

# Fwd: RPS 209-21 Galley proof

External
Inbox

R

**RPS Journal** <rpsjournalisfahan@gmail.com> Sun, Mar 13, 2022, 12:12 AM

to me

RPS 209-21 Galley proof

Subject: Proofs of [RPS 209-21]

Dear author We have finalized the above-mentioned manuscript for publication in the forthcoming issue of the RPS. Please note that certain details of page layout may still need to be amended before printing. However, the final, printed product will conform to our usual high standards for page layout and image resolution.We would be thankful for returning these proofs with your corrections **(via TRACK CHANGE MODE)**, by email Please respond within **2 working days** (even if you have no corrections), indicating the article number on all correspondence. We may proceed with publication of your article if no response is received. With many thanks in advance for your cooperation.
Kind regards,

**Jaber Emami (Pharm.D, Ph.D)**
**Professor of Pharmaceutics and Biopharmaceutics**
**Editor-in-Chief of Research in Pharmaceutical Sciences**
**Department of Pharmaceutics**
**School of Pharmacy and Pharmaceutical Sciences**
**Isfahan University of Medical Sciences**
**Isfahan, I.R. Iran**
**Tel: 0098 - (313) 792-7111**
**Fax: 0098 - (313) 668 – 0011**
**E – Mail:** emami@pharm.mui.ac.ir
rps@pharm.mui.ac.ir

**One attachment** • Scanned by Gmail

**epy muhammad luqman <epy-m-l@fkh.unair.ac.id>**

Sun, Mar 13, 2022, 1:26 AM

to RPS

I sent the revision proofs of [RPS 209-21] (attached). I have also sent a similar file at the request of Professor Jaber Emami (Pharm.D, Ph.D). Thank You

--

Dr. Epy Muhammad Luqman
Badan Kerjasama dan Manajemen Pengembangan
Universitas Airlangga
mobile : +628123090594

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