OPEN PEER REVIEW

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As a new feature for progressing towards transparency, we decided to open a new window for all of our editors as well as authors titled "**Peer Review**". We hope by this new facility, our reviewers will be more motivated and authors will be more satisfied with the review process. We believe that publishing our peer review reports could make a transparent and clear environment for all our efforts within a journal, but not all reviewers tend to publish their comments.

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- Authors' satisfactions from the review process: Increases honesty between authors and reviewers
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Peer Review

International Journal of Cancer Management
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Peer Review Report for "Ameliorative Effect of the Combination of the *Cichorium intybus* Whole Extract and Melatonin on Doxorubicin-induced Hepatotoxicity in Mice"

Author(s): Parisa Kiani Amin, Siamak Mashhady Rafie, Saeed Hesaraki, Kumarss Amini

Review Timeline:

Submit Date:	3 Oct 2021
Revised Date:	7 Mar 2022
Accepted Date:	13 Mar 2022

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE : Reviewer

8 Feb 2022

Dear secretary
I am proposing my points as:
Add significant markers to table1.
This manuscript does not seem to have been a literary or scientific theft. In addition, all references in the text are used and updated. There is a connection between the results and the photos or graphs. The discussion also has a logical connection with the text. The novelty of this study is that both antioxidants were used simultaneously.
Best regards

REFEREE : Reviewer

8 Feb 2022

Dear Secretary
There are no plagiarism abuse in this manuscript.
The referencing and citations is correct may be according to endnote style.
The English writing is good in structures.
I accept this article.
I suggest some changes to do in this article:
1. Please change the title to “Protective effect of the coadministration of the Cichorium intybus extract and Melatonin on Doxorubicin-induced hepatotoxicity in Mice”.
2. Recheck the mean quantities of total bilirubin in the control and chicory groups.
Reviewer Abbas Javaheri

REFEREE : Associate Editor

14 Feb 2022

Dear EIC,
According to the comments of the reviewers, this manuscript can be published in the IJCM journal.

REFEREE : EIC

5 Mar 2022

Dear author,
for access to the review comments please see the attached file. Also Abbreviations should be used sparingly and must be introduced in parentheses upon" first mention" in "abstract "and " full text" and also the abbreviations in the tables should be introduced in the table footnote.

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dear reviewer number 1

As you wanted to do the changes in results, we change this highlighted paragraph according your mention.

Best regards

Results: The mean sum of histological grading in the control group was 0.00 in contrast to severe damage of the hepatic parenchyma grading 11.34 in sum. The mean sum grade of the other groups include Chicory, Melatonin and Both Chicory-Melatonin were 8.17, 4.18, and 2.49 respectively. We found that the increased liver damage and TNF-α expression induced by DOX could be improved by apply therapeutic care with coadministration of the C. intybus extract and Melatonin.

Dear reviewer number 2

As you wanted to do the changes in Table and text, we operate these highlighted changes according your mention.

Best regards

3.6. Statistical analyses

First, the data obtained from the study were presented as the Mean ± SD and then analyzed by SPSS 22 using the one-way analysis of variance (ANOVA) followed by Bonferroni test for parametric data and the Kruskal–Wallis one-way analysis of variance test for non-parametric data. P-values less than 0.05 were considered as statistically significant.

Table 1. Effect of a DOX (15 mg/kg ip) alone or in combination with drugs on serum biochemical Parameters in mice. Data are mean ± SD, and analysis was done by Kruskal–Wallis for AST, GGT and Total bilirubin and one-way analysis of variance test for ALT and ALP.

Groups	AST (unit/l)	ALT (unit/l)	GGT (unit/l)	ALP (unit/l)	Total Bilirubin (mg/dl)
Control (Saline)	215.75 ± 100.20[a] (%CV = 46.44)	80.50 ± 14.27[a] (%CV = 17.72)	0.25 ± 0.50[a] (%CV = 2.0)	225.75 ± 141.54[a] (%CV = 62.69)	19.25 ± 8.53[b] (%CV = 44.31)
DOX	221.00 ± 65.84[b] (%CV = 29.79)	102.00 ± 76.63[b] (%CV = 75.12)	1.17 ± 1.94[b] (%CV = 1.65)	307.67 ± 33.90[b] (%CV = 11.01)	15.17 ± 5.15[b] (%CV = 33.94)
Chicory	150.80 ± 24.50[b] (%CV = 16.24)	62.40 ± 6.46[a] (%CV = 10.35)	0.40 ± 0.54[a] (%CV = 1.35)	214.2 ± 117.69[a] (%CV = 54.94)	32.80 ± 23.59[a] (%CV = 71.92)
Melatonin	49.67 ± 17.94[b] (%CV = 36.11)	129.33 ± 18.03[a] (%CV = 13.94)	0.50 ± 0.54[a] (%CV = 1.08)	184/83 ± 95.64[a] (%CV = 51.74)	16/0 ± 3.16[b] (%CV = 19.75)
Both	67.60 ± 11.86[b] (%CV = 8.57)	125.67 ± 10.78[a] (%CV = 8.58)	0.60 ± 0.54[a] (%CV = 0.9)	254.6 ± 61.35[a] (%CV = 24.09)	11.5 ± 1.73[b] (%CV = 15.04)

Both: DOX + Chicory / Melatonin; **a: significant difference from DOX; b: significant difference from a**

Table 2. Histopathological score of hepatic tissues from mice received high doses of DOX (15 mg/kg). They treated by Chicory extract and Melatonin. Scoring was performed as 0 = absent; 1 = low or weak; 2 = mild; 3 = moderate; and 4 = high or frequent, and also the total score. Data are mean ± SD, and analysis was done by Kruskal–Wallis one-way analysis of variance test.

Groups	Necrosis	Leucocyte infiltration	Vacuolar degeneration	Congested blood vessels	Total score
Control (Saline)	0.00 ± 0.00[a]	0.00 ± 0.00[a]	0.00 ± 0.00[a]	0.00 ± 0.00[a]	**0.00[a]**
DOX	3.67 ± 0.51[b] (%CV = 14.10)	1.83 ± 0.75[b] (%CV = 41.10)	2.50 ± 1.22[b] (%CV = 48.80)	2.17 ± 0.75[b] (%CV = 34.70)	**11.34[b]**
Chicory	2.17 ± 0.75[c] (%CV = 34.70)	1.33 ± 0.5[b] (%CV = 38.70)	1.33 ± 0.51[c] (%CV = 38.34)	1.50 ± 0.54[b] (%CV = 36.50)	**8.17[c]**
Melatonin	1.67 ± 0.51[c] (%CV =	0.67 ± 0.51[c] (%CV = 77.50)	1.00 ± 0.00[c] (%CV = 00.00)	0.67 ± 0.51[a] (%CV = 77.50)	**4.18[d]**

	31.00)				
Both	0.83 ± 0.75^{a} (%CV = 90.30)	0.33 ± 0.51^{d} (%CV = 0.00)	1.00 ± 0.00^{c} (%CV = 00.00)	0.33 ± 0.51^{a} (%CV = 154.90)	**2.49^{d}**

Both: DOX + Chicory / Melatonin; **a: significant difference from DOX; b: significant difference from a**

Table 3. Immunohistochemical evaluation of TNFα in the hepatic tissues was based at the percent of stained area in all mice (groups) that described in the histopathology. Data are mean ± SD, and analysis is carried out using one-way anova.

Factor	Control (Saline)	DOX	Chicory	Melatonin	Both
TNFα %	12.26 ± 1.35^{a}	17.54 ± 0.70^{b}	17.27 ± 0.95^{b}	14.72 ± 0.66^{c}	13.59 ± 0.98^{ac}

Both: DOX + Chicory / Melatonin; **a: significant difference from DOX; b: significant difference from a; c: significant difference from a and b**

OPEN PEER REVIEW

Revision (1)

REFEREE : EIC

13 Mar 2022

Dear Author,

This is my pleasure to announce you that your article has been accepted by the editorial committee after peer review in the International Journal of Cancer Management (IJCM). Hopefully, it will be published in future issues.