Author’s response to reviews

Title: Efficacy and safety of Curcuma longa essential oil to inactivate hydatid cyst protoscoleces

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Author’s response to reviews:

• Reviewer 1

1- By considering this fact that all protoscolices are dead after 20 min (Table 2). There is no need to evaluate the viability in time 30 min. Also, there is no consistency between Table 2 and Fig. 2.

Response: The authors should be thankful for your valuable comments. Revisions were made in the text. Regarding no consistency between Table 2 and Figure 2; the figure 2 shows the results of ex vivo test, whereas Table 2 shows the results of in vitro; therefore the results may be different.

2- How many protoscolices does every experiment tube contain in M&M?

Response: As we mentioned in the text the number of protoscoleces per mL was adjusted to 2×103 protoscoleces in a 0.9% NaCl solution and we used 0.5ml of this suspension.

3- Please add the new references in the text such as:
a- The seroprevalence rate and population genetic structure of human cystic echinococcosis in the Middle East: A systematic review and meta-analysis (2018)

b- Natural products applied against hydatid cyst protoscolices: a review of past to present (2017)

Response: The related references were added to the text as respected reviewer recommended.

- Reviewer 3

Mayor shortcomings

1) Proper use of English language requires more attention. I recommend that someone who speaks English as their first language carefully edit your manuscript. The MS cannot be accepted in the actual form.

Response: Throughout the manuscript was improved as respected reviewer suggested.

2) Although the authors evaluate the intraperitoneal toxicity of the essential oil in mice; in contrast, during hydatid cysts surgery and/or PAIR, the potential communication between the hydatid cyst and the biliary tree substantially increases the safety requirements for using protoscolicides, which can cause chemical cholangitis leading to frequently fatal subsequent sclerosing cholangitis, as it occurs when formalin is used (WHO/OIE Manual on Echinococcosis in Humans and Animals: a Public Health Problem of Global Concern. WHO-OIE., Ekert et al. (Eds), 2001.); thus, this potential adverse aspect needs to be stated and analyzed with more relevance.

Response: Revisions were made in the text.

3) Page 6, Lines 43-44. Figure 1 does not give relevant information. Give a reference in Methods section. I suggest remove this figure and add, instead figures comparing the viability of control protoscoleces vs treated protoscoleces (in Results section).

Response: Many thanks for your valuable comments. The related Figure was added to the Results section.
4) Scanning electron microscopy of protoscoleces could provide more information related to the changes provoked by the essential oil.

Response: We would like to thank you for your constructive comment. However, due to the lack of equipment and financial supports we could not able to perform the SEM as respected reviewer suggested.

5) Please revise the conclusion (abstract and text). It seems too early to state this: "therefore it might be applied as a natural protoscolicidal drug for surgeons in hydatid cyst surgery".

Response: Revision was made in the text and abstract.

6) Page 8, lines 39-40. "esthetized by Ketamine-Xylizine". This is no clear. Anesthetized? How did the animals were euthanized? By cervical dislocation? Please explain. Moreover give the doses of the cocktail of ketamine-xylazine.

Revisions were made in the text as below: “animals were fasted overnight and anesthetized by Ketamine (100mg/kg) – Xylizine (10 mg/kg); in the next step, sodium pentobarbital (70 mg/kg, i.p.) was applied as euthanasia drug; then…..”.

1) Page 3, Lines 12-13. Delete " (World Health Organization".
Revision was made in the text

2) Page 3, Lines 32-33. motionless cysts?? Explain.
Revision was made in the text

3) Page 4, Lines 51-53. Change "the mice model" to "mice".
Revision was made in the text

4) Page 6, lines 28-29. Change "the protoscoleces were washed in duplicate" to "protoscoleces were washed twice".
Revision was made in the text