**Author’s response to reviews**

**Title:** Effect of Nigella sativa and Its Bioactive Compound on Type 2 Epithelial to Mesenchymal Transition: A Systematic Review

**Authors:**

Abid Nordin (m.abid.nordin@gmail.com)

Haziq Kamal (kamalnteel@gmail.com)

Muhammad Dain Yazid (dain@ppukm.ukm.edu.my)

Aminuddin Saim (aminuddin_saim@yahoo.com)

Ruszymah Idrus (ruszyidrus@gmail.com)

**Version: 2 Date:** 09 Sep 2019

**Author’s response to reviews:**

We appreciate the time and efforts taken by the editor and reviewers in reviewing this manuscript. We have addressed all the issues indicated in the review report, and hopefully the revised version can meet the journal publication requirements.

Reviewer’s comments:

On line 27 (page 2), the word "overview" should be replaced with "review".

Authors’ Response:

We appreciate the reviewer opinion in this matter.

We would like to invite the reviewer to consider the aforementioned word in context.

The full sentence was “This systematic review is conducted to provide an overview regarding the reported effect of Nigella sativa and its bioactive compound on the type 2 EMT.”

“Overview” according to Oxford dictionary is “a general review or summary of a subject”. In the above context, the authors were reiterating the aim of this systematic review that attempts to provide “a general review or summary of a subject”, namely the reported effect of Nigella sativa and its bioactive compound on the type 2 EMT.

Next we would like to invite the reviewer to consider the impact of replacing the word “overview” with “review”.
The full sentence will be “This systematic review is conducted to provide a review regarding the reported effect of Nigella sativa and its bioactive compound on the type 2 EMT.” This can be shortened, if we may, into “conducting a review to provide a review”, which we believe to sound redundant. With that, we respectfully rebut this suggestion.

Reviewer’s comments:

In the abstract, the part of results and discussion should be combined into one part according to guidelines for manuscript submission.

Authors’ Response:

We thank the reviewer for the comment. We have combined the results and discussion part of the abstract into one on line 35 (page 2).

Reviewer’s comments:

There are some grammatical mistakes throughout the article. For example, on line 71 (page 4), "a review has been" should be replaced with "a review was".

Authors’ Response:

We thank the reviewer for the comment. We’ve sent the manuscript for proofreading and the following were made:

1. Comma was added between “bounded to their basal membrane” and “into non-polarized cell” on line 53 (page 3).

2. “EMT classification have been” was changed into “EMT classification has been” on line 58 (page 3).

3. Comma was added between “during gastrulation and neurulation” and “whereby the cell transition” on line 60 (page 3).

4. Addition of the article “were” between “secondary epithelial cells” and “involved in organogenesis” on line 62 (page 3).

5. Comma was added between “the production of ECM by the fibroblast” and “to help rebuild the damaged tissue site” on line 64 (page 3).

6. “EMT have been specifically” was changed into “EMT has been specifically” on line 68 (page 4).
7. The suggested "a review has been" was changed into "a review was" on line 71 (page 4).
8. The plural “epithelial markers” was changed to singular “epithelial marker” on line 72 (page 4).
9. The plural “mesenchymal markers” was changed to singular “mesenchymal marker” on line 73 (page 4).
10. The sentence “In terms of the elevation of mesenchymal marker, candidates such as fibroblast specific protein-1 (FSP1), discoidin domain receptor tyrosine kinase 2 (DDR2) or fibronectin has been listed” was edited into “The transition into mesenchymal phenotype was also indicated by the elevation of other mesenchymal markers such as fibroblast specific protein-1 (FSP1), discoidin domain receptor tyrosine kinase 2 (DDR2) or fibronectin.” on line 74 (page 4).
11. "a review on the molecular markers of EMT has been" was changed into "a review on the molecular markers of EMT was" on line 80 (page 4).
12. Addition of “namely the” before “repression of E-cadherin and activation of N-cadherin” on line 86 (page 4).
13. Spelling change from “dihyrdothyoquinone” to “dihydrothymoquinone” on line 98 (page 5).
14. Spelling change from “Sativa” to “sativa” on line 98 (page 5) and line 108 (page 5).
15. “studies that reports” was changed into “studies that report” on line 131 (page 6) to comply with subject-verb agreement.
16. Removal of “In terms of wound healing, inflammation and fibrosis, most model existed in vivo, and few in vitro.” that was not related to the exclusion criteria on line 132 (page 6).
17. The word “papers” was changed to “articles” on line 134, 135, 136, and 137 (page 7) of the data extraction and management.
18. Removal of apostrophe from “it’s bioactive compound” on line 149 (page 7).
19. Use of past tense in describing Figure 1 on line 153 (page 8).
20. Use of past tense in describing result findings on line 157 (page 8).
21. “investigate” was changed into “investigated” on line 165 (page 8).
22. “investigated on” was changed into “investigated” on line 167 (page 8).
23. “studies that models” was changed into “studies that model” on line 170 (page 8) to comply with subject-verb agreement.

24. “Phenotypic changes … enables” was changed into “Phenotypic changes … enable” on line 194 (page 10) to comply with subject-verb agreement.

25. Italicize the word “Nigella sativa” on line 211 (page 10).

26. Use of past tense in describing result findings on line 243 (page 12).

27. Use of past tense in describing result findings on line 248 (page 12).

28. Addition of the word “phase” on line 248 (page 12).

29. “to induced” was changed into “to induce” on line 252 (page 12).

30. Change the word “alongside” to “as well as” on line 274 (page 13).

31. “increased” was changed into “increase” on line 276 (page 13).

32. “seen reduced” was changed into “seen to be reduced” on line 285 (page 14).

33. “to resolved” was changed into “to resolve” on line 296 (page 14).

34. The word “namely” was added to reiterate the category and its list on line 299 (page 15).

35. Use of past tense in discussing the findings on line 375 (page 18).

36. “All of the inflammation study” was change into “All of the inflammation studies” on line 389 (page 19).

37. “focus” was changed into “reported” on line 389 (page 19).

38. “Among the experimental model” was change into “Among the experimental models” on line 390 (page 19).

39. Addition of hyphen into “down-regulation” on line 394 (page 19).

40. “Nigella sativa oil demonstrate” was changed into “Nigella sativa oil demonstrates” on line 394 (page 19) to comply with subject-verb agreement.

41. “properties of Nigella sativa was” was changed into “property of Nigella sativa was” on line 399 (page 19) to comply with subject-verb agreement.

42. Use of past tense for study conclusion on line 415 (page 20).

Please let us know if there is anything else that we missed.
Reviewer’s comments:

On line 120 and 121 (page 6), authors wrote that "with type 2 epithelial mesenchymal transition in an" and "inflammation or tissue fibrosis that". What is the words after "in an" or "that"? They are not complete sentences or expression.

Authors’ Response:

We thank the reviewer for the query. The paragraph that contains the sentences above described the inclusion criteria used in this review.

The sentences were clauses that made up a single continuous sentence “only primary studies that reported the association between Nigella sativa or thymoquinone with type 2 epithelial mesenchymal transition in an experimental model of wound healing, inflammation or tissue fibrosis that measures changes in the expression of the EMT markers were included.” Hence, words that come after each clause is the next clause labeled with number. The numbers were added to ease the identification of the three criteria used to select the paper.