

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 62945

Title: Thymoquinone Anticancer Activity is Enhanced when Combined with Royal Jelly in Human Breast Cancer

Reviewer's code: 00505457

Position: Peer Reviewer

Academic degree: MD

Professional title: Professor

Reviewer's Country/Territory: Germany

Author's Country/Territory: Lebanon

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Reviewer chosen by: AI Technique

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The authors Moubarak et al. assessed the influence of Thymoquinone (TQ) and Royal Jelly (RJ) alone and their combinations in different doses on cell viability, cell cycle regulation and apoptosis in MDA-MB-231 human metastatic breast cancer cells. The main finding is the enhanced anticancer effect of Thymoquinone (TQ) in combination with Royal Jelly (RJ) in human breast cancer. This is the first study describing a synergistic effect between TQ and RJ. The results could be useful for further drug development studies. The study is well structured, clear and understandable. There are only minor suggestions for correction:

- Abstract: Methods: all abbreviations should be explained (MTT, IC50) Results: The need for investigating the effect of RJ on FHS 74 Int small intestinal cells should be explained before; in the background or aim. The use of this cell line appears here for the first time.
- Introduction: Page 5: The first 2 sentences on this page are a repetition. I suggest to reconsider the 2 sentences starting with TQ.
- Materials and Methods: Materials: You should explain the need for use of FHs 74 cell line in the Introduction. Furthermore, the reader could better follow if you mentioned that the toxicity experiments on these cell lines were already performed in a previous study with TQ (also in the Introduction).
- Drug preparation and treatment: You wrote: 16,4 mg/ml of TQ crystals in 1 mL methanol. It should rather be: 16,4 mg of TQ crystals in 1 ml methanol to get a concentration of 16,4 mg/ml. Why does the stock solution have this concentration? For the assays: Why did you use the concentrations described, why max 15 μ M TQ? What happened in a combination of RJ with 20 or more μ M TQ? This remains unclear throughout the whole study. You should shortly explain the reason why you did not present the effects of TQ doses > 15 μ M.
- Immunofluorescence assay, page 10: Please declare the abbreviations (DAPI).
- Results: page 11: RJ exerted mild inhibitory effects at low doses of RJ (...) - please define low doses. Consider splitting the sentence in



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2 sentences as it is quite long and difficult to understand. page 14, Figure 2: (...)values corresponding to the % cell death of FIVE different combinations - You use the arabic sign for 5 :)