Author's response to reviews

Title: Daucus carota pentane-based fractions arrest the cell cycle and increase apoptosis in MDA-MB-231 breast cancer cells

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Author's response to reviews: see over
Dear Editor,

On behalf of my co-authors, I would like to appreciate the valuable comments raised by the referees on our manuscript (MS: 7878794731214650) entitled ‘Daucus carota pentane-based fractions arrest the cell cycle and increase apoptosis in MDA-MB-231 breast cancer cells’ submitted to BMC Complementary and Alternative medicine.

We have addressed all reviewers’ comments point-by-point and we hope that the Editors and the Reviewers will be satisfied with our response. Please find attached a revised version of the original manuscript.

With my sincere regards,

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Reviewer 1:

Major criticism:

The present work seems to be the extension of the last part of the earlier work published in Phytotherapy Research in 2013. However, in the present study authors have evaluated the cell cycle arrest and apoptosis of cancer cell lines using various approaches. In order to study the efficacy of the compound in vivo, animal studies are strongly recommended.

This paper is indeed a continuation of our work on the crude oil extract of Daucus carota spp. carota (Pharmaceutical Biology, 49(9): 955-961. 2011; Phytotherapy Research. 27(5): 737-744. 2013). In the present manuscript, we evaluated the anticancer activity of the most active fractions of the oil extract and took the work a step further by establishing their mode of action. Ongoing work in our laboratory is indeed focused on isolating the potentially potent anticancer agent. As for the suggestion of reviewer 1, we agree with him that in vivo studies are required to study the efficacy of the fractions, but we feel it is not needed at this stage because of two reasons.

1- The efficacy of the Daucus carota oil in vivo was proven by our team when tested on mice and showed a significant reduction in tumor size and occurrence in DMBA-TPA-induced squamous skin carcinoma model (Pharmaceutical Biology, 49(9): 955-961.
Logically, next step would be to fractionate the crude oil and track the biologically active fractions in vitro. Further chromatography is being conducted in our lab to isolate the major active compound(s).

2- In vitro studies were adopted at this stage to minimize animal waste when possible. Chromatography resulted in four fractions with varying potencies. Conducting animal studies on all resulted fractions will cause a big waste of animals, which we cannot justify ethically. According to the University Animal Ethical Committee, we only do animal testing if truly needed. Therefore, we are planning for the in vivo experiments as soon as we isolate the major active compound.

Minor criticism:
Furthermore, cell lines listed in the figure legends do not match the figure headings. For instance, figure 1 shows the antitumor activity of various fractions in HT 29 and Caco 2 cells whereas figure legend describes them as MDA-MB-231 and MCF-7 cells. Similar discrepancy exists in Fig 4A where HT-29 should be listed as MDA-MB-231 and Figure 4B is completely missing.

We apologize for this mistake. There was a mistake in uploading those figures. We uploaded figures related to colon cancer cells instead. This is now fixed.

Reviewer 2:

1. Cell lines described in the M& M, results and Figure legend are breast cancer lines (MCF7 and MDA-MB-231), however the figure-1A, 1B; figure-3 and figure-4 is shown for HT-29 and Caco-2 (colorectal cancer cells).

We apologize for this mistake. There was a mistake in uploading those figures. We uploaded figures related to colon cancer cells instead. This is now fixed.

2. No cell line details are given for Figure-2, -5, -6 and 7 in the figure, but in legend section it indicates the use of MDA-MB-231 cells.

The cells are indeed MDA-MB-231 cells.

3. Figure legends: Figure-4B is missing.

This was fixed.