Author’s response to reviews

Title: Immunomodulatory and Antitumour Effects of Abnormal Savda Munziq on S180 Tumour-Bearing Mice

Authors:

Ainiwaer Aikemu (ainiwa@sina.com)
Anwar Umar (anwar.umar@126.com)
Abdiryim Yusup (abdiryim@hotmail.com)
Halmurat Upur (Halmurat@263.net)
Benedicte Berké (benedicte.berke@pharmaco.u-Bordeaux2.fr)
Bernard Bégaud (bernard.begaud@u-bordeaux2.FR)
Nicholas Moore (nicholas.moore@pharmaco.u-bordeaux2.Fr)

Version: 2 Date: 4 March 2012

Author’s response to reviews: see over
Immunomodulatory and Antitumour Effects of Abnormal Savda Munziq on an S180 Tumour-Bearing Murine Model

MS: 1076773560614272

Response to reviewers and editor

Pr Nicholas Moore, MD, PhD, FRCP (Edin)
Reviewer: Leticia V Costa-Lotufo

Reviewer's report:

The manuscript described the immunomodulatory and antitumor effects of a Chinese medicinal herbal preparation called Abnormal Savda Munziq using sarcoma 180 bearing mice. Although the interest in the research field is unquestionable, the manuscript present many limitations that make it unsuitable for publication in the BMC Complementary and Alternative Medicine.

The major point that should be considered is the absence of a proper chemical characterization of the material studied. How this preparation is standardized?

ASMq is a traditional Uyghur medical preparation, that is described in the chinese pharmacopoeia. The preparation we used is commercially available from the Qikang Habo pharmaceutical company. It is prepared according to the GMP as applicable to herbal medicines, as specified in the introduction, and has a patent. It has been approved for marketing by the Chinese Medicines administration. We have added a table with the herbal composition.

Is there any active compound described?

Because it is a standardized mixture of ten medicinal herbs, there is no individualized active compound, as is often the case for traditional medicines, especially multi-herbal preparations.

Additionally, the used doses are too high.

I am not certain how the reviewer concludes that the doses are too high. Does she have dose-response data on which this is based, or is it just based on principles? the g/kg magnitude is common for oral administration of herbal medicines. In a previous study of colon cancer, we had used doses of 400, 800 and 1600 mg/kg (0.4, 0.8, 1.6 g/kg) of an ethanol extract of the product, in rats. Here we use the whole product in mice, which have a faster metabolism, so a five-time ratio of doses between the whole product in mice and an ethanol extract in rats may not be thought excessive.

Another inconsistent point is the references. For example, they mention references 3-7 in the introduction as the ones related to the previous studies of ASMq cytotoxicity. However, none of cited references mentioned ASMq preparations in the text.

You are perfectly right. There seems to have been a problem with these references and with others. All the references have been reviewed.

The discussion is generally a repetition of results section.
This has been rewritten and very much simplified.

**Level of interest:** An article of limited interest

**Quality of written English:** Not suitable for publication unless extensively edited

I have again reviewed and rewritten the paper, with my apologies. The paper was originally in Chinese, and some sinisms remained. I have tried to get rid of all of them.

**Statistical review:** No, the manuscript does not need to be seen by a statistician.
Reviewer: Takashi Kumagai

Reviewer's report:

The authors investigated the anti-cancer activity of ASMq against S180 cells in vitro, and concluded that this herbal formula inhibited the tumor growth in the transplanted mice without cytotoxicity, associated with increased serum TNF-alpha, IL-2beta and IL-2.

The manuscript is well described, and contains important findings for the progress in herbal medicine.

But there are some concerns to be addressed for publication.

In the abstract, the authors described “survival” in line 8,

Indeed that came from a previous version of the paper, and has been removed

and “The ASMq in the presence of .... plasmid DNA to fragment” in line 11. What are backgrounds for these descriptions?

Again the same problem, for which I apologize. We have shown this effect on DNA in another study on another model, but this somehow polluted the present paper. We had left the abstract verification for the last, and obviously missed out on it.

The abstract has been completely rewritten.

Minor Comments

Material and methods: 2.2 line 6; Please define control group and model group briefly.

Control group is a group of mice that were not implanted with the tumour, and did not receive ASMq; model was a group of mice that were implanted with S180 cells, but did not receive ASMq.

This has been modified in the description of methods.

2.5 & 2.6 ; Please describe more about the MTT assay and FCM the authors used.

This has been improved, hopefully, in the methods, with references to other papers where the team used them
Results

3.1; How the authors evaluated the activity and mental state of the mouse?
Is the body thin or not?
Is the skin and hair shiny?
Do the animals have a normal appetite?
Do the animals display irritability?

Please describe how the authors calculate the tumor growth velocity (TS).
A ruler was used to measure tumour size daily, plotting the tumour size against time.

3.2 line 9; Please describe what “the immune systems” mean.
This has been removed. It meant immune system markers.

3.5 line 2; All groups’ CD4 data decreased ....compared to control group. There are no * in table 4.
The significance had been unfortunately removed. This has been corrected.

Discussion

Last paragraph, line 5; a Chinese herbal medicine is deemed effective ......30% and above. This description needs a reference.
OK reference added.

☐ Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.
Thank you
Editorial requests
-----------------------
Title page- Please include a title page in the manuscript file, this should include: the title, the author list, the affiliation details for all authors, the details of the corresponding author, and the email addresses for all the authors.

Done

Abstract: Please include the abstract in the second page of the manuscript file.

Done

Introduction ? Please rename this section Background.

Done

Competing interests - Please include a "Competing interests" section between the Conclusions and Authors' contributions. If there are none to declare, please write "The authors declare that they have no competing interests”.

The questions that are asked of authors are:
Financial competing interests
In the past five years have you received reimbursements, fees, funding, or salary from an organization that may in any way gain or lose financially from the publication of this manuscript, either now or in the future? Is such an organization financing this manuscript (including the article-processing charge)? If so, please specify.

Do you hold any stocks or shares in an organization that may in any way gain or lose financially from the publication of this manuscript, either now or in the future? If so, please specify.

Do you hold or are you currently applying for any patents relating to the content of the manuscript? Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript? If so, please specify.

Do you have any other financial competing interests? If so, please specify.

Non-financial competing interests
Are there any non-financial competing interests (political, personal, religious, academic, ideological, intellectual, commercial or any other) to declare in relation to this manuscript? If so, please specify.

Authors' contributions ? Please include an Authors? contributions section within the manuscript file after the Competing interests and provide a brief summary of each author's contribution to the study.
We would be grateful if you could address the comments in a revised manuscript and provide a cover letter giving a point-by-point response to the concerns.

Done

As you will see, both reviewers have raised substantial concerns about the study. While we are ready to allow a round of revisions on the manuscript, please note that further consideration is dependent on the submission of a revised manuscript that fully and thoroughly addresses the concerns raised by the reviewers. We therefore expect you to provide details regarding the characterization of the extract and a justification for the doses employed in the revised manuscript.

This is not an extract but the actual commercial product that is produced industrially according to Chinese Good manufacturing practices concerning herbal medicines. The composition of the preparation has been patented and is described in the patent. We have added a table of the plants used in the preparation.

The doses are similar to those used for treatment of human diseases, and in line with the experience in the treatment in colon cancer in rats, taking into account differential metabolism between species, and the difference between ethanol or water extracts and the whole product (see response to reviewer 1).

Please also ensure that your revised manuscript conforms to the journal style (http://www.biomedcentral.com/info/ifora/medicine_journals). It is important that your files are correctly formatted.

We have reformatted the whole manuscript into the BMC template.