Reviewer’s report

Title: In vitro antioxidant and antiproliferative effect of the extracts of Ephedra chilensis K Presl aerial parts

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Reviewer: Mariana Belen Joray

Reviewer's report:

The present research article describes the phytochemical profile, antioxidant capacity and cytotoxic effect of three extracts obtained from Ephedra chilensis, including a GC-MS analysis of the most active extracts. The obtained results are very encouraging not only because of the potency of the active products, which in some cases resulted higher than the positive control (doxorubicin), but also because of the high selectivity that these extracts shown particularly in the case of the antitumor effect of the non-polar extracts against MCF-7 and PC-3 cells. Although I recommend this article for its publication in BMC Complementary and Alternative Medicine, there are some suggestions in order to improve the quality of the manuscript.

1. In first place, an exhaustive revision of the english language is needed all along the manuscript, title included. I highly recommend the correction by a native speaker.

2. The aim of the manuscript was to evaluate the cytotoxic activity of different E. chilensis extracts and establish relationships between this effect and the antioxidant activity. The phytochemical composition of the extracts was also explored and correlated with the mentioned effects. Three extracts with different polarity were obtain from E. chilensis with Hexane, dichloromethane and ethanol. The phytochemical content of each extract in terms of total anthraquinones, flavonoids, and phenolic compounds was determined using colorimetric assays. CH2Cl2 extract showed the highest anthraquinone and flavonoid content. While EtOH and CH2Cl2 extracts showed the highest content of phenolic compounds. Regarding the antioxidant activity, the EtOH and CH2Cl2 extracts showed an effect comparable to or even better than the positive controls Trolox and Gallic acid. This effect showed to be correlated with total phenolic content, while the other constituents did not correlate with this property. When the cytotoxic activity was evaluated against a panel of tumor cell lines, MCF-7 and PC-3 cells were the most affected by Hex and CH2Cl2 extracts. In general terms, both mentioned extracts showed a similar grade of activity against the evaluated cell lines. On the other hand, the ethanol extract was the less effective one. The reported cytotoxic effect is very interesting not only in terms of the low IC50 values obtained but also the selectivity observed when selectivity indexes were calculated for Hex and CH2Cl2 extracts over MCF-7 and PC-3 cells. However, only the most active extracts were analyzed by GC-MS. Even though in a first moment this decision makes total sense, it would be of a great value to have the information regarding the ethanol extract in order to see if any conclusion can be done in
terms of compounds that may or may not be present in the ethanol extract. In my particular experience, ethanol is a solvent in which most of the components of the plant material will be extracted, including the polar and non-polar ones (these last with a lower yield than when extracted with no polar solvents, of course), though it is possible that since the ethanol extract shows cytotoxic effect (much lower than the others but present), the activity can be due to one or more active principles that are more concentrated in the non-polar extracts and diluted by the other components in the ethanol one. So, including the CG-MS profile of the ethanol extract would be of great value in order to enrich the discussion related to the possible active principle since no activity guided isolation was performed (and as I understand was not contemplated in the aim of the article). The results are very well described but the discussion could be much more rich if an attempt to more deeply relate the three CG-MS profiles with the activity observed is done.

3. Peak number 5 and 9 in de CG-MS analysis profile of the n-hexane and CH2Cl2 extracts, respectively, correspond to the same compound but named with different nomenclatures, one should be chosen and use in both tables.

4. For a better presentation of the information, in the discussion section, first paragraph, discussion should be more focused on the phytochemical composition and avoid comments regarding the cytotoxic effect and introduce them in the third paragraph were this activity is discussed.

5. On the other hand, in the fourth paragraph of the same section, more information should be discussed about the components that the active non polar extracts have in common like the n-tetradecanoic acid and the hexadecanoic acid ethyl ester (palmitic acid ethyl ester) and also make an effort to link these aspects with the %Area of the corresponding peaks.

6. In paragraph 5 and 7 of the same section, authors describe and discus compounds that are only present in the CH2Cl2 extract. These paragraphs could be combined in one. On the other hand, in paragraph 8 there is a mistake since 6,10-dimethyl-2-undecanone is not present in CH2Cl2 extract but it is present in the hexane extract. So this information should be properly checked and corrected.

7. Finally, the conclusions will need to be revised according to the new information incorporated to the manuscript.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
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