Author's response to reviews

Title: Antiproliferative activity and induction of apoptosis by Annona muricata (Annonaceae) extract on human cancer cells

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Author's response to reviews: see over
To whom it may concerned

Object: Submission of the manuscript

Dear Sir

I the undersigned corresponding author of the manuscript title “Antiproliferative activity and induction of apoptosis by Annona muricata (Annonaceae) extract on human cancer cells” hereby declare that the manuscript which is submitted for publication in the BMC Complementary and alternative Medicine has been corrected.

Yours sincerely

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Comment of reviewer’s report

Title: Antiproliferative activity and induction of apoptosis by *Annona muricata* (Annonaceae) extract on human cancer cells

**Minor Essential Revisions**

1. **Abstract:**
   - membrane mitochondrial potential (MMP) and the cell cycle were used for apoptosis induction
   *Correction has been done*
   - sub-G01 apoptotic fraction and the G0o/G1 cell arrest # sub-G01 and G0o/G1 
   *Correction has been done*
   - membrane mitochondria potential # MMP
   *Correction has been done*

2. **Background**
   - *Annona muricata* L commonly known # *Annona muricata* L (A. muricata) commonly known
   *Correction has been done*
   - All parts of the Graviola (Annona) tree are # All parts of A. muricata are
   *Correction has been done*
   - against Human promyelotic leukemia (HL-60 cells) # against Human promyelocytic leukemia (HL-60 cells)
   *Correction has been done*

3. **Materials and Methods**
   - Yaounde, capital city of Cameroon # Yaounde, capital city of Cameroon
   *Correction has been done*
   - The total phenol was determined # The total phenol was determined
   *Correction has been done*
   - Mixture was kept in the dark--. Mixture was kept in the dark
   *Correction has been done*
   - as mg quercetin (QE)/g of dried material # as mg quercetin (QE)/g of dried material.
Correction has been done
- received only the vehicle (DMSO < 0.1%) # received only the vehicle (dimethyl sulfoxide [DMSO] < 0.1%).

Correction has been done
- For PC-3 cells, the molecules were added after 24 h of incubation….# please delete all sentences regarding PC-3 cells that is no longer used cell lines in this article.

Correction has been done
- The cells suspension was kept in the incubator (Thermocom Electron Corporation, USA) at 37°C, 5% CO2; 98% humidity # 37°C needs correction

Correction has been done
- because of membrane mitochondrial potential loss was analyzed # because of MMP loss was analyzed

Correction has been done
- please express the same way: choose G0-G1 vs G0/G1 and G2-M vs G2/M…

Correction has been done
- One way analysis of variance technique was applied # please add some comment on the distribution of the data.

4. Results:
- The interest on plant phenols is increasing in the recent decade because of their health promoting potential. It is widely known that diets containing an abundance of phenols have protective effects against a variety of diseases, particularly cardiovascular disease and cancer # these sentence(s) looks not adequate for result section; please move them to introduction or discussion section.

Correction has been done
- Novel strategies for determination of natural products with biological activity require the implementation of large-scale screening programs # these sentence(s) looks not adequate for result section

Correction has been done

- A. murica # A. muricata
- Nucleosomal DNA fragmentation is the result of activation of endogenous endonuclease # these sentence(s) looks not adequate for result section; please move them to methods section.

- The intrinsic pathway can be triggered by many stimuli including ROS. Mitochondria are the major site of ROS production and the accumulation of ROS may lead to the initiation of apoptosis # these sentence(s) looks not adequate for result section; please move them to introduction or methods section.

- Mitochondrial integrity or the loss of ##m has been linked to the initiation and Activation of apoptotic process. To determine whether A. muricata extracts induced apoptosis in HL-60 cells through mitochondrial disruption, we examined the depolarization of mitochondrial membrane by measuring the fluorescence emission shift (red to green) of the ##m sensitive cationic Rh-123 dye # these sentence(s) looks not adequate for result section; please move them to methods section.

- Figs 4A, B & C # Figures 4A, B & C.

- 17.34 % # it this right? (17.43?)

- 17.34 % to 98.91 % (Yes between 20 – 100 µg/mL of extract)

- However dose-dependent increase of fluorescence observed is ranging from 17.34 % to 98.91 % (Figures 4A, B &C) # I think this range is for Figure 4B only.

In addition, I do not understand the meaning of this sentence. What do you mean by starting with [However]?

- (21 %) # (21.75 %)

- (98 %) # (98.29 % and 98.91 %, respectively).

- To determine if the extracts of A. muricata induced cell growth inhibition was due to an
arrest at a specific point of the cell cycle, the flow cytometric analysis was carried out to quantify the apoptosis and the cell cycle distribution. These sentence(s) look not adequate for results section; please move them to methods section.

Correction has been done

-apoptotic phase (G0) # (G0) needs correction

Correction has been done

5. Discussion
- Among, these extracts the roots # Among these extracts the roots

Correction has been done

- Figs 5A, B, C # Figures 5A, B, C

Correction has been done

6. Legend
- please describe the meaning of [ctrl]

Correction has been done

- please describe the meaning of [app]

Correction has been done

- A. murica # A. muricata

Correction has been done

7. Figures
- μg/ml # μg/mL

Correction has been done

- ml # mL

Correction has been done

- please use the same font in the same figure

Correction has been done

8. Others:
- Please check the error by yourself once more

Correction has been done