Reviewer's report

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

Version: 4 Date: 16 October 2014

Reviewer: WAN KYU EO

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Minor Essential Revisions

1. Abstract:
   - membrane mitochondrial potential (MMP) and the cell cycle were used for apoptosis induction # membrane mitochondrial potential (MMP) and the cell cycle were used for assessment of apoptosis induction
   - sub-G01 apoptotic fraction and the G0o/G1 cell arrest # sub-G01 and G0o/G1 needs correction
   - membrane mitochondria potential # MMP

2. Background
   - Annona muricata L commonly known # Annona muricata L (A. muricata) commonly known
   - All parts of the Graviola (Annona) tree are # All parts of A. muricata are
   - against Human promyeoltic leukemia (HL-60 cells) # against Human promyelocytic leukemia (HL-60 cells)

3. Materials and methods
   - Yaounde the capital city of Cameroon # Yaounde, capital city of Cameroon
   - The total phenol was determined # The total phenol was determined
   - Mixture was kept in the dark--. Mixture was kept in the dark
   - as mg quercetin (QE)/g of dried material # as mg quercetin (QE)/g of dried material.
   - received only the vehicle (DMSO < 0.1%) # received only the vehicle (dimethyl sulfoxide [DMSO] < 0.1%)
   - 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.
   - The cells suspension was kept in the incubator (Thermocom Electron Corporation, USA) at 37°C, 5% CO2; 98% humidity # 37°C needs correction
   - because of membrane mitochondrial potential loss was analyzed # because of MMP loss was analyzed
- please express the same way: choose G0-G1 vs G0/G1 and G2-M vs G2/M…
- 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.

- 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
- 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 % # (17.43?)
- 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) looks not adequate for result section; please move them to methods section

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

5. Discussion
- Among, these extracts the roots # Among these extracts the roots
- Figs 5A, B, C # Figures 5A, B, C

6. Legend
- please describe the meaning of [ctrl]
- please describe the meaning of [app]
- A. murica # A. muricata

7. Figures
- μg/ml # μg/mL
- ml # mL
- please use the same font in the same figure

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

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

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

Declaration of competing interests:
'I declare that I have no competing interests'