Reviewer's report

**Title:** Anti-angiogenic potential of an ethanol extract of Annona atemoya seeds in vitro and in vivo

**Version:** 3  **Date:** 3 August 2014

**Reviewer:** Rajaa El Bekay

**Reviewer's report:**

In this manuscript Jin-Mu Yi and coauthors studied the anti-angiogenic potential of an ethanol extract of Annona atemoya seeds both in vitro and in vivo. The authors describe that EEAA was able to significantly inhibit the angiogenic properties of HUVECs in vitro as well as angiogenic factor-induced blood vessel formation in vivo. EEAA down-regulated the expression of VEGF and HIF-1alpha/2alpha at the mRNA and protein levels, respectively, in cancer cells under hypoxic conditions. Finally they concluded that EEAA shows a strong anti-angiogenic potential in both in vitro and in vivo systems, and we suggest that EEAA may be a valuable herbal source for anticancer drug development.

The Question posed by the authors is well defined, and the methodology is appropriate and well described although the mechanisms underlying of the anti-angiogenic effects of EEAA on HUVEC were not fully detailed. The manuscript adheres to the relevant standards for data deposition.

Discussion and conclusions are adequately supported by the data, but they should be shortened, there are many repetitions throughout the text.

The writing of this manuscript is acceptable.

**Minor changes**

Material should be removed from supplemental information and placed in the main text.

In discussion section, authors should remove all sentences that were already stated in results section. For example: HIF-1#. NCI-H460 tumor cells were subjected to a hypoxic environment (1%O2) to mimic physiological tumor conditions (page 16, line 11).

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**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