The rational used by the authors for the present study is the previous demonstration that the lack of iNOS in the apoE knockout model of hypercholesterolemia leads to a dramatic reduction in the size of atherosclerotic lesions and that Illicium verum, which is widely used for culinary and medicinal purposes, including conditions of inflammation. The authors clearly demonstrated beneficial effects of Illicium v. on pathogenic atherosclerotic plaques and vascular inflammation. Their data suggest that this natural product exerts beneficial effects probably through attenuation of the iNOS inflammatory response to atherosclerosis. Their data led to the conclusion that Illicium v. is a promising novel therapeutic drug for hyperlipidemia-atherosclerosis treatment.

- Major Compulsory Revisions

Introduction

The rational and questions posed by the authors in the Introduction section are well defined, but the authors should take in account that in addition to anti-inflammatory drugs, there are other agents that can reduce the occurrence of atherosclerosis without altering blood lipid profiles in this murine model. For instance, studies such as that from Leal MA et al. Mechanisms of enhanced vasoconstriction in the mouse model of atherosclerosis: the beneficial effects of sildenafil. Curr Pharm Biotechnol.2015;16(6):517-30, could improve this section.

Methods

Comment 1.
The authors stated, “Blood was collected from the aorta under light anesthesia”. My concerning is about the ethical problems collecting blood samples under light anesthesia. How or in which vessel was it collected?

Comment 2.
It is not clear the division of animal groups. The authors say that the mice fed on high fat diet were divided into 5 groups: control, high fat diet saline, Illicium v 100, Illicium v. 200 mg/kg and atorvastatin. However, when one looks at the tables and figures, they are labeled as Con, HFD, illicium 100, illicium 200 and atorvastatin. It looks like only one group is HFD and that Con is not a HFD, which is not true. For example in the above text, the authors stated that all animals
were HFD but in table 1 the authors talk about a control without HFD. Thus, the authors should labeled in more clear way the different groups.

Comment 3.
If the Con is without HFD, why this group (Table 2) exhibits ~500 mg;dl of cholesterol?

Comment 4.
Table 2 show a lipid profile different from most of the data that have been published.
For example, these values for the group HFD are very different from those published by Balarini et al. Journal of Translational Medicine 2013, 11:3.

Comment 5.
The authors must give a clear information to the reader in the methods section and figure legend about which part of the aorta was the focus of the analysis and quantification of the lipid deposition.

Statistical analysis
The authors stated that they used ANOVA for repeated measures in all experiments. However, they do not say clearly if it was one or two-way ANOVA. For instance, panel B of figure 2 and 3 do not look like appropriated for repeated measures Anova but a two-way Anova. It should also say which statistical program was used.

Results.
Comment 1.
What about the heart rate? Was it modified by the treatments?

Comment 2.
In the section 3.4. Illicium v. attenuates formation of atherosclerotic plaque lesions, the authors do not indicate in which figures are the data

Comment 3.
Could the authors explain why there are not significant differences among the values shown in table 1A? The means look like very different (0 vs. 100 groups) and the SEM very small. The same question is for graph B group 10.

Comment 4.
The graph of Fig 2A is correctly presented in the line format, because it is a temporal data. However, Fig 2B should not be presented as a line format because it deals with independent data in the X-axis.

- Minor Essential Revisions

Title
Although ApoE-/- is well known, it is recommended to do not use the abbreviated form. I would suggest to use “apolipoprotein E knockout mice”

Tables and Figures
Most of the values of table 2 should not be separated with decimals (example: 1,112,00 should be 1.112)
Similarly, values at Y-axis labels show a non-necessary decimal.

**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' below