Reviewer's report

Title: Suppression of low-density lipoprotein oxidation, vascular smooth muscle cell proliferation and migration by a herbal extract of Radix Astragali, Radix Codonopsis and Cortex Lycii

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Reviewer: Hsiu-Chung Ou

Reviewer's report:

Chan et al. present a study in which they test the ability of herbal extract of Radix Astragali, Radix Codonopsis and Cortex Lycii to suppress LDL oxidation and vascular smooth muscle cell proliferation. The paper is written and organized well and the results are easy to follow. However, there are a few things that need to be clarified.

My specific comments are below:

Major comments:

1. There are several different components of SR10 that may be responsible for protection against oxidative modification of LDL and PDGF-BB-induced proliferation and migration. Are any specifics known about which may be more likely to be participating in their model?

2. How easy would it be to achieve comparable levels of SR10 in vivo as were used on this study, and what is known about the beneficial effects of these doses in humans with atherosclerosis? The authors make no mention as to whether these mg/ml concentrations used in the in vitro study could ever be reached in the body after consumption of SR10. Thus the question as to whether the author's results reflect pharmacological phenomena rather than physiologically useful effects exists for this study. At the very least this issue needs to be discussed in this manuscript or references provided that could shed some perspective on the results of this study as related to the concentrations of SR10 used.

3. The authors mention about ROS and ERK-mediated signaling pathways play important roles on smooth muscle proliferation in background, however, there was no data exploring whether ROS and ERK signaling are involved in the effects of SR10 on suppression of oxidative modification of LDL and PDGF-induced proliferation and migration, it is therefore unclear whether SR10 is in fact acting through ROS and ERK pathway to confer it's protection.

4. During mitogenic stimulation, cell cycle progression is initiated by induction of cyclin D, following by induction of cyclin E and A, activation of cdk4 and cdk2, and phosphorylation of Rb. In addition, the cdk inhibitors, P53 and its downstream protein P21 and P27, serve as negative regulators that inhibit
cyclin/cdk activity and phosphorylation of Rb, resulting in G1 arrest. Why only cycline D1 was selected for determination in this study? The author should provide more details mechanisms to elucidate how SR10 modulate the expression of G1 cell cycle-regulating proteins in smooth muscle cells stimulated by PDGF.

Minor comments:

1. Some references did not match with statement, for example, in Methods section, cell proliferation assay, “MTT assay was performed to measure the cell viability” cited with reference 10; in Methods section, Western blot analysis of cyclin D1, “The experiment was performed as described previously” cited with reference 14.

2. In Methods section, Measurement of LDL peroxidation, copper (II) chloride is not consistent with CuSO4 in Fig 2. legend.

3. In Fig. 5B, no statistical data are given in the immunoblotting of cyclin D1.

4. In Fig. 6A, it will be better to recognize where the migrated cells are if the authors put arrows for indication.

**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'