Reviewer's report

Title: Standardized butanol fraction of WIN-34B suppresses cartilage destruction via inhibiting the production of matrix metalloproteinase and inflammatory mediator in osteoarthritis human cartilage explants culture and chondrocytes

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Reviewer: YUN JONG LEE

Reviewer's report:

Minor essential revisions

1. The duration of cartilage explants culture was 21 days and the conditioned media was collected at 7, 14, and 21 day. And, GAG and type II collagen assays were done at 7, 14, and 21 day (Figure 3). Please, correct the description about the time of these assays in Methods.

2. Cytotoxicity was determined in cartilage explants using LDH test and in isolated chondrocytes using BrdU test, according to Method section. But, the legend of Fig 2. says that “cytotoxicity of IL-1b ... healthy peripheral blood mononuclear lymphocytes...”. Does Fig 2B. present the cytotoxicity effect in PBMC or chondrocytes?

3. To evaluate the effect on MAPK pathways, chondrocytes were cultured and stimulated, according to Method section. However, the legend of Fig. 7. says that cartilage explants were used. Which is right?

It is important to interpret the results – if Fig. 2B presents the cytotoxicity for CA or MF in isolated chondrocytes, a high concentration of these compounds was toxic to chondrocytes. Because changes in MAPK pathways could be affected by other stimuli other then inflammatory IL-1b, comparison between WINI-34B and CA or MF seems not appropriate.

4. Above all, they did not show any scientific evidence on the concentrations used in in-vitro experiment. Because it is a major limitation of this study, the authors should address the issue in Discussion.

1) Ten ng/mL of IL-1b is a very high, supraphysiologic level – Fig 3 showed that 1-2.5 ng/mL was adequate for the stimulation of cartilage explants.

2) If higher concentrations of the compound are needed to diffuse into the cartilage and make an effect on chondrocytes, further higher levels should be administered in in-vivo study. But, they showed the cytotoxic effect of CA and MF, the major lipophilic component of WIN-34B, in PBMC.

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