Reviewer’s report

Title: Berberine moderate glucose metabolism through GnRH-GLP-1 and MAPK pathway in intestine

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Reviewer: Lihong Fan

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Berberine is the main active component of an ancient Chinese herb Coptis chinensis French, which has been used to treat diabetes for thousands of years. The efficacy of berberine for treatment of type 2 diabetes has been confirmed in several clinical trials, but the exact underlying mechanism is not clear. In this study, the authors investigated the effect of berberine on glucose metabolism in diabetic rats and concluded that berberine may moderate blood glucose and insulin secretion through decreasing GnRH-GLP-1 pathway. It makes sense for the authors to provide such a preliminary explanation for the pharmacological mechanism of berberine.

- Major Compulsory Revisions
  1. The authors propose the hypothesis that berberine acts directly in the terminal ileums, and suppresses gastrointestinal movement. Could the authors provide some more direct evidence? such as the observation of gastrointestinal movement after berberine administration, etc.
  2. The authors have done immunohistochemical straining for the detection of GLP1R and MAPK10. To give more convincing evidence, the authors should provide the western blotting results of the examined proteins.

- Minor Essential Revisions
  The spelling mistakes or figure should be revised, the following are some examples:
  1. p.3 “glucosereducing” should be “glucose reducing”
  2. p.11, (FDR=1.01-13). “-13” should be superscript.
  3. In Figure 4, the size of the immunostaining pictures for GLP1R and MAPK10 should be adjusted to the same.

- Discretionary Revisions
  None

Level of interest: An article of importance in its field

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.