Reviewer’s report

Title: Multi Component Chinese Medicine Jinzhida improve cognition by reducing endoplasmic reticulum stress and increasing insulin signal transduction in type 2 diabetic rats

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Reviewer: Sawsan Abuhamdah

Reviewer’s report:

Reviewer Report
Journal: BMC Complementary and Alternative Medicine
Reviewer: Dr Sawsan Abuhamdah, The University of Jordan (s.abuhamdah@ju.edu.jo)
Authors: Xiaohui Chang, Lina Liang, Libin Zhan, Xiaoguang Lu, Xiang Shi, Xin Qi, Zhaolan Feng, Meijuan Wu, Hua Sui, Luping Zheng, Fulaing Zhang, Jie Sun, Changchuan Bai, Nan Li and Guozhu Han.

Title: Multi Component Chinese Medicine Jinzhida improve cognition by reducing endoplasmic reticulum stress and increasing insulin signal transduction in type 2 diabetic rats.

Major Compulsory Revisions

The author must respond to these before a decision on publication can be reached. For example, additional necessary experiments or controls, statistical mistakes, errors in interpretation.

1- Title does not reflect the idea of research properly and suggested to be replaced with red one.

2- Number of authors for the article are too much (8), also there is mismatch between the covering letter (15 authors) and authors listed in the article.

3- No abbreviations should be used in the abstract part, such as T2DM-DM, (ERS). JNK (FSI) (ITT)

4- Authors also must be consistent in (JZD) abbreviation used in the article as it is sometimes written between brackets and sometimes not, see abstract section.

5- Conclusions in abstract is not correct,

6- Proposed mechanism is that JZD reduce ERS and improve insulin signal transduction and insulin

7- This conclusion not clear? How it is demonstrated in results!

8- 6-Key words: are very weakly selected:

9- Suggested to be changed to the following:

10- Diabetes, cognitive decline, step down test, Morris water, immunobloting
analysis Hippocampus.

11-Reference no 1 in the introduction section is quite old, 2010, should be replaced with new statistics about this prevalence of diabetes.

12-Cognitive decline & diabetic encephalopathy (DE) are mixed termed used throughout the article. Authors should select only one term and use in all the text.

13-Large numbers of abbreviations used in the introduction section
   Without listing these meaning. Suggested to have a list for all.
   Such as: DE, T2DM, GRP78/Bip and activate JNK, AD IRS-1

14-The term: the activity of Jun NH2-terminal not understood.

15- May and colleagues: not clear?? Our team or our lab.

16- (TCMs) TCMs, same abbreviation, but not consistent

17-This paragraph not written correctly, needs revision.

Multi-component Chinese medicine theory is a new theory system of TCMs, which was firstly put forward by the Tianjin University of Traditional Chinese Medicine Zhang Boli professor in 2006[12]. It is based on TCMs theory, following the Chinese medicine prescription compatibility

When assessing the work, please consider the following points:

1. Is the question posed by the authors well defined?

   Yes, but the use of multi component medicine, is difficult way to study the pharmacological effect especially in complex structure like the brain, in addition constituents lack scienctic evidence for selection of these herbal constituents and ratios. Are these constituents only gave effect when present together, does single constituents alone tested and was unsuccessful.

2. Are the methods appropriate and well described?

   No, methods and techniques weekly presented,

   compatibility formula. The Multi component Chinese Medicine Jinzhida (JZD) from green tea, ginseng and polygala are complex extracts made of theanine, tea polyphenols, ginsenosides and polygalic acid and were

   How the formula is considered compatible, how plants constituents were authenticated properly?

   Authors in methods descried the use of three doses 39 mg/kg, 104 mg/kg and 390 without justification why the section of these numbers???
Were the mixed herbal constituents soluble in water???

Eight week-old male should be corrected to Eight weeks-old male

a high-fat diet (source is lacking)

Authors were not clear with the name of control rats: sometimes called these rats challenge group, mock group, other places called treatment group. Are these represents same group.

What means by the HDE group in Improvement of behavioral by JZD paragraph

How many rats used for the study is not clear and confusing.

randomly divided into three treatment groups and a mock treatment group of 7 each. Rats in the three treatment groups received different concentrations of JZD 1ml/100g orally twice a day for 35 days. The DE and control (Cont) group rats #10 rats# received isotonic Na chloride as control

22 treatment.

3 treatment plus control will be 7 by 4 = 28.
How many for control group 7 or 10.
Why no control to be diabetic without treatment.

Behavioural experiment listed without any background of the test, and aims of using this or its importance in cognitive decline testing and memory, not in the methods section or introduction, the reader will not know the link between these and the study.

There should be clear paragraph about these two important behavioural test, why to use two tests instead of one, each should highlight important point in conclusions and results.!!! These all lacking in the text.

The protein concentration in the supernatant was detected using a UV spectrophotometer (NanoVue TM, GE Healthcare, USA).

Information is lacking about the assay, and reference, for example Lowry assay or Bradford???

Source of all chemicals used the study are all lacking, tris, sample buffer NaCL........

Western blot analysis
No idea how antibodies types have been selected?????

The relative intensities were calculated by dividing by anti-# actin. Not correct statement
After 35 days treatment, time of experiment was not clear. And behavioural testing D1 and D2 ?? this is confusing

We obtained the similar results in the retention test (Table 2). in Improvement of behavioral by JZD paragraph

What is the retension test???

3. Are the data sound?

Idea of the paper is great, but data analysis was so bad to get a conclusion.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?

Yes it follows the rule of : abstract, introduction, methods, results and discussion

Aim of the study is poorly highlighted at the end of introduction section.

Results & discussion is poorly understandable.

5. Are the discussion and conclusions well balanced and adequately supported by the data?

First paragraph in discussion is not correct and needs rewriting. No similar pathological deficit in both diseases

In recent years, clinical and experimental studies have demonstrated similar pathological changes in AD and DE [22, 23], including amyloid plaques and neurofibrillary tangles.

Tea paragraph needs rewriting

Tea as a traditional medicine was used in the Chinese medicine prescription has undergone a very this paragraph should be well cited

5 long history periods. The earliest Chinese medicine monographs, "Shen Nong 's Herbal Classic" has been recorded on the medicinal Green Tea “tea, bitter taste, drink make people think, littlelie, light-weight, eyesight,” Another famous ancient Chinese medical scientist Hua Tuo said in his book “food theory”, ”long term drinking tea could make people clever”. In addition, “Chuan-xiong-cha-tiao Fang” was also widely used as a famous tea therapy prescription. So green tea extracts, polyphenols and theanine, were used as the principal drug in the prescription11 of JZD.

What means by of replenishing the primordial qi,
6. Are limitations of the work clearly stated?
No limitation described for the work, and future direction.

7. Do the authors clearly acknowledge any work upon which they are building both published and unpublished?
In the introduction part
-the databases in English and Chinese were searched from their inceptions to February 2007. Which data bases authors means, not cited or referenced.

In the introduction part
-Each of these substances has a clear mechanism of action which has been shown to have neuroprotective functions.

For this important paragraph, reference is missing.

8. Do the title and abstract accurately convey what has been found?
• Title does not reflect the idea of research properly and suggested to be replaced with red one.
• Number of authors for the article is too much (8), also there is mismatch between the covering letter (15 authors) and authors listed in the article.
• No abbreviations should be used in the abstract part, such as T2DM-DM, (ERS). JNK
• Authors also must be consistent in (JZD) abbreviation used in the article as it is some times written between brackets and some times not in abstract section.
• Conclusions in abstract is not correct,
• proposed mechanism is that JZD reduce ERS and improve insulin signal transduction and insulin
  o This conclusion not clear? How it is demonstrated in results!

9. Is the writing acceptable?
• Many language errors. In introduction paragraph
• May and colleagues: not clear?? Should be Our team or our lab.
  •
  • (TCMs) TCMs, same abbreviation, but not consistent
• This paragraph not written correctly, needs revision.
• Multi-component Chinese medicine theory is a new theory system of TCMs, which was firstly put forward by the Tianjin University of Traditional Chinese Medicine Zhang Boli professor in 2006[12]. It is based on TCMs theory, following the Chinese medicine prescription compatibility
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• Aim of the study is poorly highlighted in the end of introduction section.

In statistical paragraph

A value of p<0.05 was considered to be statistically significant. Not correct should be

A p value of <0.05 was considered

Figure 2: legand describe A & B but not C &D.
Figure 3: Abbreviation on the figure not in the legand.
Figure 4: concs of antibodies use should be listed, should be labled as immunoblott of rat hipp
Figure 5 not clear, is it data analysis of immnublot figure 4.
Figure 6 & Figure 7 no lable, is it repetition or not

Final Decision:

Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Dr.Sawsan.Abuhamdah
Amman, Jordan
17 Feb/2013

Level of interest: An article of importance in its field

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

'I declare that I have no competing interests'