

OPEN PEER REVIEW REPORT 1

Reviewer 1: Gentian Vyshka, Faculty of Medicine, University of Medicine in Tirana, Albania **Comments to the authors:**

I have mentioned the weaknesses in the review; provided a thorough revision is made, I think the paper is not fit actually in its present form for publication.

The issue and arguments are of very high importance; however, it seems that several sources, are scrutinizing the effect and efficacy of different alleged protective agents with regard to neuroprotection against chronic high glucose level.

I suggest authors to include in the references, and above all, discuss and compare advantages and disadvantages of all available studies, mainly with regard to their methodology, reproducibility of results, and applicability in the clinical field; with regard to inclusion and mentioning of other sources I mean following papers (but not only):

- 1. Han J, Tan P, Li Z, Wu Y, Li C, et al. (2014) Fuzi Attenuates Diabetic Neuropathy in Rats and Protects Schwann Cells from Apoptosis Induced by High Glucose. PLoS ONE 9(1): e86539. doi:10.1371/journal.pone.0086539
- 2. Weijie Yao, Xinwei Yang, Jiayue Zhu, Biane Gao, Renhui Liu, and Liping Xu, "Tang-Luo-Ning, a Traditional Chinese Medicine, Inhibits Endoplasmic Reticulum Stress-Induced Apoptosis of Schwann Cells under High Glucose Environment," Evidence-Based Complementary and Alternative Medicine, vol. 2017, Article ID 5193548, 9 pages, 2017. doi:10.1155/2017/5193548

Under this precise aspect, the dedicated reader might find a diversity of agents, mainly from complementary or alternative medicine research; such a fact will produce confusion.

It is highly important therefore that authors group and mentions the main and most prestigious previous studies on the same theme; compare respective methodologies; and underscore the novelties that offer the actual manuscript.

Under the formal aspect of the paper, I do found very hard to understand the abstract, which is flooded with acronyms; some of them even not clarified at that stage (RSC96, ONOO-, CCK8); even if acronyms are explained in the main text later, abstract should be kept with a minimum of those, and when indispensable, clarified already at the very start of their usage.

Even in the abstract there is confusion on the terms vis-à-vis the title: do you mean nitrosation, or nitrosylation? If there is no important chemical difference within two terms, please be consistent and use only one.

The paper needs a thorough grammatical correction and editing (in the abstract there is written rsults, not results.... etc).

What do you mean with Japanese colleagues, Japan...; when talking about CCK8... is this a personal communication; a brand name; whatever?

There is no paragraph(s) with the subheading of 'conclusion'. This will render even more difficult for the reader - who will sustain a big burden to understand the scarcely detailed introduction and methodology - to pick up the novelties, the advantages, the benefits and the practical aspects of the potential clinical use of 3-N-Butylphthalide.