Reviewer’s report

Title: Melatonin and health: an umbrella review of health outcomes and biological mechanisms of action

Version: 0 Date: 29 Aug 2017

Reviewer: Rita Rezzani

Reviewer’s report:

The Authors in this manuscript critically evaluated the evidence from systematic reviews on the effects of melatonin on health and identify its potential mechanisms of action involved.

The present manuscript has a very interesting message and aim and the results are well explained and discussed. I think that the present review will help in a better understanding on the mechanisms of action of exogenous and endogenous melatonin.

Very good article. The manuscript has a clear message and it is well written. However, I have some minor and compulsory comments:

- there are few editing and misspelling errors in the text, check and correct them;

- control in all the text (included the Abstract) to report correctly the abbreviations;

- in all the text sometimes the numbers are write as digit and sometimes as letter, please formatted the text;

- the Authors used to define melatonin the term "hormone", but this term is not adequate, please correct with an appropriate definition (such as indoleamine);

- it will be better to not use abbreviation in the heading title.

Background

- page 3, lines 7-34: shorten/summarize this part about the light environmental because it is not the main topic of the review.

Introduction

- page 4, line 10: add also a brief explanation/definition of the physiopathological link between melatonin and aging.
Methods
- the Authors should explain why decided to start they research from year 1996 and not before;

Results
- briefly explain also in the text the data summarized in Table 1.

Effectiveness
- page 10, line 22: the Authors write that 6 SRs had very large levels of heterogeneity, but in the square brackets cited 7 reference (30-36), check and correct.

Melatonin receptor agonists
- page 12, line 12: add also a brief explain/define the melatonin receptor agonists cited (agomelatine, tasimelteon, ramelteon);

Discussion
- page 12, lines 53-55: briefly explain/discuss the sentence "except for some auto-immune conditions such as rheumatoid arthritis, asthma or organ transplant", also adding specific reference(s).

Mechanism of action
- page 13, lines 2-13: please provide one or more references for each melatonin effects.

Safety
- page 13, line 51: a table can help to summarize the adverse effects observed in the referred articles.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.
Unable to assess

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

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