Review of: "Antinociceptive activities of a novel diarylpentanoid analogue, 2-benzoyl-6-(3-bromo-4-hydroxybenzylidene)cyclohexen-1-ol, and its possible mechanisms of action in mice"

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Potential competing interests: The author(s) declared that no potential competing interests exist.

This is a study that aims to investigate the antinociceptive effect of a new compound on acute inflammatory pain and thermal stimuli in murine models. BBHC, a compound synthesized by the research group itself, when injected intraperitoneally, generates an important antinociceptive effect, compared to reference analgesic drugs, such as morphine and acetylsalicylic acid. BBHC was also effective against peripheral nociception with involvement of TRPV1 receptors, in addition to participating in the glutamatergic pain pathway.

Below are considerations about the work, which seems to have been very well conducted and which may be another step towards the discovery of a new potentially effective analgesic drug.

INTRODUCTION

1. Justification is relevant. Apparently, the group seems to be up to date on the process of creating a new compound and potential analgesic drug, in addition to constantly updating on the work generated in the laboratory.

2. In the introduction, I suggest clarifying the objective of the work, regarding the route of administration of the compound. It is important to situate the reader as to how the work is carried out: is it peripheral or central? Does it have an effect on local pain? Does it have effect in local injection, without systemic effect? As it is a new drug, it may be interesting to assess this point.

MATERIALS AND METHODS

1. The article makes it very clear how the synthesis of the drug was carried out, preparation of solutions, aspects related to the use of animals in research (authorization of the ethics committee for the use of animals in research, environmentalization of animals, allocation, number of animals per group) and the standardization of the technique.

2. Choice of study method is pertinent.

3. Again, I suggest performing an experiment relating the new compound to local action (eg using the formalin test itself or carrageenan or prostaglandin injection). In humans, the use of drugs is usually carried



out in a systemic way, but in veterinary medicine we have the local injection of drugs as an important way to contain pain. It would be interesting to expand the possibility of uses of BBHC. In addition, the mechanism of action of some analgesic drugs may vary when injected locally.

- 4. How was the pre-selection of the animals carried out? Size? Weight? Behavior? This needs to be detailed in the work so that there are no selection biases.
- 5. Choice of tests is relevant.
- 6. Figure I Better describe the image in the caption. What is I and what is II?

RESULTS

1. I suggest transforming Table 1 into a graph for better visualization of these results.

DISCUSSION

1. The tests are well explained at this point, as well as the inflammatory process generated in each of the tests, when applicable.

2. Good textual guidance: the description of the experiment, as well as the discussion of the results, was done in a chronological way, placing the reader in each of the phases of the experiment.

FINAL CONSIDERATIONS

The article was very well written, the tests were well performed, there was concern about ethics in the use of experimental animals. It is work that opens new perspectives for studies in pain and analgesia, as well as the creation of new analgesic compounds.

As a suggestion, to evaluate the involvement of BBHC in the cannabinoid, serotonergic, noradrenergic and dopaminergic systems, pathways described in the literature as potential drug targets for pain relief.