

# Review of: "Uncovering Insights Into the Bio-Efficiency of Zingiber Officinale Roscoe: Understanding Components That Contribute Significantly to Ginger's Anti-inflammatory and Antioxidant Potential in Relationship With Modern Drying Methods"

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Potential competing interests: No potential competing interests to declare.

The work deals with the evaluation of the components of ginger, their effectiveness in anti-inflammatory and antioxidant capacity, and the influence on these biological properties of modern drying methods.

The argument is not so original, since this drug has been well studied over the past years, particularly in relationship to the changes in phytochemical components with drying. For example, please check Dalsasso et al., 2022 (<https://doi.org/10.1016/j.foodres.2022.111043>).

In general, I saw several problems after reading the manuscript, starting from its rationale approach and in the methodology section. Moreover, some analytical data regarding the antioxidant capacity by the ABTS method and the scavenging of nitric oxide lack their description in the methodological section. The data and the discussion about the molecular docking evaluations are very interesting, although they have not been enforced by a careful data report and discussion of the GC-MS plots, from which these considerations are deriving. Only five lines have been dedicated to the data pattern of samples for GC-MS (see paragraph 3.1), where I have inferred that, as in paragraph 2.2.1, "Ligands were modeled via their nomenclature obtained from the GC-MS result." This is the central point of this manuscript, and this is valid for all the subsequent considerations regarding the interest section on the computational analyses in paragraphs 3.4, 3.5, and 3.6. (I repeat, the Authors have to better clarify why in paragraphs 3.5 and 3.6 only data on FD and OD samples are present, lacking data on RW ones. This is not clear for the reader.)

I have specifically asked the Authors to reply to the comments in a point-to-point manner, following the reported sequence of questions arising from the manuscript, here listed afterwards.

- The sentence in the Abstract "In general, the findings could imply that dried ginger has the ability to enhance the anti-inflammatory and antioxidant activities of ginger by 12.90-17.91% and 4-11.2%, respectively, when compared to the usual drugs Vitamin C and Aspirin." needs to be better explained in terms of relative concentrations, since the measured biological activity is strongly dependent on the concentration. What is the reference concentration of the assayed ginger extract? What are the concentrations of the reference compounds, vitamin C and aspirin? Please

rewrite the sentence.

- I ask the Authors to better explain the sentence “This drawback can impede investigations into the specific phytoconstituents responsible for ginger's bioactive properties.” Since it is not clear why possible problems in the drying of the drug can be negative for the investigations of the phytochemicals. For their absence or too low concentrations after drying? The investigations are possible in every case; the results can be very different, in my opinion. Please clarify.
- The sentence “Although freeze-drying is not cost-effective, it has been reported to minimize nutrient loss through vaporization, retain sensory properties (such as taste and aroma), and improve the shelf life more effectively than oven-drying and sun-drying techniques.” is not clear. It is known that freeze-drying, for its characteristics, can be effective in the retaining of non-volatile components, but sometimes can be detrimental to the volatile composition, with slight changes in comparison to other drying methods. Please check An et al., 2016, <https://doi.org/10.1016/j.foodchem.2015.11.033>.
- The sentence “This investigation will involve analyzing their interaction with human antioxidant and anti-inflammatory genetic receptors, and evaluating their ability to bind to these genes.” needs more clarification, especially with regards to the genes involved in the reported interactions between ginger phytocomponents and receptors. Are these genes those expressing these receptors? Or did the Authors want to express a different concept? Please clarify.
- As regards the section describing the plant material, some more information is needed about its cultivation. Where is the farm? How was the cropping managed, integrated, organic, or else? Was the farm an experimental farm or a commercial farm? How was the water supply to the cultivation managed? Was the ginger of a particular variety? How were the ginger samples for freeze-drying pre-frozen? At what temperature and time of exposition? How were the results expressed? On fresh weight or on dry weight? If on dry weight, how were these data obtained? Please add this information.
- All over the manuscript, the Authors are pleased to correctly write the chemical formulas; for example, “Na<sub>2</sub>CO<sub>3</sub>” has to be corrected to “Na<sub>2</sub>CO<sub>3</sub>.” Please correct where necessary.
- As for the analysis of total flavonoids, the Authors are asked to clarify the measure unit used for the data expression. What are CE equivalents?
- I see a problem in the DPPH experiment. The sentence “The control experiment substituted methanol for the extract.” was checked? Why was the control experiment not performed with methanol/water 80:20, exactly as the extract? This could be very important, due to the fact that the DPPH molecule can suffer from solvation problems in water-alcoholic solutions and the DPPH solubilization in the working solutions has to be carefully checked during the set-up of the experiment. Please clarify.
- As regards the GC-MS analysis description, the Authors have to better describe what type of sample was injected into the gas-chromatographic system. Was the sample treated to extract the volatile fraction or not? Please clarify.
- The paragraphs of the results have to be numbered consecutively just like the methods description. Please shift paragraph 3.1, regarding the GC-MS data, to the last section of the biochemical assays, after the section on the antioxidant and anti-inflammatory assays, and just before the paragraph on protein-ligand interactions.
- The reported number in the text of total phenolic in RW-G of 59.97 mg/100g GAE is not coherent with Figure 1, where

the value 595.97 is reported. Please correct.

Moreover, I see that the content in raw samples is the lowest in both assays (total phenols and total flavonoids). This seems strange. I repeat the question. Did the Authors express the reported level on 100g of fresh matter, or on 100g of dry matter? Please, explain and clarify this important point, reporting a clear justification of the minor content in phytochemicals in raw samples. The same comment is valid for data in Figure 2.

- As regards the chapter of protein interactions with ligands, I have not well understood why the RW compounds are listed in Table 2 and not in Table 3. Are the compounds in Table 3 given as examples? This is because, for example, I see from the text that FD1, FD3, FD4, FD5, and FD6 cleaved better to the anti-inflammatory active site than aspirin, and I see on Table 2 only the patterns of FD1 and FD4. Data on Table 2 need to be better discussed. Please, clarify.
- In the Discussion section, the sentence “FD-G and OD-G possess more anti-inflammatory and antioxidant properties than RW-G.” is very important and needs to be validated. Are the data all in the same type of weight matter? Dried or fresh? Check the data, please.

Finally, the comment to be made is that the manuscript in its present form shows a lot of problems and is, in the present form, of low scientific value. Only after a careful reorganization and rewriting can it be considered of sufficient value for the final evaluation as a publication.