

# Review of: "On the pros and cons of utilizing crude herbal preparations as opposed to purified active ingredients, with emphasis on the COVID pandemic"

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The article is interesting and touches on a very topical topic. However some remarks are needed.

*Artemisia* should appear in the title of the article, since the authors focus specifically on this plant taxa.

It is not clear which species of *Artemisia* the authors refer to in the cases they have studied: is it *A. annua* or other species? Specify better. Indeed, as the authors rightly point out, the genus *Artemisia* is a very broad genus of Asteraceae, with an equally broad spectrum of active medicinal constituents, each with specific biological activities.

Therefore, in my opinion, given the complexity of the subject matter, there are two issues that the authors should further explore:

- 1) The issue of **safety**, because herbal preparations from raw materials are not always safe. For example, they can contain toxic substances (i.e. heavy metals such as cadmium, lead, arsenic, mercury, which can cause toxic and mutagenic effects) accumulated from the environment, during cultivation, as well as during storage and processing processes. A significant presence of these substances can affect the safety and quality of herbal preparations. Furthermore, the presence of thujone in herbal preparations based on *Artemisia* spp. must be considered, since thujone is a toxic ketone for which cases of poisoning have been documented due to repeated ingestion of infusions of *Artemisia* spp.
- 2) The second issue concerns the main active principle of *Artemisia* spp. to which the scientific research has attributed an action against Sars-CoV-2, **artemisinin**, which is the same active ingredient against malaria. Despite the understandable enthusiasm of many researchers for the use of herbal remedies based on *Artemisia* spp., the debate is still open, because there is a serious risk that this could lead to a possible increase in the **resistance of *Plasmodium falciparum* to antimalarial drugs**. In fact, in some endemic areas such as sub-Saharan Africa (about 90% of malaria cases worldwide), artemisinin-based combined antimalarial therapies could become ineffective in the next few years precisely because of the uncontrolled use of *Artemisia* spp. for the prevention of COVID-19.