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Comment *תגובה*

In Reference to: "Let it Bee: The busy bee and the turbulent Corona"

[by R. Ofir, Negev, Dead Sea and Arava Studies, 2020, 12 (2), pp. 44–46]

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I have read the Perspective article entitled "Let it Bee: The busy bee and the turbulent Corona" by Ofir, R., recently published in "Negev, Dead Sea and Arava Studies" (2020, 12 [2]: 44–46). First, I would like to congratulate the author on her unique viewpoint and clear presentation.

The manuscript suggests that bee venom can be used to reduce cytokine storm that underly the life-threatening symptom of COVID-19 patients. Although bee venom had been shown to reduce inflammation in chronic patients and to possess health-promoting activities both *in vitro* and *in vivo*, I interpret the results differently. As bee stung typically causes low-grade local inflammation and pain (Carpena et al., 2020), the mechanism of action underlying the reduction of chronic pain and inflammation is probably due to hormetic action - enhancing the tolerance to more severe challenges (Calabrese and Mattson, 2017). For instance, bee venom phospholipase A2, listed in the manuscript, will result in arachidonic acid release. Enzymatic and non-enzymatic metabolism will result in the generation of PGE2 and other lipid-derived mediators that will cause both local inflammation (redness) and pain (Carpena et al., 2020). However, the result, in the long run, will be the reduction of the signaling cascade and enhanced tolerance to other inflammatory and pain stimuli. To my understanding, this hormetic action is the molecular mechanism underlying its therapeutic action.

This suggests that bee venom may have a beneficial preventive action and should be used only prior to COVID-19 infection, and not as a therapeutic treatment after infection suggested by the author. When experiencing the lethal cytokine storm, it is better to use conational treatment at this time.

References

Calabrese, E. J., & Mattson, M. P,. 2017. How does hormesis impact biology, toxicology, and medicine?. NPJ aging and mechanisms of disease, 3 (1), 1–8.

Carpena, M., Nuñez-Estevez, B., Soria-Lopez, A., & Simal-Gandara, J,. 2020. Bee Venom: An Updating Review of Its Bioactive Molecules and Its Health Applications. Nutrients, 12 (11), 3360.