Anti-inflammatory property of propolis

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Dear Editor-in-Chief,

The recent article by Weina Gao and colleagues, on July issue of this Journal, showed that Brazilian green propolis have a positive effect on innate and adaptive immunity in aged mice.⁽¹⁾ This role should be mainly attributed to flavonoids contained in propolis.⁽²⁾ The Authors reported that Brazilian propolis had 189.12 mg/g total polyphenols, 98.46 mg/g flavonoids, 1.95 mg/g cinnamic acid and 23 mg/g artemillin-C.⁽¹⁾ Yet, the participation of any single molecule to the reported evidence in aged animals might have involved different spectra of activity and different molecular targets in promoting the beneficial action observed by the Authors.⁽¹⁾ Artemillin C, namely (E)-3-[4-hydroxy-3,5-bis(3-methylbut-2-enyl)phenyl]prop-2-enoic acid, is one of the major component in Brazilian propolis and recent reports have stressed its ability to block the serine/threonine protein kinase known as PAK-1.⁽³⁾ PAK proteins are critical effectors that link the Rho family of GTPases to the cytoskeleton reorganization and nuclear signaling; These proteins serve as targets for the small GTP binding proteins Cdc42 and Rac and have been implicated in a wide range of biological activities, for example PAK1 regulates cell motility and morphology, furthermore the role of Cdc42 GTPases activating protein in aging has been recently reported.⁽⁴⁾

The involvement of PAK1 in inflammatory and neurodegenerative disorders suggests that this molecules is targeted in aging mechanism. Few natural PAK1-blockers such as rosmarinic acid, curcumin and caffeic acid extend the lifespan of the nematode *Caenorhabditis elegans* or fruit flies.⁽⁵⁾ PAK1 promotes reproduction, whereas it inactivates HSP16.2 gene and shortens lifespan, as do also PI-3 kinase (AGE-1), mTOR, and insulin-like signalling (ILS) (Daf-2) in this nematode.⁽⁵⁾ It is arguable that caffeic acid and particularly artemillin-C play a role in slowing aging cellular mechanism and synergistically exert an anti-inflammatory action with propolis flavonoids.⁽⁴⁾ This suggestive

speculation may appear contradictory when data from serum in aged mice, showing a marked increase in inflammatory cytokines on increasing Brazilian propolis assumption, are considered.⁽¹⁾ The Authors concluded that this evidence assessed the improvement in inflammatory response caused by propolis in aged mice.⁽¹⁾ This circumstance addresses the positive role exhibited by nature-derived phytochemicals on stressed, dysregulated, aged or infected (inflamed) cells. Therefore, while a wide literature exists reporting the anti-inflammatory role of flavonoids,⁽⁶⁾ many data from clinics should suggest a pro-inflammatory role exerted by polyphenols in restoring health, prevent cancer onset and degenerative disorders.⁽⁷⁾ Fundamentally, as like as in propolis, the most proper idea about the activity of nature-derived polyphenols and phenolic substances, should deal with the concept of immune modulation, depending on the cell nature and homeostatic balance, not merely an improvement given by inhibition or promotion coming from the molecular nature of these molecules. Propolis is widely used as an anti-inflammatory raw substance, especially during allergy and airway inflammatory disorders. The interesting paper by Weina Gao *et al.*, would suggest that in elderly people Brazilian propolis may ensure a health promoting action by activating the immune response.⁽¹⁾ This is formally true but literature reports many data with potentially misleading evidence about. A combination therapy (anti-inflammatory drugs plus propolis) in aged adults showed encouraging results⁽⁸⁾ and, moreover, due to yet contradictory results from clinics,⁽⁹⁾ respect to *in vitro* and animal evidence,^(1,10) a more cautious, critical and less enthusiastic debate about this substance has to be taken into account in the next future.

Looking forward to a kind reply from yours.

Conflict of Interest

No potential conflicts of interest were disclosed.

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