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Letter to Editor

A Brief Perspective on Anti-inflammatory Effects of Thymol and Carvacrol

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Dear Editor

We eagerly read the recent paper published by Gholijani N et al. entitled “The Suppression of Adjuvant-induced Inflammation and the Inhibition of the Serum and Tissue IL-17, TNF-α and IL-1β levels by Thymol and Carvacrol” in "Herb Med J". This study adequately indicated the anti-inflammatory properties of the two mentioned plant-derived compounds. Thus, the authors intend in this letter to point to a few important notes in confirming this study. Inflammation is a defensive mechanism in the body that removes or deactivates pathogens. Although it is beneficial for the body, inflammation can be harmful if it is induced without being controlled properly. Moreover, inflammation plays a role in restoring homeostasis to the body after the onset of the disease and is useful in improving the damages (1). It is documented that cytokines, including TNF-α, IL-17 and IL-1β, play substantial roles in inflammatory responses (2). One of these cytokines is TNF-α which is secreted by mononuclear phagocytes. TNF-α can induce acute phase proteins and is considered as a pyrogenic factor (3). Another cytokine is IL-17 which is produced by Th17, NK cells and neutrophils. It could exacerbate inflammation via increased immune cells proliferation and indirect neutrophil recruitment (4). IL-1β is recognized as a mediator of acute inflammatory response against infections (5). Moreover, adjuvants can be used as exacerbation factors for immune responses in animal models (6). Today, chemical drugs such as corticosteroids are used to reduce inflammation. But, important adverse effects of these drugs are well known and unavoidable (7). Today, researchers have shown that herbal medicines with low cost and minimal side effects are good alternatives to synthetic drugs (8).

Among these plants, peppers species are widely used as medicinal plants. Carvacrol (2-methyl-5-(1-methylethyl)-phenol) and Thymol (2-isopropyl-5-methylphenol) are the most important active ingredients of these plants especially *Zataria multiflora* and *Satureja hortensis* (Figure-1). These compounds are monoterpenoid phenols which are chemically very similar and only the position of their hydroxyl group differs (9). Several researches have documented that carvacrol exhibits various biological activities including but not limited to antioxidant, antimicrobial, antispasmodic, anti-inflammatory, analgesic, immunomodulatory and chemopreventive activities (10-12). Thymol had also beneficial properties including antioxidant, anti-inflammatory, antiseptic, antibacterial, antifungal, antinociceptive, properties. Numerous investigations have been carried out on the properties of these compounds, among which we now refer to a number of them concerning their anti-inflammatory properties and to confirm this study (13-15).

Many researches showed anti-inflammatory effects of carvacrol. Carvacrol could inhibit neutrophil elastase and production of E2, F1 and F2 prostaglandins. It

also can inhibit cyclooxygenase-2 (COX-2) activity (16-18). In addition to carvacrol, thymol showed anti-inflammatory effects through inhibition of human neutrophil elastase. Another study indicated that carvacrol and thymol, particularly carvacrol, play their anti-inflammatory roles via inhibited inflammatory edema and leukocyte migration (19).

Conclusion

Further studies about the anti-inflammatory effects of herbal compounds can lead to the development of useful herbal treatments to reduce inflammation. For this purpose, comprehensive investigation of signaling pathways involved in turning on and off the inflammation such as NF-kBA which plays a central role in inflammation, activation of lymphocytes, cell survival and the JAK/STAT pathway which is involved in the signaling of cytokines. Moreover, inflammatory mechanisms can be further investigated by adding inflammatory cytokines antagonists. In addition, techniques for silencing the gene in inflammatory conditions can provide more information about the anti-inflammatory mechanisms of plant compounds. Taken together, elucidation of cellular and molecular players in inflammation and immune responses would lead to more optimized application of herbal medicines.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. Chovatiya R, Medzhitov R. Stress, inflammation, and defense of homeostasis. Molecular cell. 2014;54(2):281-8.
2. Kim Y-K, Na K-S, Myint A-M, Leonard BE. The role of pro-inflammatory cytokines in neuroinflammation, neurogenesis and the neuroendocrine system in major depression. Progress in Neuro-Psychopharmacology and Biological Psychiatry. 2016;64:277-84.
3. Kalliolias GD, Ivashkiv LB. TNF biology, pathogenic mechanisms and emerging therapeutic strategies. Nature reviews Rheumatology. 2016;12(1):49-62.
4. Chehimi M, Vidal H, Eljaafari A. Pathogenic Role of IL-17-Producing Immune Cells in Obesity, and Related Inflammatory Diseases. Journal of clinical medicine. 2017;6(7):68.
5. Chen KW, Groß CJ, Sotomayor FV, Stacey KJ, Tschopp J, Sweet MJ, et al. The neutrophil NLRC4 inflammasome selectively promotes IL-1β maturation without pyroptosis during acute Salmonella challenge. Cell reports. 2014;8(2):570-82.
6. Bagavant H, Nandula SR, Kaplonek P, Rybakowska PD, Deshmukh US. Alum, an aluminum based adjuvant, induces Sjögren's Syndrome-like disorder in mice. Clinical and experimental rheumatology. 2014;32(2):251.
7. Torres A, Sibila O, Ferrer M, Polverino E, Menendez R, Mensa J, et al. Effect of corticosteroids on treatment failure among hospitalized patients with severe community-acquired pneumonia and high inflammatory response: a randomized clinical trial. Jama. 2015;313(7):677-86.
8. Bahmani M, Saki K, Rafieian-Kopaei M, Karamati SA, Eftekhari Z, Jelodari M. The most common herbal medicines affecting Sarcomastigophora branches: a review study. Asian Pacific journal of tropical medicine. 2014;7:S14-S21.
9. Miladi H, Zmantar T, Chaabouni Y, Fedhila K, Bakhrouf A, Mahdouani K, et al. Antibacterial and efflux pump inhibitors of thymol and carvacrol against food-borne pathogens. Microbial pathogenesis. 2016;99:95-100.
10. Alagawany M, El-Hack MA, Farag MR, Tiwari R, Dhama K. Biological effects and modes of action of carvacrol in animal and poultry pro-duction and health-a review. Advances in Animal and Veterinary Sciences. 2015;3(2s):73-84.
11. Guimarães AG, Oliveira GF, Melo MS, Cavalcanti SC, Antoniolli AR, Bonjardim LR, et al. Bioassay-guided Evaluation of Antioxidant and Antinociceptive Activities of Carvacrol. Basic & clinical pharmacology & toxicology. 2010;107(6):949-57.
12. Silva FV, Guimarães AG, Silva ER, Sousa-Neto BP, Machado FD, Quintans-Júnior LJ, et al. Anti-inflammatory and anti-ulcer activities of carvacrol, a monoterpene present in the essential oil of oregano. Journal of medicinal food. 2012;15(11):984-91.
13. Marchese A, Orhan IE, Daglia M, Barbieri R, Di Lorenzo A, Nabavi SF, et al. Antibacterial and antifungal activities of thymol: a brief review of the literature. Food chemistry. 2016;210:402-14.
14. Gholijani N, Gharagozloo M, Farjadian S, Amirghofran Z. Modulatory effects of thymol and carvacrol on inflammatory transcription factors in lipopolysaccharide-treated macrophages. Journal of immunotoxicology. 2016;13(2):157-64.
15. Kumar D, Rawat DS. Synthesis and antioxidant activity of thymol and carvacrol based Schiff bases. Bioorganic & medicinal chemistry letters. 2013;23(3):641-5.
16. da Silva Lima M, Quintans-Júnior LJ, de Santana WA, Kaneto CM, Soares MBP, Villarreal CF. Anti-inflammatory effects of carvacrol: evidence for a key role of interleukin-10. European journal of pharmacology. 2013;699(1):112-7.
17. Landa P, Kokoska L, Pribylova M, Vanek T, Marsik P. In vitro anti-inflammatory activity of carvacrol: Inhibitory effect on COX-2 catalyzed prostaglandin E 2 biosynthesisb. Archives of pharmacal research. 2009;32(1):75-8.
18. Hotta M, Nakata R, Katsukawa M, Hori K, Takahashi S, Inoue H. Carvacrol, a component of thyme oil, activates PPARα and γ and suppresses COX-2 expression. Journal of lipid research. 2010;51(1):132-9.
19. Fachini-Queiroz FC, Kummer R, Estevao-Silva CF, Carvalho MDdB, Cunha JM, Grespan R, et al. Effects of thymol and carvacrol, constituents of Thymus vulgaris L. essential oil, on the inflammatory response. Evidence-Based Complementary and Alternative Medicine. 2012;2012.

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