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Opinion

Immunomodulatory and Anti-Inflammatory Phytochemicals for the Treatment of Inflammatory Bowel Disease (IBD)

- Turning Strong Rationale into Strong Evidence? -

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Key Words

inflammatory bowel disease, Crohn's disease, phytochemicals

Inflammatory bowel disease (IBD) comprises two types of chronic and relapsing intestinal inflammation conditions including Crohn's disease and ulcerative colitis [1]. Although the exact etiology of IBD remains elusive, the interaction of host's immune system with diet and microbiome of intestinal tract in genetically susceptible individuals seems to play a pivotal role in the pathogenesis of IBD [2]. Encoding regions for nucleotide oligomerization domain 2 (NOD2) and interleukin 23 T helper 17 (Th17) pathway are the most prominent genetic components of IBD pathogenesis [3,4]. NOD2 recognizes bacterial peptidoglycan and triggers the inflammatory cascade [5], and interleukin 23 is integral to immune defense against non-self-antigens and chronic intestinal inflammation [6]. On the other hand, breakdown and alteration of normal microbiome increases the risk of intestinal colonization with pathogenic organisms and inflammatory diseases [7].

Dietary factors are known to influence gut microbiome and have the potential to shape the interplay between gut microbiome and immune responses involved in the pathogenesis of IBD [2]. Dietary factors can affect gut colonization of microorganisms in long term; they can mimic pathogenic antigens and trigger intracellular transduction and transcription pathways leading to modulation of inflammatory responses [8,9]. Exposure to stimuli such as reactive oxygen species, bacterial antigens and even innocent antigens activate nuclear factor (NF)-κB. This cascade results in the production of chemokines, pro-inflammatory cytokines, and infiltration of lymphocytes to the intestinal mucosa and disturbance of epithelial barrier leading to chronic intestinal inflammation. Phytochemicals including ellagic acid, curcumin, flavonoids, quercetin and green tea polyphenols can modulate NF-κB pathway [10-14]. Besides cytokine overproduction, overexpression of COX-2, the rate-limiting enzyme of

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prostaglandin production, is also involved in either acute or chronic intestinal inflammation. Phytochemicals such as grape juice and black raspberry powder have the ability to inhibit COX-2 and prostaglandin production [15,16].

Research on immunomodulatory and anti-inflammatory activities of phytochemicals in preventing and treating intestinal inflammation, and in modulating the gut microbiome and colitis symptoms is still at its infancy. Most of the evidence have come from animal studies [10-16], thus evidence from well-designed randomized controlled trials in this area are lacking. The shortcomings of available drugs to treat IBD and their side effects highlight a real need to additional therapies that could confer, either as alternative or adjunct, a better control of disease. In this context, phytochemicals are interesting candidates owing to their multimechanistic mode of action, potential safety, and wide availability [1,2]. Moreover, limited bioavailability of phytochemicals which is generally considered as an obstacle against their maximal systemic effects is less of a problem in IBD, as the site of action is intestine where the phytochemical is almost completely bioavailable upon oral use. While all these points emphasize the great therapeutic potential of phytochemicals for the treatment of IBD, important questions as to the dose-response association, clinical efficacy, precise mechanism(s) of action, and long-term tolerability still remain to be answered.

Conflict of interest

The authors declare that there are no conflicts of interest.

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