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Invited Commentary

Green tea catechins suppress NF-κB-mediated inflammatory responses: relevance to nutritional management of inflammation

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Blood loss after trauma induces several systemic inflammatory responses culminating in the dysfunction and failure of organs. In this issue of the *British Journal of Nutrition*, Relja *et al.*[1] have examined the inflammatory signals at the subcellular, cellular and tissue levels after haemorrhage-induced hepatic injury and resuscitation in rats. Hepatic injury and resuscitation induced the expression of intercellular adhesion molecule-1, neutrophil infiltration and necrosis in the liver, and augmented serum alanine transaminase and IL-6 levels. It also induced IκBα phosphorylation and the activation of NF-κB. Pre-treatment with green tea extract (GTE: catechins >80 %, with >40 % of epigallocatechin gallate (EGCG)) suppressed the inflammatory responses at all levels, including neutrophil infiltration, intercellular adhesion molecule-1 expression and the release of IL-6, and, importantly, suppressed the activation of NF-κB.

The inflammatory responses occurring in the liver after haemorrhage are parallel to the inflammatory events occurring after inducing ischaemia, and EGCG is also active in the latter setting[2–5]. The anti-inflammatory efficacy of EGCG demonstrated in all these studies generates a unifying hypothesis. Hepatic injury induced by ischaemia[2] caused oxidative stress with enhanced production of reactive oxygen species and TNF-α; both mediated the expression of nuclear factors and kinases, activating the signal transduction pathways to trigger cell death. The liver that stained positive for NF-κB in the ischaemia group remained negative in the EGCG-pre-treated group. Neutrophil infiltration that was enhanced in the ischaemia group was significantly reduced after EGCG. Ischaemia-induced myocardial injury[3] also caused significant neutrophil infiltration, an increase in plasma IL-6, and activation of IκB kinase and NF-κB in the tissues. EGCG pre-treatment significantly reduced myocardial damage, neutrophil infiltration and plasma IL-6, and also suppressed the NF-κB pathway. Intestinal injury induced by ischaemia[4] also resulted in an enhanced production of reactive oxygen species, neutrophil infiltration and activation of NF-κB. EGCG pre-treatment significantly deactivated NF-κB, decreased neutrophil infiltration and lowered reactive oxygen species production. All these studies support the conclusion derived by Relja *et al.* and collectively point out that induced inflammatory responses are mediated through NF-κB-dependent mechanisms, and EGCG *per se* or in combination with other catechins suppresses NF-κB activation and alleviates inflammation.

There are enumerable reports on the efficacy of EGCG *per se* or EGCG in combination with other catechins (epigallocatechin or epicatechin gallate or gallocatechin gallate)[5–9] on inflammatory responses induced by different exogenous and endogenous factors. The inflammatory inducers include polymicrobial sepsis[10], lipopolysaccharide[5–7,11], *Staphylococcus aureus* enterotoxin B[12], *Helicobacter pylori* infection[13], IL-1β alone[8,14–16] or in combination with β-amyloid[17] or oxygen tension[18] or TNF-α[9,19] or TNF-α alone[20–22], UV-B[23–25], repetitive oxidative stress[26], cigarette smoke condensate[27], phorbol 12-myristate 13-acetate[28–30], trinitrobenenesulphonic acid[31]- or acetic acid[32]-induced colitis, receptor activator for the NF-κB ligand[33,34] or high glucose[35]. Most importantly, all these studies document that consequent to the down-regulation of NF-κB pathways, EGCG or catechin combination suppressed the levels of several pro-inflammatory cytokines (TNF-α[11,12,28,32,35] IL-6[17,24,28], IL-8[16,17,20,27,28], interferon-γ[12,32]), chemokine (Fractalkine[22]) and enzymes (matrix metaloproteinases-1, -3, -9[27], -13[8,15,18], NO synthase[6,10,14,25,27,32]; cyclo-oxygenase-2[17,19,30], glucosyl/lactosyl and Gb3 transferases[21]), growth factors (vascular endothelial growth factor[17]), cell adhesion molecules (intercellular adhesion molecule-1, vascular cell adhesion molecule-1 and E-selectin[9]) and monocyte chemotactic protein-1[29]. In this regard, the study of Relja *et al.* is well justified in the use of GTE, since other tea catechins act synergistically with EGCG. It is important to use GTE with a greater percentage of EGCG to counteract inflammation. These preclinical studies on the induced inflammatory responses promote the hypothesis that green tea catechins have the potential to suppress the NF-κB-mediated inflammatory pathway into a salient concept relevant to nutritional management of inflammation. The emerging concept is that EGCG or GTE has the potential to block the NF-κB pathway, which plays a critical role in inflammation induced by various factors and also in malignancy. These aforementioned studies pave the way for phase I and II clinical trials using GTE or EGCG to control trauma, haemorrhage or ischaemia-induced inflammation.

There is no conflict of interest.

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