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Flavonoid fraction of Bergamot juice reduces LPS-induced inflammatory response through SIRT1-mediated NF-κB inhibition in THP-1 monocytes.

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Plant polyphenols exert anti-inflammatory activity through both anti-oxidant effects and modulation of pivotal pro-inflammatory genes. Recently, Citrus bergamia has been studied as a natural source of bioactive molecules with antioxidant activity, but few studies have focused on molecular mechanisms underlying their potential beneficial effects. Several findings have suggested that polyphenols could influence cellular function by acting as activators of SIRT1, a nuclear histone deacetylase, involved in the inhibition of NF-κB signaling. On the basis of these observations we studied the anti-inflammatory effects produced by the flavonoid fraction of the bergamot juice (BJe) in a model of LPS-stimulated THP-1 cell line, focusing on SIRT1-mediated NF-κB inhibition. We demonstrated that BJe inhibited both gene expression and secretion of LPS-induced pro-inflammatory cytokines (IL-6, IL-1β, TNF-α) by a mechanism involving the inhibition of NF-κB activation. In addition, we showed that BJe treatment reversed the LPS-enhanced acetylation of p65 in THP-1 cells. Interestingly, increasing concentrations of Sirtinol were able to suppress the inhibitory effect of BJe via p65 acetylation, underscoring that NF-κB-mediated inflammatory cytokine production may be directly linked to SIRT1 activity. These results suggest that BJe may be useful for the development of alternative pharmacological strategies aimed at reducing the inflammatory process.

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