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Beta-caryophyllene protects against diet-induced dyslipidemia and vascular inflammation in rats: Involvement of CB2 and PPAR-γ receptors

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Abstract

Beta-caryophyllene (BCP) is a phytocannabinoid possessing selective agonistic activity to cannabinoid type-2 receptors (CB2R) and peroxisome proliferator-activated receptors-α (PPAR-α). However, few studies reported the contribution of PPAR-γ receptors in BCP effects. The aim of this study was to investigate the BCP effects on diet-induced dyslipidemia and vascular inflammation as well as the involvement of CB2R and PPAR-γ receptors. Wistar rats were fed a high-fat diet and administered 10% fructose for 12 weeks. Treatment with pioglitazone, BCP, BCP + CB2R antagonist, AM630, or BCP + PPAR-γ antagonist, BADGE was started from the 9th week and continued till the 12th week. BCP significantly ameliorated all diet-induced alterations in a CB2R-dependant manner as it improved glycemic parameters, dyslipidemia, and vascular oxidative stress and inflammation. It also downregulated proatherogenic adhesion molecule (VCAM-1) and restored vascular eNOS/iNOS expression balance. PPAR-γ was involved in BCP-evoked suppression of vascular inflammation, VCAM-1 and restoration of normal vascular eNOS/iNOS balance thus normal NO level. Furthermore, part of BCP hypolipidemic effects (lowering total cholesterol, LDL, VLDL) involved both CB2R and PPAR-γ receptors. BCP treatment was superior to pioglitazone in anti-inflammatory and anti-atherosclerotic measures. BCP may represent a more potent alternate to pioglitazone avoiding its side effects in the treatment of insulin resistance and vascular inflammation.

Keywords: Beta-caryophyllene; Cannabinoid receptor 2; High fat/fructose diet; Insulin resistance; PPAR-γ; Vascular inflammation.

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