Format: Abstract

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Cannabidiol, a Major Non-Psychotropic Cannabis Constituent Enhances Fracture Healing and Stimulates Lysyl Hydroxylase Activity in Osteoblasts.

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Abstract

Cannabinoid ligands regulate bone mass, but skeletal effects of **cannabis** (**marijuana** and hashish) have not been reported. Bone fractures are highly prevalent, involving prolonged immobilization and discomfort. Here we report that the major non-psychoactive **cannabis** constituent, **cannabidiol** (CBD), enhances the biomechanical properties of healing rat mid-femoral fractures. The maximal load and work-to-failure, but not the stiffness, of femurs from rats given a mixture of CBD and Δ(9) -tetrahydrocannabinol (THC) for 8 weeks were markedly increased by CBD. This effect is not shared by THC (the psychoactive component of **cannabis**), but THC potentiates the CBD stimulated work-to-failure at 6 weeks postfracture followed by attenuation of the CBD effect at 8 weeks. Using micro-computed tomography (μCT), the fracture callus size was transiently reduced by either CBD or THC 4 weeks after fracture but reached control level after 6 and 8 weeks. The callus material density was unaffected by CBD and/or THC. By contrast, CBD stimulated mRNA expression of Plod1 in primary osteoblast cultures, encoding an enzyme that catalyzes lysine hydroxylation, which is in turn involved in collagen crosslinking and stabilization. Using Fourier transform infrared (FTIR) spectroscopy we confirmed the increase in collagen crosslink ratio by CBD, which is likely to contribute to the improved biomechanical properties of the fracture callus. Taken together, these data show that CBD leads to improvement in fracture healing and demonstrate the critical mechanical role of collagen crosslinking enzymes.

KEYWORDS: CANNABIDIOL; COLLAGEN CROSSLINKING; FRACTURE HEALING; FTIR; LYSYL HYDROXYLASE; μCT

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