

Unheated *Cannabis sativa* extracts and its major compound THC-acid have potential immuno-modulating properties not mediated by CB₁ and CB₂ receptor coupled pathways

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International Immunopharmacology 6 (2006) 656–665.

Available online 7 November 2005.

Abstract

There is a great interest in the pharmacological properties of cannabinoid like compounds that are not linked to the adverse effects of Δ^9 -tetrahydrocannabinol (THC), e.g. psychoactive properties. The present paper describes the potential immuno-modulating activity of unheated *Cannabis sativa* extracts and its main non-psychoactive constituent Δ^9 -tetrahydrocannabinoid acid (THCa). By heating Cannabis extracts, THCa was shown to be converted into THC. Unheated Cannabis extract and THCa were able to inhibit the tumor necrosis factor alpha (TNF- α) levels in culture supernatants from U937 macrophages and peripheral blood macrophages after stimulation with LPS in a dose-dependent manner. This inhibition persisted over a longer period of time, whereas after prolonged exposure time THC and heated Cannabis extract tend to induce the TNF- α level. Furthermore we demonstrated that THCa and THC show distinct effects on phosphatidylcholine specific phospholipase C (PC-PLC) activity. Unheated Cannabis extract and THCa inhibit the PC-PLC activity in a dose-dependent manner, while THC induced PC-PLC activity at high concentrations. These results suggest that THCa and THC exert their immuno-modulating effects via different metabolic pathways.

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