Abstract

Background: *Cannabis sativa* L. extracts (CSE) are used for treating inflammatory conditions, but little is known about their immunomodulatory effects. We investigated a novel CSE with high (14%) CBD and low (0.2%) THC concentration in comparison with pure CBD on primary human lymphocytes.

Methods: Proliferation, cell cycle distribution, apoptosis/necrosis and viability were analysed with standard methods. Genotoxicity was evaluated with the comet-assay. The effect on T lymphocyte activation was evaluated via CD25/CD69 marker expression, degranulation assays and the production of cytokines. The influence on the transcription factors was analysed using Jurkat reporter cell lines. Specific CB2 receptor antagonist SR144528 and TRPV1 receptor antagonist A78416B were used to study the involvement of CB2 or TRPV1 receptors.

Results: CSE inhibited the proliferation of activated T lymphocytes in a dose-dependent manner without inducing apoptosis, necrosis, or affecting cell viability and DNA integrity. The inhibitory effect was mediated via the suppression of T lymphocytes activation, particularly by the suppression of CD25 surface marker expression. Furthermore, CSE interferes with the functionality of the T lymphocytes, as indicated by inhibition of degranulation, IL-2, and IFN-γ production. AP-1-and-NFAT-reporter activation was reduced implicating an AP-1-and-NFAT-mediated mode of action. The effects were in part reversed by SR144528 and A78416B, showing that the effects were mainly mediated by CB2 and TRPV1 receptors.

Conclusion: CSE and CBD have immunomodulatory effects and interfere with the activation and functionality of T lymphocytes. A comparison between CSE and CBD

suggests that the immunosuppressive effect of CSE is mostly due to the effect of CBD.