Cannabidiol Displays Antiepileptiform and Antiseizure Properties In Vitro and In Vivo

S Nicholas A. Jones, Andrew J. Hill, Imogen Smith, Sarah A. Bevan, Claire M. Williams, Benjamin J. Whalley, and Gary J. Stephens

School of Pharmacy (N.A.J., A.J.H., I.S., S.A.B., B.J.W., G.J.S.) and School of Psychology (N.A.J., A.J.H., C.M.W.), University of Reading, Whiteknights, Reading, United Kingdom

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ABSTRACT

Plant-derived cannabinoids (phytocannabinoids) are compounds with emerging therapeutic potential. Early studies suggested that cannabidiol (CBD) has anticonvulsant properties in animal models and reduced seizure frequency in limited human trials. Here, we examine the antiepileptiform and antiseizure potential of CBD using in vitro electrophysiology and an in vivo animal seizure model, respectively. CBD (0.01–100 M) effects were assessed in vitro using the Mg2 -free and 4-aminopyridine (4-AP) models of epileptiform activity in hippocampal brain slices via multielectrode array recordings. In the Mg2 -free model, CBD decreased epileptiform local field potential (LFP) burst amplitude [in CA1 and dentate gyrus (DG) regions] and burst duration (in all regions) and increased burst frequency (in all regions). In the 4-AP model, CBD decreased LFP burst amplitude (in CA1, only at 100 M CBD), burst duration (in CA3 and DG), and burst frequency (in all regions). CBD (1, 10, and 100 mg/kg) effects were also examined in vivo using the pentylenetetrazole model of generalized seizures. CBD (100 mg/ kg) exerted clear anticonvulsant effects with significant decreases in incidence of severe seizures and mortality compared with vehicle-treated animals. Finally, CBD acted with only low affinity at cannabinoid CB1 receptors and displayed no agonist activity in [35S]guanosine 5-O-(3-thio)-triphosphate assays in cortical membranes. These findings suggest that CBD acts, potentially in a CB1 receptor-independent manner, to inhibit epileptiform activity in vitro and seizure severity in vivo. Thus, we demonstrate the potential of CBD as a novel antiepileptic drug in the unmet clinical need associated with generalized seizures.