Cannabinoid induced vasorelaxation of human mesenteric arteries

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Cannabinoid induced vasorelaxation has been well studied in animal models. Research has shown that cannabinoids cause vasorelaxation through cannabinoid receptors, ion channel, the endothelium, metabolites and/or nuclear receptor-mediated mechanisms. These mechanisms are influenced by both the cannabinoid ligand, vessel used and species studied. To date the vascular effects of cannabinoids in human arteries have not been fully investigated. Therefore the aim of the present study was to investigate the vasorelaxant effects of a range of cannabinoids in human mesenteric arteries.

With ethical approval and following written informed consent, human mesenteric arteries were taken from patients receiving colorectal surgery and either used fresh or stored overnight at 4°C. Arteries were dissected, cleaned and mounted on a Mulvany-Halpern myograph. Arteries were bathed in oxygenated physiological salt solution at 37°C under a set tension of 90% of 100 mmHg. U46619 and endothelin-1 were added to increase tension by a minimum of 5 mN. Once a stable contraction had been achieved, the vasorelaxant effects of anandamide (AEA), 2-arachidonyl-glycerol (2-AG), \( \Delta^9 \) tetrahydrocannabinol (THC), cannabidiol (CBD) and CP55,940 were assessed as cumulative concentration-response curves.

CBD (\( R_{\text{max}} \) 38.1%, \( n=10 \)), THC (\( R_{\text{max}} \) 24.8%, \( n=9 \)) and AEA (\( R_{\text{max}} \) 22.3%, \( n=7 \)) caused modest vasorelaxation that was significantly different to vehicle controls (\( P<0.05 \) Students unpaired t-test).

CP55,940 (\( R_{\text{max}} \) 57.7%, \( n=9 \)) was the most efficacious cannabinoid tested, producing vasorelaxation that was significantly greater than CBD (\( n=10, P<0.05 \), ANOVA), THC (\( n=9, P<0.001 \), ANOVA) and AEA (\( n=7, P<0.001 \), ANOVA). The endocannabinoid 2-AG (\( R_{\text{max}} \) 47.7%, \( n=10 \)) was more efficacious than AEA (\( n=9, P<0.001 \), ANOVA).

The results of the present investigation demonstrate the ability of cannabinoids to cause vasorelaxation of human blood vessels. However, cannabinoids demonstrated less potency and efficacy in human mesenteric arteries than in rat mesenteric arteries. Also in contrast to animal studies, we found that 2-AG has much greater efficacy in human mesenteric arteries than AEA.