CBG studies

> Psychopharmacology (Berl). 2016 Oct;233(19-20):3603-13. doi: 10.1007/s00213-016-4397-4. Epub 2016 Aug 9.

Cannabigerol is a novel, well-tolerated appetite stimulant in pre-satiated rats

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Abstract

Rationale: The appetite-stimulating properties of cannabis are well documented and have been predominantly attributed to the hyperphagic activity of the psychoactive phytocannabinoid, Δ(9)-tetrahydrocannabinol (Δ(9)-THC). However, we have previously shown that a cannabis extract devoid of Δ(9)-THC still stimulates appetite, indicating that other phytocannabinoids also elicit hyperphagia. One possible candidate is the non-psychoactive phytocannabinoid cannabigerol (CBG), which has affinity for several molecular targets with known involvement in the regulation of feeding behaviour.

Objectives: The objective of the study was to assess the effects of CBG on food intake and feeding pattern microstructure.

Methods: Male Lister hooded rats were administered CBG (30-120 mg/kg, per ora (p.o.)) or placebo and assessed in open field, static beam and grip strength tests to determine a neuromotor tolerability profile for this cannabinoid. Subsequently, CBG (at 30-240 mg/kg, p.o.) or placebo was administered to a further group of pre-satiated rats, and hourly intake and meal pattern data were recorded over 2 h.

Results: CBG produced no adverse effects on any parameter in the neuromotor tolerability test battery. In the feeding assay, 120-240 mg/kg CBG more than doubled total food intake and increased the number of meals consumed, and at 240 mg/kg reduced latency to feed. However, the sizes or durations of individual meals were not significantly increased.

Conclusions: Here, we demonstrate for the first time that CBG elicits hyperphagia, by reducing latency to feed and increasing meal frequency, without producing negative neuromotor side effects. Investigation of the therapeutic potential of CBG for conditions such as cachexia and other disorders of eating and body weight regulation is thus warranted.

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Chemotherapy-induced cachexia dysregulates hypothalamic and systemic lipoamines and is attenuated by cannabigerol

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Abstract

Background: Muscle wasting, anorexia, and metabolic dysregulation are common side-effects of cytotoxic chemotherapy, having a dose-limiting effect on treatment efficacy, and compromising quality of life and mortality. Extracts of Cannabis sativa, and analogues of the major phytocannabinoid Δ9-tetrahydrocannabinol, have been used to ameliorate chemotherapy-induced appetite loss and nausea for decades. However, psychoactive side-effects limit their clinical utility, and they have little efficacy against weight loss. We recently established that the non-psychoactive phytocannabinoid cannabigerol (CBG) stimulates appetite in healthy rats, without neuromotor side-effects. The present study assessed whether CBG attenuates anorexia and/or other cachectic effects induced by the broad-spectrum chemotherapy agent cisplatin.

Methods: An acute cachectic phenotype was induced in adult male Lister-hooded rats by 6 mg/kg (i.p.) cisplatin. In total 66 rats were randomly allocated to groups receiving vehicle only, cisplatin only, or cisplatin and 60 or 120 mg/kg CBG (po, b.i.d.). Feeding behavior, bodyweight and locomotor activity were recorded for 72 hours, at which point rats were sacrificed for post-mortem analyses. Myofibre atrophy, protein synthesis and autophagy dysregulation were assessed in skeletal muscle, plasma metabolic profiles were obtained by untargeted 1H-NMR metabonomics, and levels of endocannabinoid-like lipoamines quantified in plasma and hypothalami by targeted HPLC-MS/MS lipidomics.

Results: CBG (120 mg/kg) modestly increased food intake, predominantly at 36-60hrs ($p<0.05$), and robustly attenuated cisplatin-induced weight loss from 6.3% to 2.6% at 72hrs ($p<0.01$). Cisplatin-induced skeletal muscle atrophy was associated with elevated plasma corticosterone (3.7 vs 13.1ng/ml, $p<0.01$), observed selectively in MHC type IIx ($p<0.05$) and IIb ($p<0.0005$) fibres, and was reversed by pharmacological rescue of dysregulated Akt/S6-mediated protein synthesis and autophagy processes. Plasma metabonomic analysis revealed cisplatin administration produced a wide-ranging aberrant metabolic phenotype ($Q2\hat{Y}=0.5380$, $p=0.001$), involving alterations to glucose, amino acid, choline and lipid metabolism, citrate cycle, gut microbiome function, and nephrotoxicity, which were partially normalized by CBG treatment ($Q2\hat{Y}=0.2345$, $p=0.01$). Lipidomic analysis of hypothalami and plasma revealed extensive cisplatin-induced dysregulation of central and peripheral lipoamines (29/79 and 11/26 screened, respectively), including reversible elevations in systemic N-acyl glycine concentrations which were negatively associated with the anti-cachectic effects of CBG treatment.

Conclusions: Endocannabinoid-like lipoamines may have hitherto unrecognized roles in the metabolic side-effects associated with chemotherapy, with the N-acyl glycine subfamily in particular identified as a potential therapeutic target and/or biomarker of anabolic interventions. CBG-based treatments may represent a novel therapeutic option for chemotherapy-induced cachexia, warranting investigation in tumour-bearing cachexia models.

Keywords: Cachexia; Cannabigerol; Cannabinoid; Chemotherapy; Cisplatin; Lipoamine.

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A cannabigerol-rich Cannabis sativa extract, devoid of [INCREMENT]9-tetrahydrocannabinol, elicits hyperphagia in rats

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Abstract

Nonpsychoactive phytocannabinoids (pCBs) from Cannabis sativa may represent novel therapeutic options for cachexia because of their pleiotropic pharmacological activities, including appetite stimulation. We have recently shown that purified cannabigerol (CBG) is a novel appetite stimulant in rats. As standardized extracts from Cannabis chemotypes dominant in one pCB [botanical drug substances (BDSs)] often show greater efficacy and/or potency than purified pCBs, we investigated the effects of a CBG-rich BDS, devoid of psychoactive [INCREMENT]-tetrahydrocannabinol, on feeding behaviour. Following a 2 h prefeed satiation procedure, 16 male Lister-hooded rats were administered CBG-BDS (at 30-240 mg/kg) or vehicle. Food intake, meal pattern microstructure and locomotor activity were recorded over 2 h. The total food intake was increased by 120 and 240 mg/kg CBG-BDS (1.53 and 1.36 g, respectively, vs. 0.56 g in vehicle-treated animals). Latency to feeding onset was dose dependently decreased at all doses, and 120 and 240 mg/kg doses increased both the number of meals consumed and the cumulative size of the first two meals. No significant effect was observed on ambulatory activity or rearing behaviour. CBG-BDS is a novel appetite stimulant, which may have greater potency than purified CBG, despite the absence of [INCREMENT]-tetrahydrocannabinol in the extract.