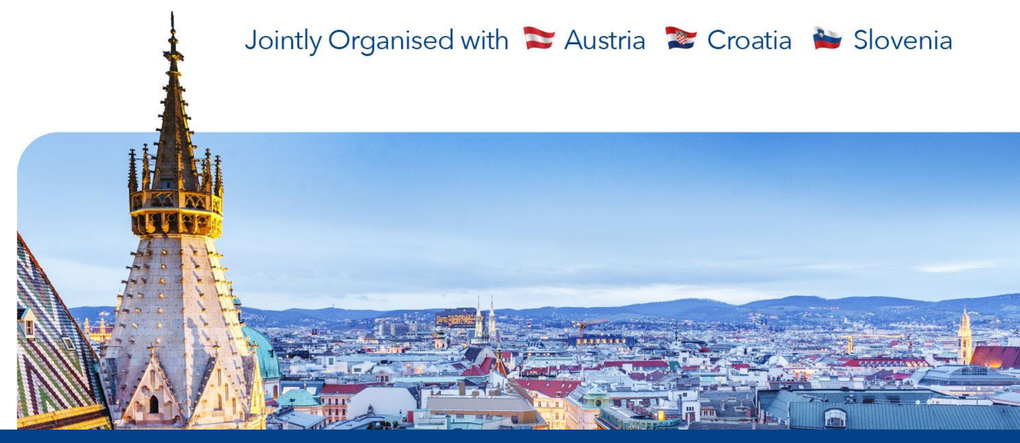
Cannabidiol prevents cisplatin-induced atrophy in a model of myotubes in culture

Phelipe Sanchez, Olivier Le Bacquer

44th ESPEN CONGRESS
3–6 Sept 2022
VIENNA ESPEN CONGRESS
ON CLINICAL NUTRITION & METABOLISM
www.espen.org www.espencongress.com
eat & move
Jointly Organised with Austria Croatia Slovenia



Cannabidiol prevents cisplatin-induced atrophy in a model of myotubes in culture

P. SANCHEZ[1], O. LE BACQUER[1]
1. Université Clermont Auvergne, INRAE, UNH (Unité de Nutrition Humaine), Clermont-Ferrand, France.

PT 36

INTRODUCTION

Chemotherapy-induced cachexia (CIC) is a severe muscle wasting syndrome and aggravates cancer-cachexia in patients [1]. Currently, there are no official guidelines for the management of muscle wasting. Cannabidiol (CBD) is a bioactive phytocannabinoid produced from Cannabis Sativa. Recent studies demonstrated the beneficial effect of CBD on maintaining muscle function and metabolism in obese models and mdx dystrophic mice [2-4].

AIM

The aim of this study was to evaluate the effect of CBD on muscle atrophy in response to cisplatin, in a model of myotubes in culture.

METHOD

After differentiation, C2C12 cells (a model of myotubes) were incubated in the presence of 50µM cisplatin for 24-48h with or without increasing dose of CBD (1-5µM). Cell viability was measured using a CellTiter-Glo® 3D Cell Viability Assay. Myotube diameter was analyzed by microscopy. Protein synthesis and proteolysis were measured by Western Blot using the SUnSET technique (puromycin incorporation into nascent proteins), and polyubiquitination of total proteins, respectively. Activation of Akt and S6K1 pathways and cleaved-caspase 3 levels were quantified by Western blot. Results were analyzed by one-way ANOVA and expressed as mean ± sem.

RESULTS

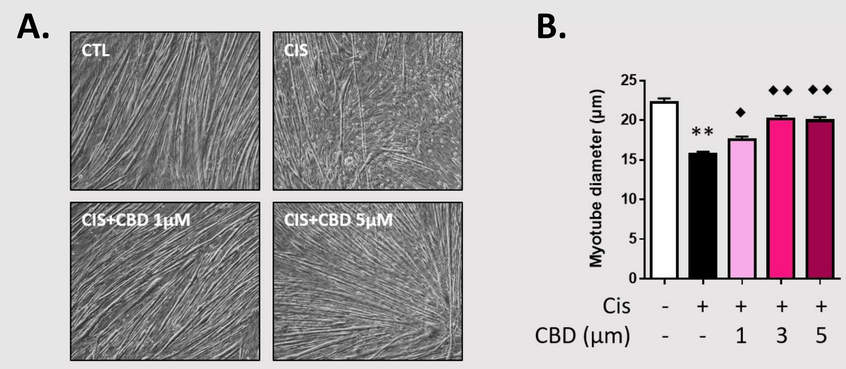


Figure 1. Cannabidiol prevents cisplatin-induced myotube atrophy in C2C12. A) Representative pictures of myotube morphology at 24 h of incubation. B) Myotube diameter of treated cells. Results are expressed as mean ± sem. ** p<0.01 *vs.* CTL, ◆ p<0.05 *vs.* Cis, ◆◆ p<0.01 *vs.* Cis.

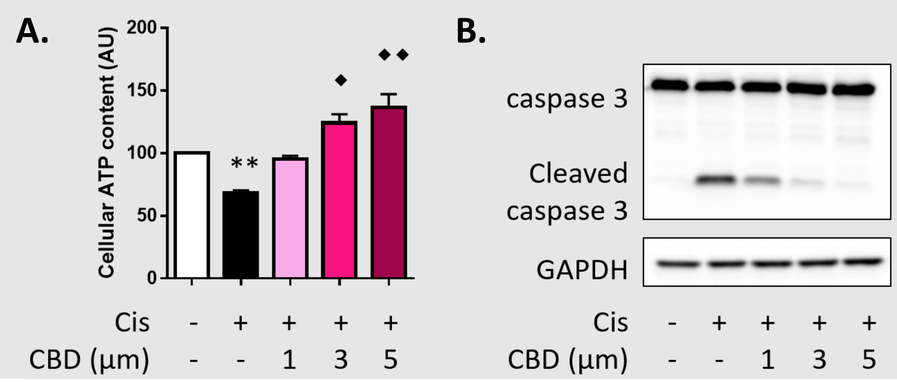


Figure 2. Cannabidiol prevents cisplatin-induced cell death in C2C12. A) Cellular ATP content was measured as indicative of cell viability at 48h of incubation. B) Representative Western Blot of cleaved-caspase 3 levels in response to cisplatin and cannabidiol treatment, at 24 h of incubation. Results are expressed as mean ± sem. ** p<0.01 *vs.* CTL, ◆ p<0.05 *vs.* Cis, ◆◆ p<0.01 *vs.* Cis.

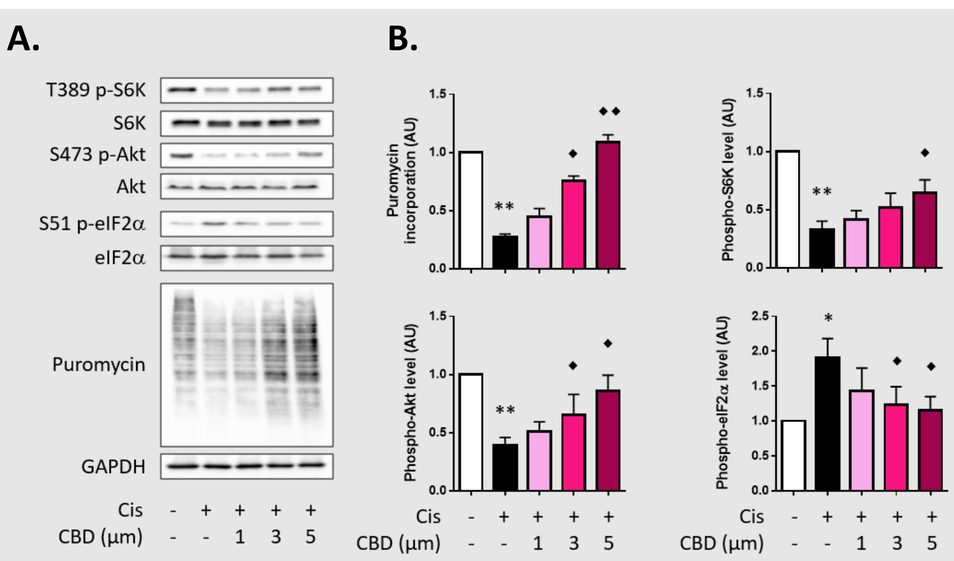


Figure 3. Cannabidiol helps maintaining protein synthesis in cisplatin-treated C2C12. A). Representative western blot of the phosphorylation state of Akt (ser473), S6K (thr389), eIF2a (ser51), and puromycin incorporation in response to cisplatin and cannabidiol treatment, at 24 h of incubation. B) Quantification of puromycin incorporation, and phosphorylation state of Akt, S6K and eIF2a signals from (A). Results are expressed as mean ± sem. * p<0.05 *vs.* CTL, ** p<0.01 *vs.* CTL, ◆ p<0.05 *vs.* Cis, ◆◆ p<0.01 *vs.* Cis.

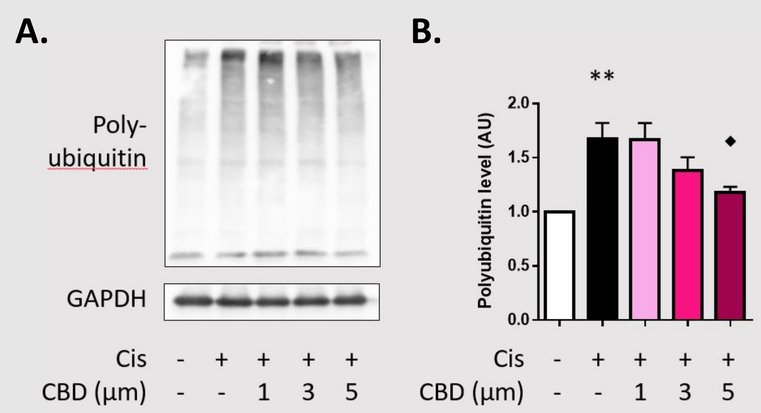


Figure 4. Cannabidiol reduces proteolysis in cisplatin-treated C2C12. A). Representative western blot of total protein polyubiquitination in response to cisplatin and cannabidiol treatment, at 24 h of incubation. B) Quantification of polyubiquitination signal from (A). Results are expressed as mean ± sem. ** p<0.01 *vs.* CTL, ◆ p<0.05 *vs.* Cis.

CONCLUSIONS

These results demonstrate that, in a model of myotubes in culture, cannabidiol prevents cisplatin-induced cell death and myotube atrophy by maintaining protein homeostasis. This suggests cannabidiol could be useful in the treatment of cancer cachexia.

ACKNOWLEDGEMENT

This study was supported by the INRAE AlimH department.

REFERENCES

1. Fearon K et al. Definition and classification of cancer cachexia: an international consensus. Lancet Oncol. 2011 May;12(5):489-95.
2. Iannotti FA et al. Effects of non-euphoric plant cannabinoids on muscle quality and performance of dystrophic mdx mice. Br J Pharmacol. 2019 May;176(10):1568-1584.
3. Bielawiec P et al. Attenuation of Oxidative Stress and Inflammatory Response by Chronic Cannabidiol Administration Is Associated with Improved n-6/n-3 PUFA Ratio in the White and Red Skeletal Muscle in a Rat Model of High-Fat Diet-Induced Obesity. Nutrients. 2021 May 11;13(5):1603.
4. Bielawiec P et al. Chronic Cannabidiol Administration Attenuates Skeletal Muscle De Novo Ceramide Synthesis Pathway and Related Metabolic Effects in a Rat Model of High-Fat Diet-Induced Obesity. Biomolecules. 2020 Aug 26;10(9):1241.

CONTACT INFORMATION

olivier.le-bacquer@inrae.fr