PERSPECTIVES IN **HYPERTENSION**

Full-spectrum CBD oil: a promising ally against hypertension?

JOSIANE CRUZ

Federal University of Paraíba, Brazil



Introduction

Hypertension is a chronic, multifactorial condition marked by persistently high blood pressure, influenced by genetic and lifestyle factors such as smoking, obesity, and inactivity. It often progresses silently but can cause serious damage to vital organs, contributing to cardiovascular and renal diseases. Its global prevalence has doubled from 2009 to 2019, now affecting around 1.2 billion adults (World Health Organization, 2019).

Treatment involves lifestyle changes and antihypertensive medications, but long-term effectiveness can be limited due to tolerance and the need for combination therapies. Although 82 natural compounds have been FDA-approved for hypertension, many patients fail to achieve full blood pressure control. Incomplete understanding of the disease mechanisms highlights the need for further research and innovative therapies (World Health Organization, 2019).

Cannabis-Derived Phytocannabinoids: Historical Use and Cardiovascular **Therapeutic Potential**

Phytocannabinoids from the Cannabis plant, used medicinally since ancient times in civilizations like China, Egypt, and Greece, are now being investigated for their therapeutic potential. (Rock & Parker, 2021)

Among over 100 phytocannabinoids, cannabidiol (CBD) and $\Delta 9$ -tetrahydrocannabinol ($\Delta 9$ -THC) are the most abundant and active. Δ9-THC is psychoactive, while CBD is non-psychoactive, well-tolerated, and predominant in Cannabis sativa. These compounds act via cannabinoid

receptors CB1 and CB2, which are part of the endocannabinoid system (ECS), a homeostatic regulator involving endogenous ligands like anandamide (AEA) and 2-AG (Jarvis et al., 2017).

CBD, a lipophilic molecule, crosses biological barriers efficiently and exhibits strong antioxidant and anti-inflammatory properties. Studies have also demonstrated its vasodilatory and hypotensive effects, highlighting its potential for treating cardiovascular diseases (Stanley et al., 2015).

Early Evidence from Cardiovascular Studies

Research on the cardiovascular effects of Cannabis compounds began in the 1970s. Early studies showed that Δ9-THC and CBD could reduce blood pressure in animal models. These findings raised interest in the role of the endocannabinoid system in cardiovascular regulation (Adams et al., 1977). Anandamide, an endogenous cannabinoid, was found to induce complex cardiovascular responses and lower blood pressure and heart contractility in hypertensive rats, effects mediated by CB1 receptors (Malinowska et al., 2001; Varga et al., 1995). Anandamide also reduced blood pressure in angiotensin II-induced hypertension, suggesting ECS interaction with hormonal (Bátkai et al., 2004).

Fitocanabinoide such as Δ9-THC also lowers blood pressure, however its therapeutic use is limited by rapid tolerance. CBD, on the other hand, is nonpsychoactive, well tolerated, and does not induce tolerance. In humans, a single 600 mg dose of CBD reduced both systolic and diastolic blood pressure and blunted the response to stress, supporting its potential as an antihypertensive agent (Jadoon et al., 2017).







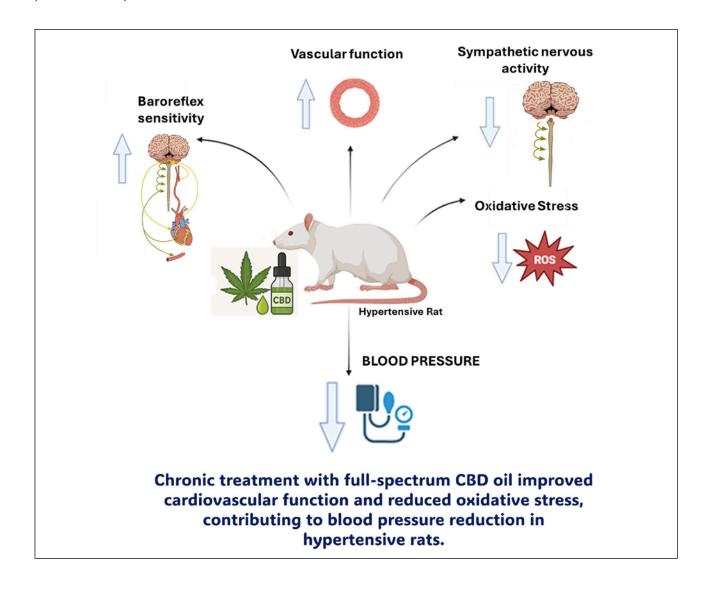
Our Study: CBD in Renovascular Hypertension

In our study, we evaluated the chronic effects of full-spectrum CBD (a cannabidiol rich extract that also contains a variety of other naturally occurring compounds from the Cannabis sativa plant) in the 2-kidney, 1-clip (2K1C) model of renovascular hypertension, a condition caused by reduced blood flow to the kidneys and driven by high levels of angiotensin II vasoactivity hormone. Male Wistar rats underwent either 2K1C or SHAM surgery. Six weeks later, they received chronic oral treatment with cannabis oil containing CBD (20 mg/kg, administered every 12 hours for 14 days by intragastric gavage). A combination of in vivo, in vitro, and ex vivo techniques was used to assess cardiovascular outcomes.

The results were promising. chronic full-spectrum CBD oil treatment significantly reduced blood pressure, improved vascular function, and

decreased oxidative stress in the arterial wall, factors strongly linked to hypertension progression. Furthermore, CBD enhances baroreflex sensitivity, a brain-controlled mechanism that helps the heart and blood vessels respond to changes in blood pressure, and reduces sympathetic nervous system overactivity, which is commonly elevated in hypertensive states (Flôr et al., 2024).

These findings suggest that full-spectrum CBD oil possesses multi-target antihypertensive properties, contributing to blood pressure reduction through mechanisms involving improved autonomic regulation, vascular tone, and oxidative balance. Although further clinical investigations are needed to confirm these effects in humans, our results support the therapeutic potential of full spectrum CBD oil in hypertension management, particularly in cases resistant to conventional treatment.









Importantly, our study was made possible through collaboration with ABRACE, a nonprofit association that produces cannabis oil at low cost, thereby ensuring accessibility for the Brazilian population. This partnership underscores the vital role of community-based organizations in advancing scientific research and promoting equitable access to emerging therapies.

By bridging scientific innovation with social commitment, this research highlights CBD's therapeutic promise and advocates for broader public and governmental engagement in the discussion around medicinal Cannabis. Such efforts are essential to expand access and improve outcomes for the millions of individuals affected by hypertension in Brazil and globally.

Final remarks

Chronic full-spectrum CBD oil treatment demonstrates significant antihypertensive effects by enhancing baroreflex sensitivity, improving vascular function, reducing sympathetic nervous system activity, and mitigating arterial oxidative stress. These findings position CBD as a promising candidate for the treatment of renovascular hypertension and its associated cardiovascular complications.

References:

Bátkai, S., Pacher, P., Osei-Hyiaman, D., Radaeva, S., Liu, J., Harvey-White, J., Offertáler, L., Mackie, K., Rudd, M. A., Bukoski, R. D., & Kunos, G. (2004). Endocannabinoids Acting at Cannabinoid-1 Receptors Regulate Cardiovascular Function in Hypertension. Circulation, 110(14), 1996–2002. https://doi.org/10.1161/01.CIR.0000143230.23252.D2

Flôr, A. F. L., Duarte-Maia, S., Fernandes-Costa, F., Souza, R. M. P. de, braga, V. de A., do Amaral, S. L., Mascarenhas, S. R., Brito-Alves, J. L., Colombari, D. S. A., & Cruz, J. C. (2024). Chronic cannabidiol treatment induces cardiovascular improvement in renovascular hypertensive rats. Journal of Hypertension. https://doi.org/10.1097/ HJH.000000000003865

Jadoon, K. A., Tan, G. D., & O'Sullivan, S. E. (2017). A single dose of cannabidiol reduces blood pressure in healthy volunteers in a randomized crossover study. JCI Insight, 2(12). https://doi.org/10.1172/jci.insight.93760

Josiane Cruz - josianecruz@cbiotec.ufpb.br

Jarvis, S., Rassmussen, S., & Winters, B. (2017). Role of the Endocannabinoid System and Medical Cannabis. The Journal for Nurse Practitioners, 13(8), 525–531. https://doi. org/10.1016/j.nurpra.2017.05.014

Malinowska, B., Kwolek, G., & Göthert, M. (2001). Anandamide and methanandamide induce both vanilloid VR1- and cannabinoid CB1 receptor-mediated changes in heart rate and blood pressure in anaesthetized rats. Naunyn-Schmiedeberg's Archives of Pharmacology, 364(6), 562–569. https://doi.org/10.1007/s00210-001-0498-6

Remiszewski, P., Jarocka-Karpowicz, I., Biernacki, M., Jastrząb, A., Schlicker, E., Toczek, M., Harasim-Symbor, E., Pędzińska-Betiuk, A., & Malinowska, B. (2020). Chronic Cannabidiol Administration Fails to Diminish Blood Pressure in Rats with Primary and Secondary Hypertension Despite Its Effects on Cardiac and Plasma Endocannabinoid System, Oxidative Stress and Lipid Metabolism. International Journal of Molecular Sciences, 21(4), 1295. https://doi.org/10.3390/ ijms21041295

Rock, E. M., & Parker, L. A. (2021). Constituents of Cannabis Sativa (pp. 1-13). https://doi. org/10.1007/978-3-030-57369-0 1

Stanley, C. P., Hind, W. H., Tufarelli, C., & O'Sullivan, S. E. (2015). Cannabidiol causes endothelium-dependent vasorelaxation of human mesenteric arteries via CB 1 activation. Cardiovascular Research, 107(4), 568-578. https://doi.org/10.1093/cvr/cvv179

Varga, K., Lake, K., Martin, B. R., & Kunos, G. (1995). Novel antagonist implicates the CB1 cannabinoid receptor in the hypotensive action of anandamide. European Journal of Pharmacology, 278(3), 279-283. https://doi. org/10.1016/0014-2999(95)00181-J

Whelton, P. K., Carey, R. M., Aronow, W. S., Casey, D. E., Collins, K. J., Dennison Himmelfarb, C., DePalma, S. M., Gidding, S., Jamerson, K. A., Jones, D. W., MacLaughlin, E. J., Muntner, P., Ovbiagele, B., Smith, S. C., Spencer, C. C., Stafford, R. S., Taler, S. J., Thomas, R. J., Williams, K. A., ... Wright, J. T. (2018). 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/ APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension, 71(6). https:// doi.org/10.1161/HYP.0000000000000065

Williams, R. B., Ng, L. K. Y., Lamprecht, F., Roth, K., & Kopin, I. J. (1973). ?9-Tetrahydrocannabinol: A hypotensive effect in rats. Psychopharmacologia, 28(3), 269-274. https://doi. org/10.1007/BF00429307

World Health Organization. (2019). World Health Organization annual report 2019 WHO.









