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Influence of cannabidiol on vascular function in hypertension

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Introduction Cannabidiol has been suggested to be a beneficial treatment of cardiovascular disorders. It directly relaxes human and rat arteries and augments endothelial function in Zucker diabetic fatty rats [1]. The aim of the study was to determine the influence of cannabidiol on vascular function in hypertensive rats.

Methods Experiments were performed in the isolated endothelium-intact thoracic aortae isolated from male spontaneously (SHR) or deoxycorticosterone acetate and high salt-diet treated (DOCA-salt) hypertensive Wistar rats or their appropriate normotensive controls Wistar Kyoto (WKY) or uninephrectomized Wistar (UNX) rats using organ bath technique[2]. Aortae were incubated for 2h with cannabidiol (10 µM) or vehicle (10 µl), then cumulative concentration-response curves were conducted: (1) to acetylcholine (0.0001 - 3 µM) in phenylephrine pre-constricted aortae and (2) to phenylephrine (0.0001 - 30 µM) and a thromboxane A_2 analog U46619 (0.0001 - 3 µM). In each individual preparation only one experimental curve was determined. Results are shown as means ± SEM of *n* animals as (1) % of relaxation of phenylephrine (10 µM)-induced contraction or (2) % of contraction of KCl (60 mM)-induced tone, respectively. Statistical comparisons were made using Student's unpaired *t*-test. $P<0.05$ was considered as significant.

Results Cannabidiol by itself did not change basal tone but its incubation increased potency of acetylcholine-induced vasorelaxation without changes in maximal response in both model of hypertension but not in respective normotensive strains when compared to vehicle-treated artery (Table 1). Treatment with cannabidiol attenuated the phenylephrine- and U46619-induced vasoconstrictor potency (Table 1). The maximal response was reduced only in phenylephrine-evoked vasoconstriction in normo- and hypertensive animals; R_{max} (cannabidiol vs vehicle): WKY 52.5±3.7 vs 79.8±2.5; SHR 54.7±4.2 vs 74.5±3.1; UNX 51.6±3.9 vs 82.8±4.0; DOCA-salt 82.4±2.3 vs 92.3±2.7, $P<0.05$.

Conclusions The beneficial effect of cannabidiol in hypertension (model-independently) may be partially due to improved endothelium-dependent vasorelaxation and/or reduced vasoconstriction.

References

1. Wheal AJ *et al*. (2017). *Front Pharmacol* 8:248.

2. Baranowska-Kuczko M *et al*. (2016). *Life Sci* 151:288-299.

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Table1. Potency (pEC_{50}) of acetylcholine and vasoconstrictors in aortae.

Group		Acetylcholine	Phenylephrine	U46619
WKY	vehicle	6.9±0.1(8)	7.4±0.1 (6)	7.6±0.1(8)
	cannabidiol	6.8±0.1(8)	7.0±0.1* (6)	7.2±0.1*(8)
SHR	vehicle	7.1±0.1(6)	7.2±0.1(5)	8.3±0.1(5)
	cannabidiol	8.0±0.2*(6)	6.7±0.1*(5)	7.3±0.1*(5)
UNX	vehicle	7.3±0.1(5)	7.5±0.1(6)	8.0±0.1(5)
	cannabidiol	7.6±0.1(5)	6.7±0.1*(6)	7.2±0.1*(5)
DOCA-salt	vehicle	7.2±0.1(5)	7.6±0.1(5)	8.4±0.1(5)
	cannabidiol	7.6±0.1*(5)	7.2±0.1*(7)	7.4±0.1*(5)

* $P<0.05$ compared to the respective vehicle control, *n* in brackets