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Meldonium Therapy Improves the Right Ventricle Function

Kigitovica D, Korzh S, Videja M, Vilks K, Makrecka-Kuka M, Liepinsh E, Skride A, Dambrova M, Vilskersts R

2023

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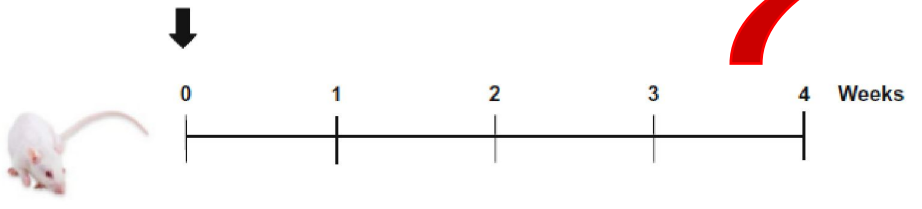
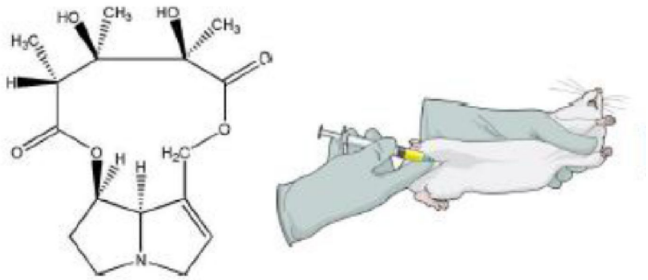
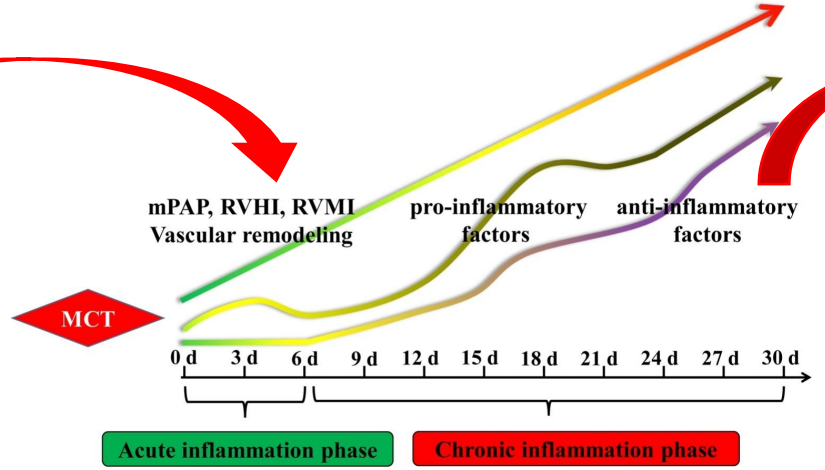
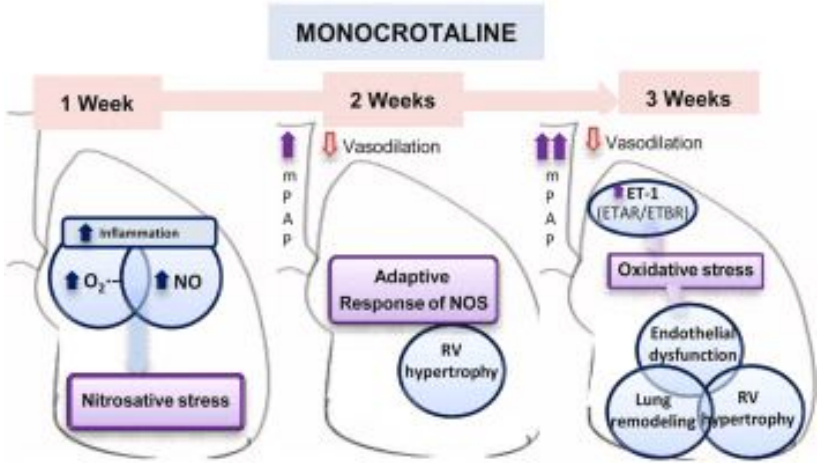
Experimental model



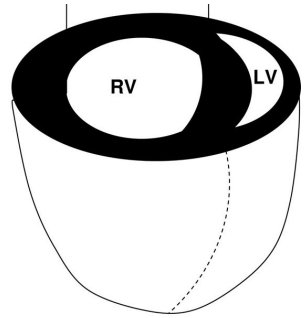


Bueno-Beti C, et al, 2018
Turck R, et al, 2019





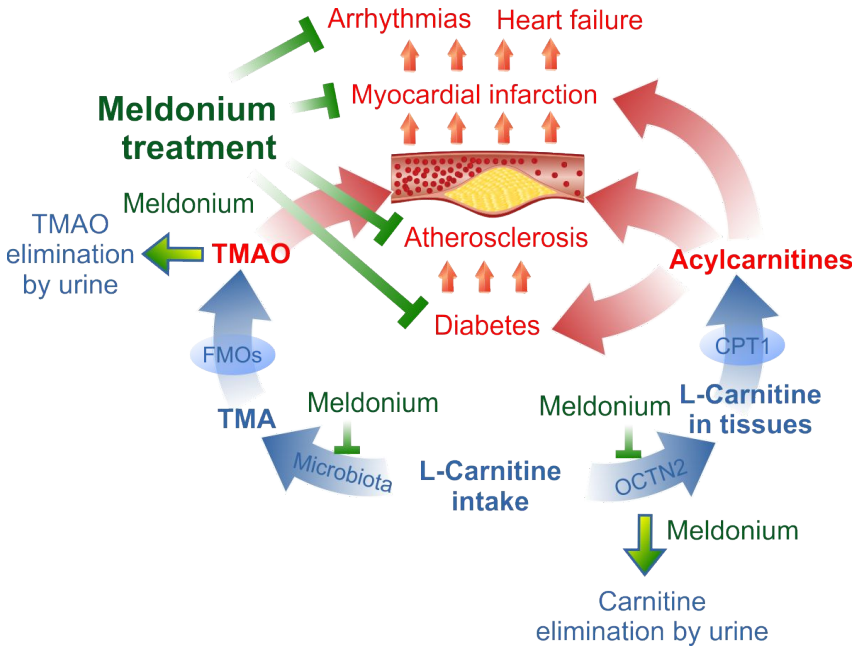
Thang C, et al, 2021
Zimmer A, et al, 2021



RVF
Death

Voelkel NF, et al, 2006

Meldonium

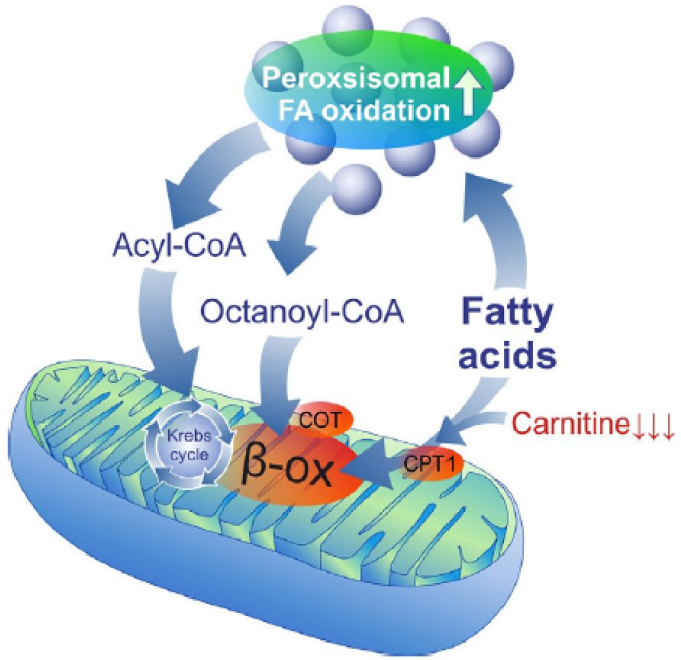


REVIEW ARTICLE

Fatty acid metabolism in pulmonary arterial hypertension: role in right ventricular dysfunction and hypertrophy

Megha Talati, Anna Hemnes

Division of Allergy, Pulmonary, and Critical Care Medicine, Department of Medicine, Vanderbilt University Medical Center, Nashville, Tennessee, USA



Dambrova M, et al,2016

Methods

34 Male Sprague-Dawley rats

Saline

Control (n=10)

MCT

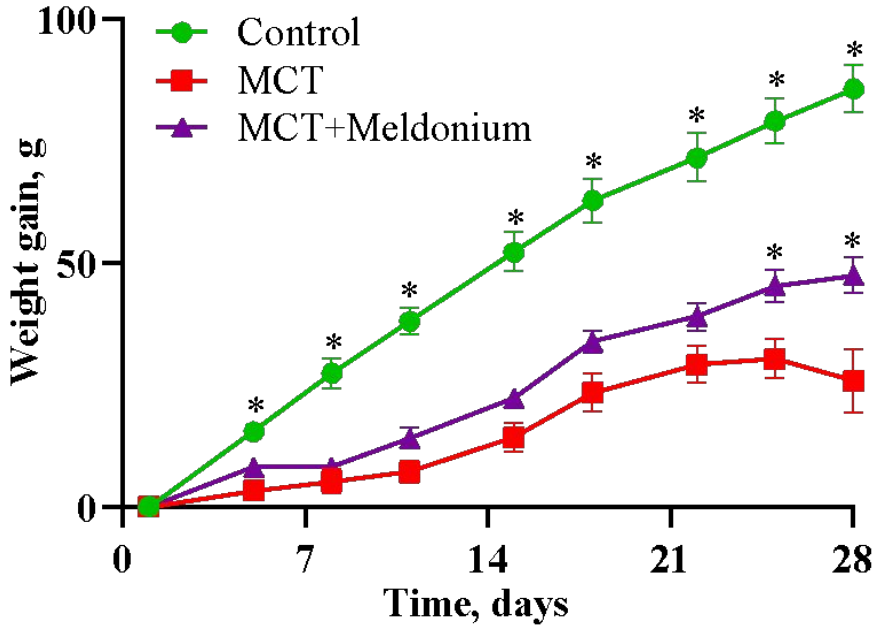
MCT (n=12)

MCT

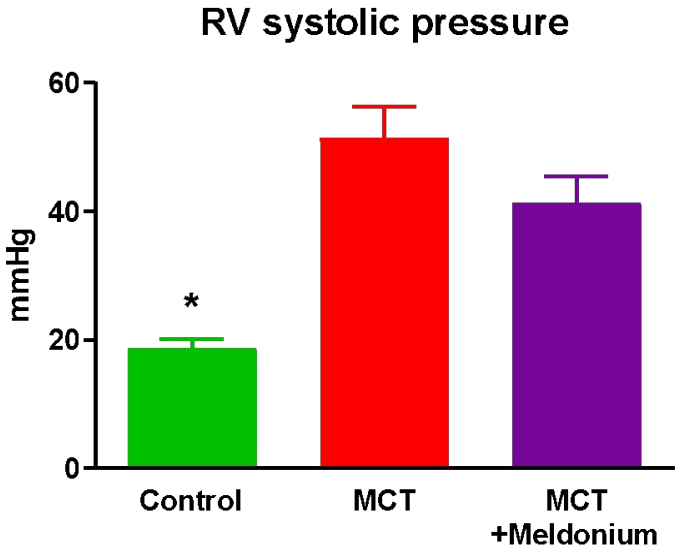
MCT+Meldonium (n=12)

4 weeks

Effect of meldonium on body weight change

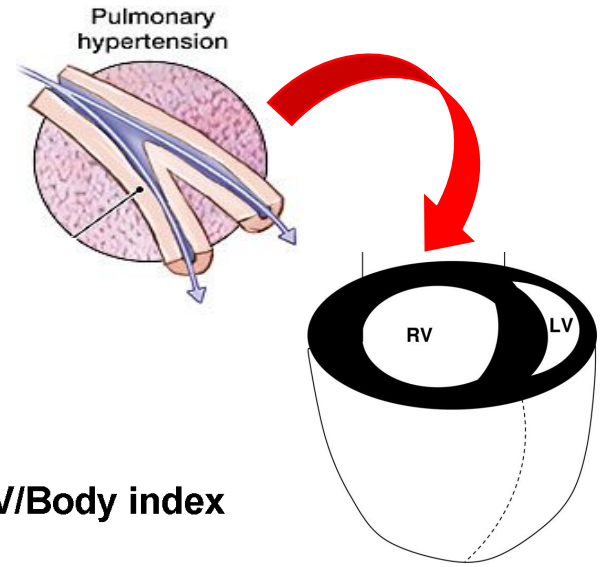


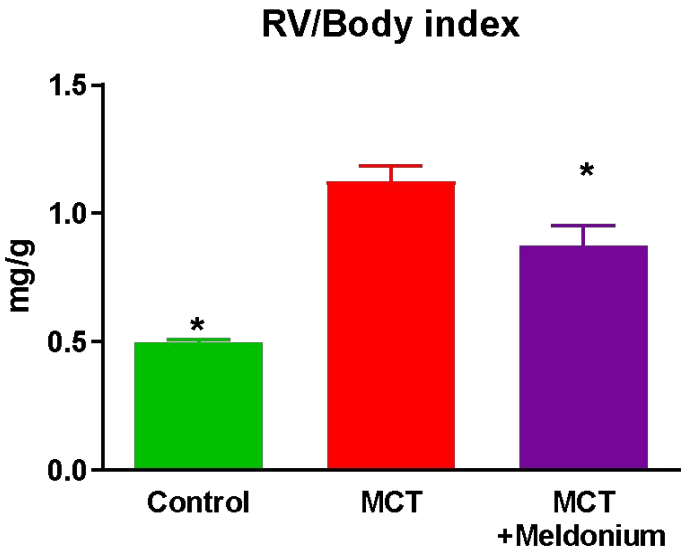
Results are shown as the mean ± SEM of 10-12 animals. * p<0.05 vs. MCT group, Two-way repeated measures ANOVA with Tukey's multiple comparisons test.

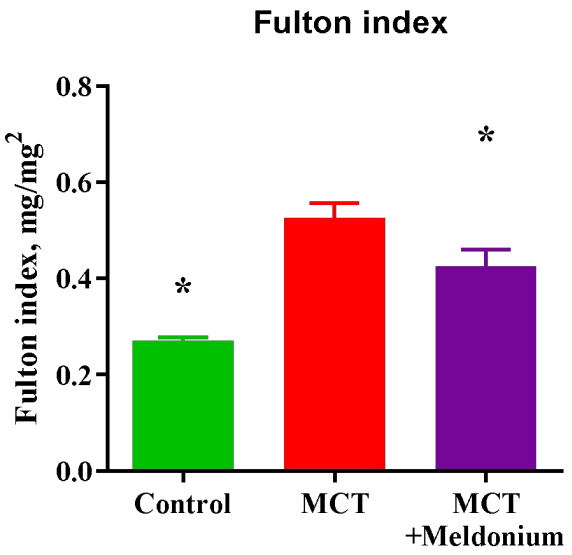


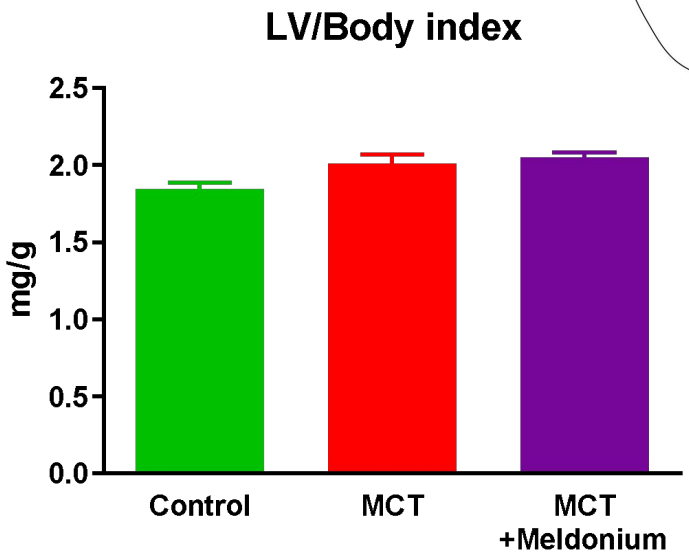
Results are shown as the mean ± SEM of 10-12 animals. * p<0.05 vs. MCT group, One-way ANOVA with Dunnett's multiple comparisons test.

Effect of meldonium on weight of heart ventricles



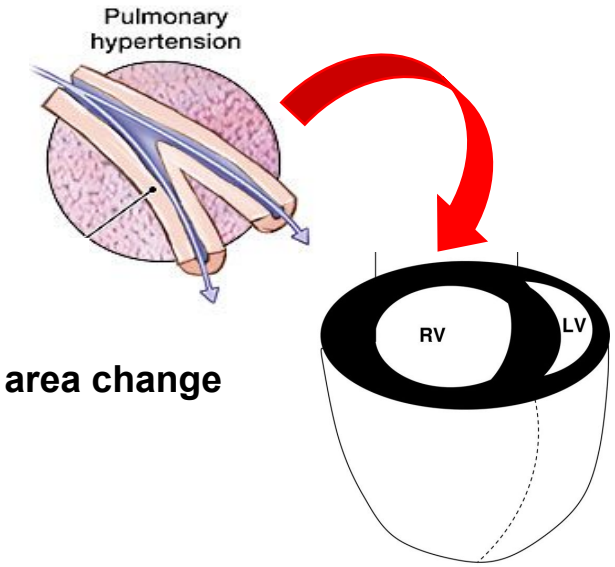


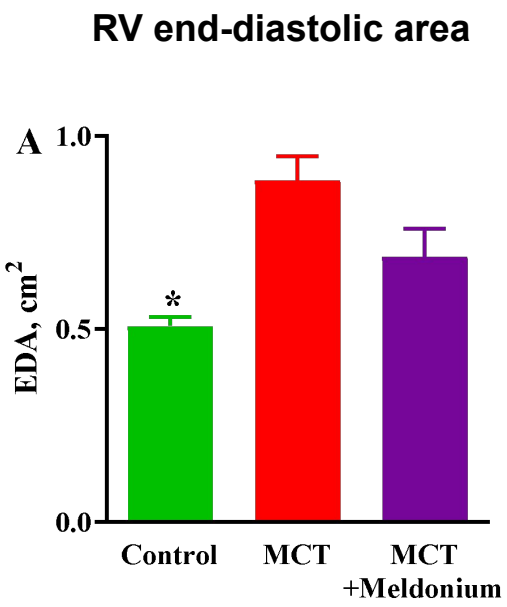


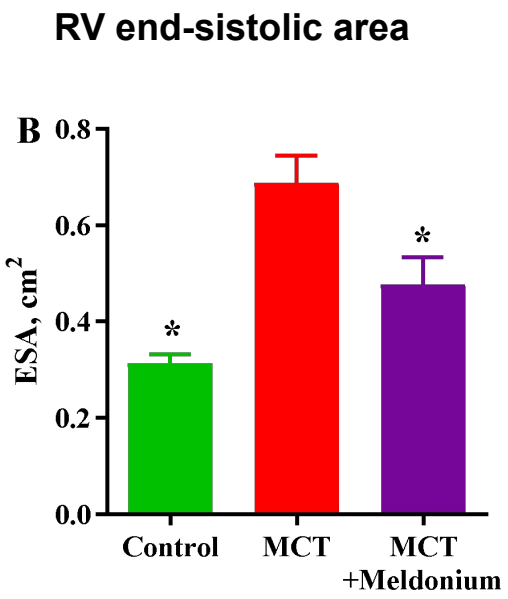


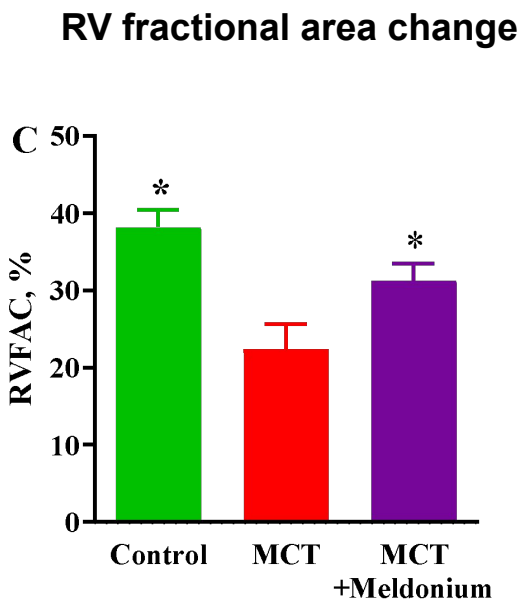
Results are shown as the mean ± SEM of 10-12 animals. * p<0.05 vs. MCT group, One-way ANOVA with Dunnett's multiple comparisons test.

Effect of meldonium on right ventricle



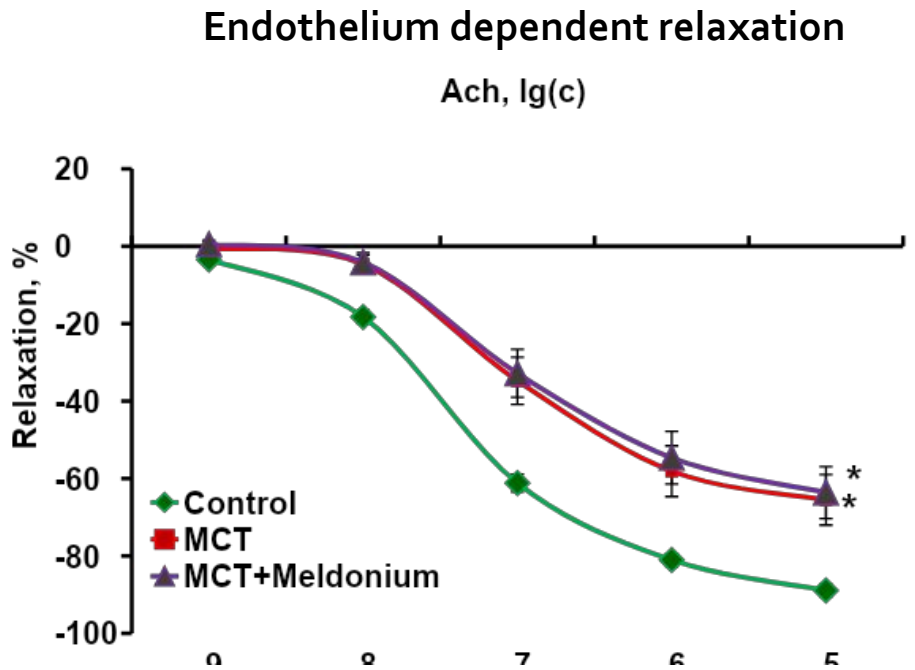


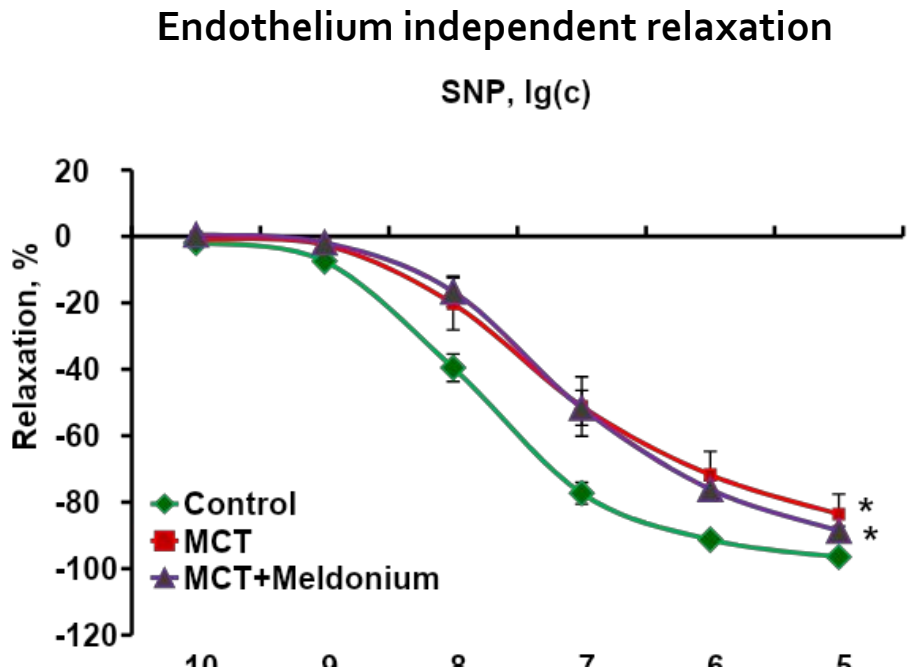




Data are shown as the mean ± SEM of 9 to 10 animals. * p<0.05 vs. MCT group, One-way ANOVA with Dunnett's multiple comparisons test.

Effects of meldonium on vascular reactivity of pulmonary arteries



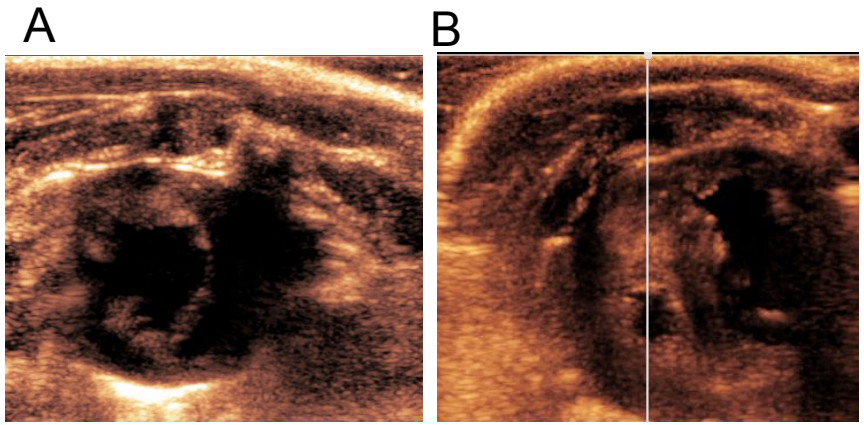


* p<0.05 vs MCT group; Two-way repeated measures ANOVA with Tukey's multiple comparisons test

Effects of administration of meldonium on the dimensions and functioning of the left ventricle

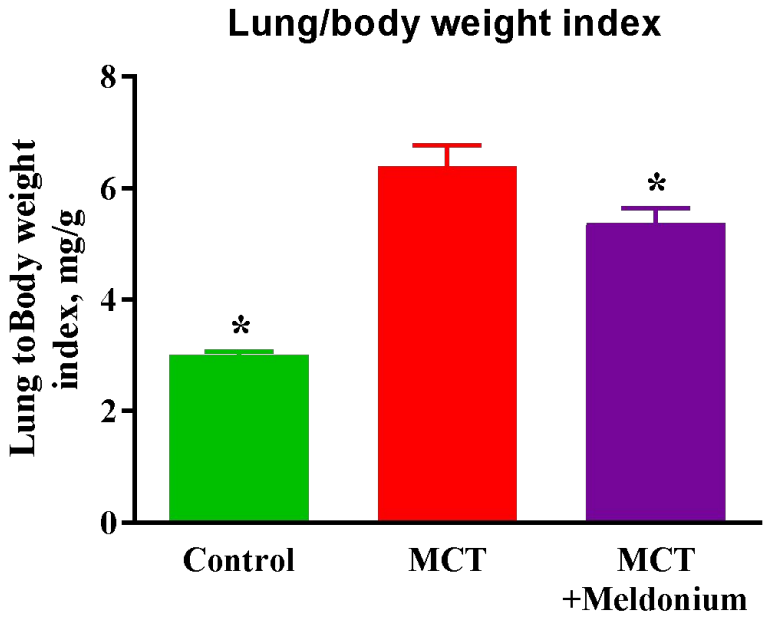
	Control	MCT	MCT +Meldonium
HR, bpm	310±8	298±8	305±6
EF, %	81±1	82±1	80±3
FS, %	45±1	46±1	45±3
CO, l/min	0.39±0.02*	0.25±0.03	0.25±0.03
LVPWs, mm	3.2±0.1	2.9±0.1	3.0±0.1
LVPWd, mm	1.7±0.1	1.7±0.1	1.7±0.1
IVSs, mm	3.1±0.1	3.3±0.1	3.0±0.2
IVSd, mm	1.6±0.1	1.8±0.2	1.6±0.1
LVIDs, mm	4.9±0.1	3.9±0.3	4.3±0.5
LVIDd, mm	9.0±0.2*	7.2±0.5	7.7±0.5
ESV, ml	0.30±0.02	0.19±0.04	0.27±0.06
EDV, ml	1.55±0.09*	0.96±0.15	1.10±0.15

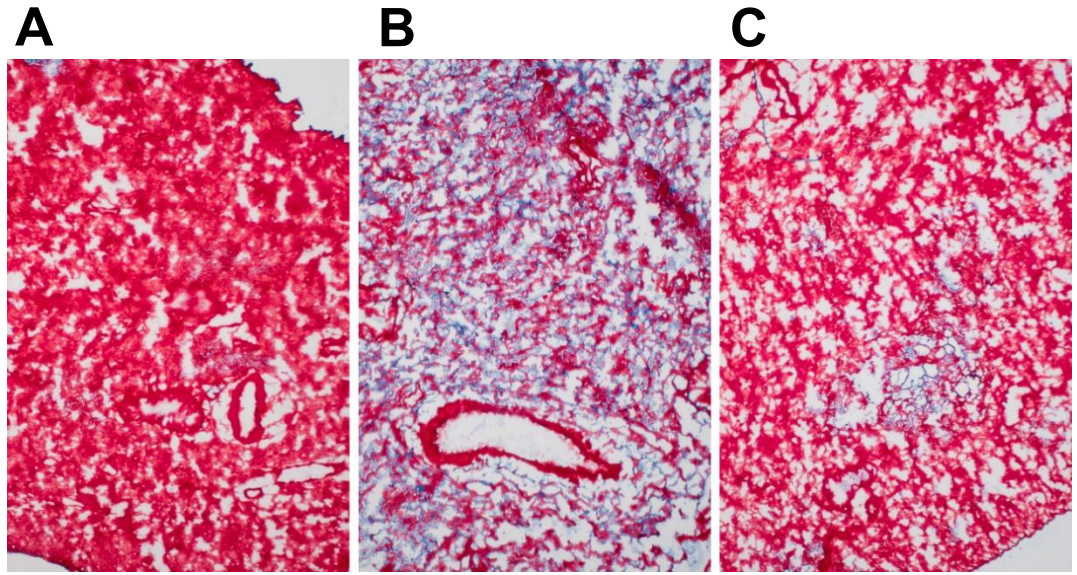
Data are shown as the mean±SEM of 10 to 12 animals. * $p<0.05$ vs. MCR group, One-way ANOVA with Dunnett's multiple comparisons test.



Illustrative images of heart ventricle (A) from control and (B) MCT group animal 4 weeks after the administration of MCT

Effect of meldonium on the lung to body weight index

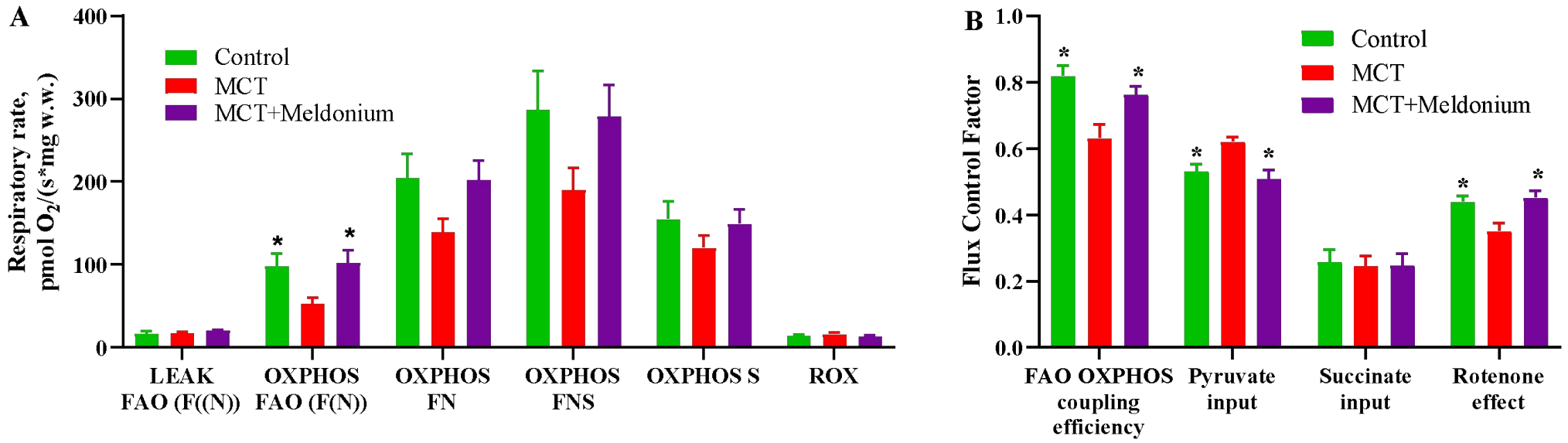




Illustrative images of Masson's-trichrome stained sections of the lungs (A) control, (B) MCT and (C) MCT+Meldonium groups

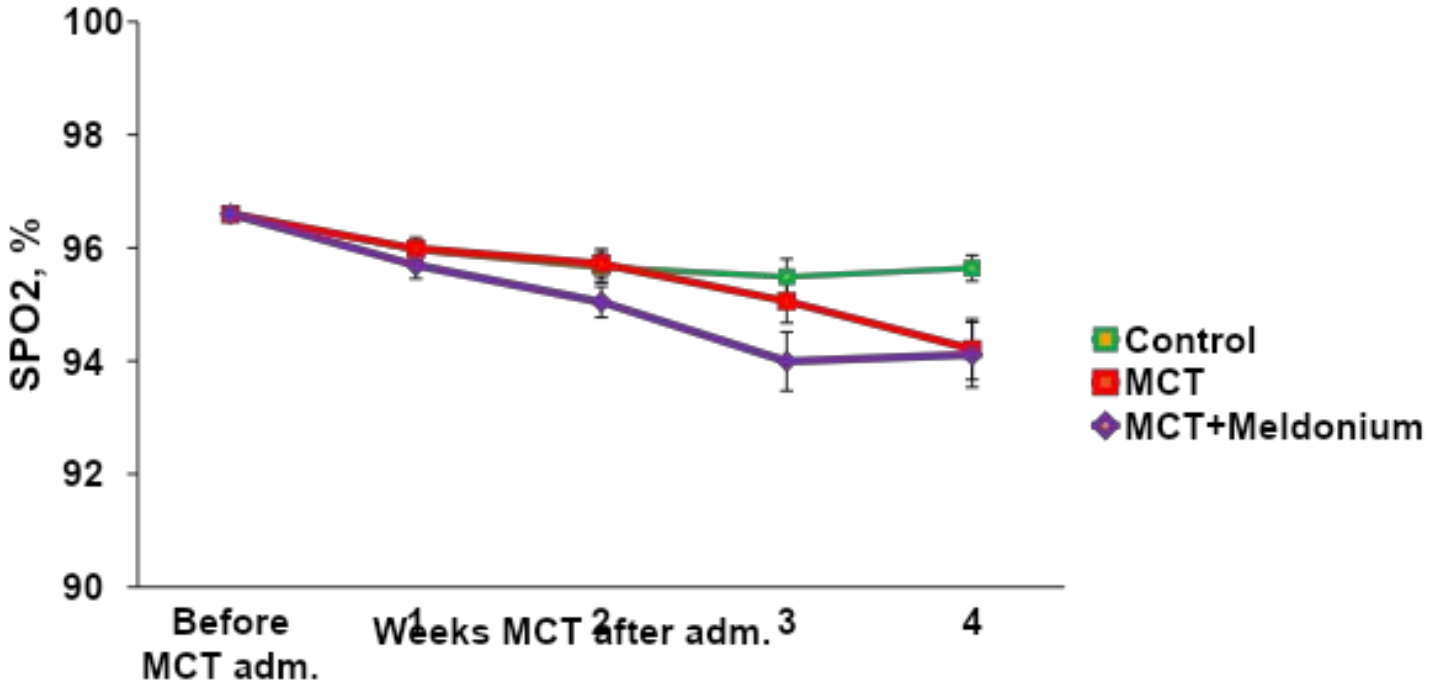
Data are shown as the mean ± SEM of 10 to 12 animals. * $p<0.05$ vs. MCT group, One-way ANOVA with Dunnett's multiple comparisons test.

Effect of meldonium on mitochondrial functionality in the right ventricular cardiac fibers



The results are presented as the mean ± SEM of 10-12 animals. * p<0.05 vs. MCT group, One-way ANOVA with Dunnett's multiple comparisons test. Flux control factor, the contribution of each substrate/pathway to the respiration rate; S, succinate; F, fatty acid oxidation-dependent pathway; N, NADH pathway; LEAK, substrate-dependent state; OXPHOS, oxidative phosphorylation-dependent state; ROX, residual oxygen consumption.

Changes of Oxygen saturation (SpO_2) after meldonium administration



Results are shown as the mean±SEM of 10 rats. * p<0.05 vs. Control group, Two-way repeated measures ANOVA with Tukey's multiple comparisons test

Conclusions

Meldonium decreased dilation, improved function of RV and protected functionality of cardiac mitochondria in experimental model of PH and RV failure.

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THANK YOU!

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