Chronic (-)-epicatechin administration does not affect contracting skeletal muscle microvascular oxygenation

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Abstract

The flavanol -(-)epicatechin (EPI) is a naturally occurring component of cocoa, consumption of which is associated with numerous cardiovascular health benefits. Chronic EPI reportedly augments mouse skeletal muscle capillarity and mitochondrial density (Nogueira et al, J Physiol, 589, 2011). These effects may translate to improved skeletal muscle O_2 delivery-utilization matching (i.e. ↑ microvascular O_2 pressure (PO_2mv)) during contractions. We tested the hypothesis that EPI would elevate PO_2mv at rest and contractions. Rats were administered EPI (2mg/kg , n=5) or water (CON; n=5) via oral gavage twice daily for 21 days. PO_2mv was measured via phosphorescence quenching in the spinotrapezius muscle at rest and during 180 s of 1 Hz twitch contractions. EPI did not change resting baseline PO_2mv (EPI=29±4; C=30±2 mmHg; p>0.05). Following the onset of contractions the time delay (EPI=9±1; C=8±2 s; p>0.05) and time constant (time to 63% of transient response, EPI=16 ±4; C=23±3 s; p>0.05) of the PO_2mv fall were not altered by EPI nor was contracting steady-state PO_2mv (EPI=18±4; C=19±2 mmHg; p>0.05). Despite previous reports of the efficacy of EPI to improve the O_2 transport pathway, the present data indicate that chronic EPI treatment (2mg/kg) does not improve skeletal muscle microvascular oxygenation at rest or during contractions.
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Background

Chronic intake of the flavanol epicatechin (EPI) is associated with reduced risk and prevalence of cardiovascular disease (Janszky et al., 2009) as well as reductions in MAP (Ellinger et al., 2012).

In mice EPI improves exercise capacity secondary to increases in skeletal muscle capillarity and mitochondrial volume density (Nogueira et al., 2011).

Given that EPI promotes endothelial function and vasodilation it is plausible that augmented vascular control also underlies improvements in exercise performance (Grassi et al., 2005).

Hypothesis

Chronic EPI supplementation in healthy rats would

1) reduce MAP at rest and during contractions
2) improve exercise performance ($\dot{V}O_2$peak and time-to-fatigue (T_{lim}))
3) increase skeletal muscle O_2 delivery-utilization matching (i.e. ↑ microvascular O_2 pressure (PO_2mv)) at rest and during in situ contractions

Methods

10 Young adult male Sprague-Dawley rats.

Supplementation: Administration of either EPI (2mg/kg , n=5) or water (CON; n=5) via oral gavage twice daily for 21 days.

5 days of acclimatization to high speed running on a custom built motor driven treadmill (~5 min).

Timeline

Pre-intervention performance testing	21 day intervention	Post-intervention performance testing	PO_2mv protocol

Performance testing

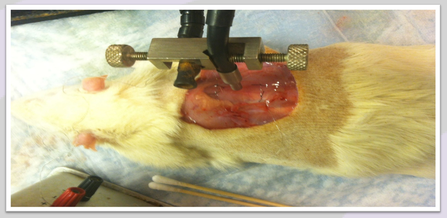
T_{lim} - motor-driven treadmill at 5% grade. Initial speed 20 m/min. Increased by 5 m/min every 15 min until exhaustion (Copp et al., 2009).

$\dot{V}O_2$peak - via metabolic chamber placed on the treadmill. Ramp increase of ~5-10 m/min every minute at 5% grade until a plateau in $\dot{V}O_2$ with increasing speed.

Microvascular O_2 pressure

Allows assessment of the O_2-delivery ($\dot{Q}O_2$) to O_2-utilization ($\dot{V}O_2$) balance which constitutes the driving force for blood-myocyte O_2 flux

Surgical exposure of spinotrapezius under anesthesia with sutured electrodes:



Preparation- phosphorescence quenching of the spinotrapezius at rest and 180 s of 1Hz twitch contractions (~5-8 V, 2 ms pulse duration) (Behnke et al., 2001).

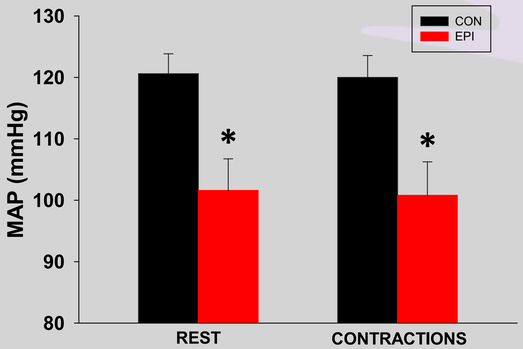
Modeling- PO_2mv curve fitting utilizing a time delay and exponential fit

Results

Body mass was not different between groups (CON: 387±14; EPI: 399±20 g, P>0.05)

There were no differences in arterial blood pH, PO_2, PCO_2 or [lactate] between control and EPI groups at rest or during exercise (P>0.05).

Figure 1: EPI reduced MAP at rest and during steady-state contractions



* P<0.05 compared to control

Figure 2: EPI did not alter post-intervention $\dot{V}O_2$peak

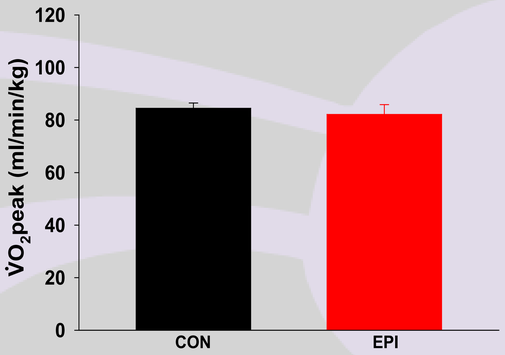


Figure 3: EPI did not alter post-intervention T_{lim}

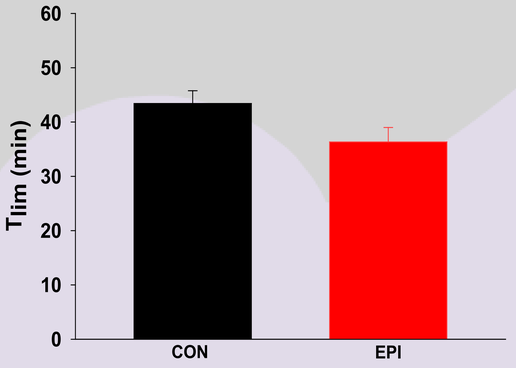


Figure 4: EPI did not affect spinotrapezius PO_2mv during contractions.

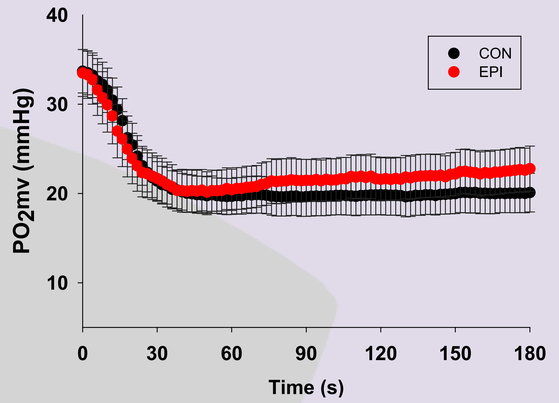


Table 1: Spinotrapezius PO_2mv kinetics

	CON	EPI
PO_2mv$_{(baseline)}$, mmHg	33.2 ± 2.5	33.4 ± 2.6
ΔPO_2mv, mmHg	15.1 ± 1.1	14.4 ± 1.3
Time constant, s	17.4 ± 2.6	14.0 ± 3.2
Time delay, s	7.9±1.3	7.8±1.1
PO_2mv$_{(steady-state)}$, mmHg	21.3 ± 2.0	22.0 ± 2.2
Mean response time, s	25.2 ± 2.8	21.8 ± 4.2

Conclusions

- EPI was efficacious in lowering MAP consistent with previous reports.
- Exercise performance was not improved with EPI.
- Despite the reduction in driving pressure, chronic EPI treatment (4mg/kg) did not alter PO_2mv in situ.

References

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