Capsaicin Analog Supplementation is not Effective to Improve 10-km Running Time-Trial Performance in Amateur Athletes: A Randomized, Crossover, Double-Blind and Placebo-Controlled Study

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Abstract

Background: To investigate the acute effect of capsaicin analog supplementation on 10-km time-trial running performance and physiological responses in amateur athletes.

Methods: Twenty-one participants (age = 29.3 ± 5.5 years), completed two randomized, double-blind trials: capsaicin analog condition [Capsiate (CAP) = 24 mg] or a placebo condition. The participants consumed two doses of 12 mg of capsaicin or placebo capsule 45 minutes before and immediately at the start of each trial. The time required to complete 10-km in minutes, lactate concentration, maximum heart rate (HR), and rating of perceived exertion (RPE) were recorded.

Results: 10-km time-trial performance (CAP= 44.4 ± 6.3 min *vs* placebo= 45.3 ± 6.8 min, $P = 0.823$) was not statistically significant different between conditions. No statistically significant differences between conditions were detected for lactate concentration ($P = 0.507$), HR ($P = 0.897$) and RPE ($P = 0.517$).

Conclusion: Capsaicin analog supplementation did not improve performance and physiological responses in a 10-km running time-trial in amateur athletes.

Background

Long-distance running is one of the most widespread individual sports modalities and have become even more popular in the last decade (Hagan, 2018). Long-distance running promotes several systemic and muscle adaptations (Li et al., 2019), increases maximal oxygen uptake ($\dot{V}O_{2max}$) (Paavolainen, Nummela, & Rusko, 2000) and time to exhaustion (Hausken, 2019). The oxidative system demand of long-distance runners is about 3-fold higher compared with physically active people (Skovgaard et al., 2014; Vuorimaa, Häkkinen, Vähäsöyrinki, & Rusko, 1996) and a relative increase of type IIa at expense of type IIb, results in the ability to increased fat metabolism (Giovanelli et al., 2016). In consequence, long-distance running provokes a calcium imbalance, which results in inefficiency of muscular contraction (Pearcey et al., 2015). Therefore, different ergogenic and thermogenic compounds were strategically used to optimize performance in middle and long-distances running (Schubert & Astorino, 2013).

Capsiate (CAP) is an analog of capsaicin, belonging to an 8-methyl-N-vanillyl-trans-6-nonenamide natural phytochemical compound found primarily in red peppers (Ludy, Moore, & Mattes, 2012) and also in the analog of a sweet pepper species (CH-19 sweet) which has the same molecular structure as capsaicin, except for the substitution of NH for O in the alkyl chain that alters the pungency factor (Ohnuki et al., 2001). This phytochemical has been used as a nutritional strategy to improve performance in different intensities and exercises distances (de Freitas, Billaut, et al., 2019; de Freitas et al., 2018). The dose of capsaicin in studies remains not well established for humans. Previously studies from our research group have used 12 mg of CAP 45 minutes before the exercise trials and there was found an improvement in performance for short duration aerobic exercise (Costa et al., 2020; de Freitas, Billaut, et al., 2019; de Freitas et al., 2018) and in combined exercise protocol (5-km running plus strength exercise), was 24 mg of CAP in two doses of 12 mg with 45 minutes interval between doses (de Freitas, Cholewa, et al., 2019).

On the other hand, another study used a dosage of CAP of 150 mg administrated 60 minutes before exercise protocol (30 minutes of aerobic exercise at 50% of maximal ventilatory threshold on a stationary ergometer), shows a better endurance performance, demonstrating higher fat oxidation during exercise under CAP condition compared to placebo condition (Shin & Moritani, 2007). Therefore its already known that the peak concentration of CAP occurs around 45 minutes after ingestion and bioavailability is approximately 25 minutes, so it is in the plasma for up to 105 minutes (Chaiyasit, Khovidhunkit, & Wittayalertpanya, 2009; Rollyson et al., 2014).

In skeletal muscle, CAP phosphorylates the transient vanilloid-1 receptor (TRPV1), which results in the release of available calcium in the sarcoplasmic reticulum, optimizing the myosin-muscle actin interaction, consequently improving the processes of force generation and optimizing the efficiency in depleting intramuscular triglycerides and preserve muscle glycogen, thus increasing the time to exhaustion (Lotteau, Ducreux, Romestaing, Legrand, & Van Coppenolle, 2013). Moreover, TRPV1 is activated in the putative pain neural circuit (Watanabe, Kawada, Kurosawa, Sato, & Iwai, 1988) increasing fat metabolism, at least in part, due to β-adrenergic stimulation induced by CAP supplementation. Therefore, the CAP ingestion may increase fat metabolism by both stimulating lipolysis and inhibiting lipogenesis (Yoshioka et al., 1995), which could potentiate longer distance performance.

Regarding the potential ergogenic effect of CAP, previous studies from our research group demonstrated that 12 mg of acute CAP supplementation was effective to improve a 1.500 meters running time-trial performance with a lower rate of perceived exertion (RPE) (de Freitas et al., 2018). Recently, an investigation about running performance and CAP verified the effect of acute CAP supplementation on short (400-meter) and moderate distance (3000-meter) running time trial performance in physically active men but they did not find differences for heart rate (HR) and RPE (Costa et al., 2020). Despite several studies have been conducted investigating the potential effect of CAP on performance mainly in rodents (Kim, Park, & Lim, 2016), short and moderate distances (de Freitas et al., 2018; Yoshioka et al., 1995) or high-intensity intermittent exercises in human (de Freitas, Billaut, et al., 2019; Opheim & Rankin, 2012) there is no evidence of CAP supplementation effects during long-distance running, such as 10-km time-trial. Furthermore, previous studies at the literature demonstrating the benefits of CAP on performance were conducted in physically active men, therefore, it is a lack of study investigating the effect in experienced runners.

Thus, the objective of this study was to verify the acute effect of CAP supplementation on 10-km running time trial performance and physiological responses in amateur athletes. We hypothesize that acute CAP supplementation could be a ergogenic strategy to improve long-distance performance (10-km) with lower lactate concentration, HR and RPE in this athletes compared to placebo condition.

Methods

Study design

This is a randomized, crossover, double-blind and placebo-controlled study with experimental trials conducted in the morning (6 to 9 AM) under similar weather conditions (relative humidity: 60–90%; wind: 5–29 $km.h^{-1}$ km/h; temperature: 19–26 °C; altitude: 475 meters) to minimize the chronobiologic variance. The participants were instructed about the protocol and were requested to maintain their training and nutritional habits during the study. The participants visited the track for two 10-km running test under CAP or placebo conditions separated by a 1-week. The trials were performed on a 400 m official outdoor track.

Participants

Amateur athletes previously experience (more than one year) in at least 10-km with time faster than 60 minutes (~ 17% slower in relation the mean velocity of the world record for the distance of 10-km) (Jones & Carter, 2000), were invited to participate in the study. The general characteristics of participants have been showed at (Table 1). Twenty-one men enrolled in this study (Fig. 1). The subjects were required to be 18–35 years old and do not present any cardiovascular, muscle or joint contraindications to exercise or are in use of any ergogenic aid supplementation. Participants were advised to abstain from chili peppers or other spicy foods, caffeinated, supplement or ergogenic substance, energetic or alcoholic beverages and strenuous physical exercise within 24 hours prior to testing, to consume the same diet, and to maintain the same physical exercise regimen 48 hours prior to testing. Also, they were instructed to consume breakfast at home as usual before each experimental trial. The Research Ethics Committee (protocol number 3.654.560/2019), approved the study protocol which was conducted according to the 2013 Revision of the Declaration of Helsinki. The subjects signed a consent form and were informed about the purpose of the study and possible risks.

Table 1
General characteristics of participants

Variables	**(N = 21)**
Age (years)	29.3 ± 5.4
Weight (kg)	74.2 ± 11.3
Height (cm)	176 ± 0.0
Fat mass (%)	12.7 ± 3.8
Fat Free Mass (kg)	64.3 ± 7.2
$\dot{V}O_2max$ ($ml.kg^{-1}.min^{-1}$)	62.7 ± 8.4
Data are presented in mean and SD.	

Procedures

Supplementation protocol

The participants were randomized by a random sequence generator (www.Random.org) in placebo and CAP condition trial by a researcher who not participate in this study (double-blinded) at the first trial and performed a second trial in a cross-over manner. In both conditions, subjects ingested two capsules of 12 mg of CAP (24 mg) or placebo according our previous study that demonstrated benefits of this dose (Conrado de Freitas et al., 2018). Subjects ingested one capsule 45 minutes before the test and the second one immediately before to start 10-km running test. This strategy of CAP supplementation was applied to use peak concentration occurring at about 45 minutes after intake and a bioavailability of approximately 25 minutes, to remain the plasma level elevated up to 105 minutes (Chaiyasit et al., 2009; Rollyson et al., 2014). The product used for this study contained 50% extract from capsicum (capsicum annuum L.) from India (Purifarma-Gemini Pharmaceutical Industry Ltda, Anapolis, GO, Brazil) and 50% of maltodextrin. The correction factor in assay calculation was used by Pharma Nostra (Campinas, Brazil) to guarantee 100% of capsinoids (Capsiate) in each capsules of 12 mg. The capsules were identical and without flavour. It was delivered to each subject by an independent person who did not participate in the research team in order to secure double-blinding.

10-km time-trial running test

All subjects performed the trial without the presence of opponents or another competitor on the track. The trial was preceded by a self-determined warm-up of 10 min, the same in both trials. All participants were encouraged to give their best performance and, in each lap, they were cheered by the research team. Participants freely choose their pacing strategy during the performance and the time in minutes was recorded every 400 m. The overall mean velocity for each trial was calculated by dividing the total distance covered by the total time of the test duration. All subjects had access to mineral water during the run *ad libitum*.

Blood lactate

Twenty-five microliters of blood were collected from the volunteer's right ear lobe before, immediately after, and 3, 5 and 7 minutes after trial. The lactate concentration was determined by electroenzymatic methods using an automated analyser (YSI 2300 STAT®, Yellow Springs, Ohio, EUA). Peak lactate concentration was defined for each participant as the highest post-exercise lactate concentration value (Peserico et al., 2018).

Rating of perceived exertion and heart rate

Rating of perceived exertion was evaluated by the 6–20 points Borg scale and peak of heart rate (Polar Vantage NV, Electro Oy, Finland) was recorded immediately after the 10-km was completed.

Incremental test

To determine aerobic fitness, the participants performed a maximal incremental test on the treadmill (Inbramed ATL®, Porto Alegre - Brazil) until exhaustion. The maximum oxygen uptake ($\dot{V}O_{2max}$) was determined by the latest 30 seconds mean from the last stage completed in the incremental test. Gas exchanges were measured breath-by-breath using a gas analyzer (Model Quark PFT Ergo – Cosmed® – Rome, taly). Before each test, the gas analyzer was calibrated according to the manufacturer's recommendations. The participants performed three minutes of warm-up at 8 $km.h^{-1}$. Each stage of the test lasted one minute and the first stage was performed at 9 $km{\cdot}h^{-1}$, with speed increments of 1 $km{\cdot}h^{-1}$ per stage until voluntary exhaustion by the participants (Alves Pasqua et al., 2018). The maximal velocity (V_{max}) from the incremental was assumed as the highest velocity in the stage completed before exhaustation. Later, the mean from the Vmax was compared to the mean velocity of the 10-km running time trial test (Table 2).

Table 2
Dietary intake and macronutrient distribution 24 h before each trial.

	Placebo	CAP	*P*-value
Total intake (kcal)	1.7 ± 661	1.8 ± 476	0.322
Protein (g)	97.2 ± 41.7	107.2 ± 47.7	0.221
Carbohydrate (g)	213.6 ± 97.4	206.6 ± 69.3	0.900
Lipids (g)	61.0 ± 28.4	66.9 ± 26.0	0.112
Total intake ($kcal.kg^{-1}$)	24.8 ± 9.2	21.8 ± 10.9	0.357
Protein ($g.kcal^{-1}$)	1.3 ± 0.5	1.2 ± 0.7	0.669
Carbohydrate ($g.kcal^{-1}$)	3.0 ± 1.4	2.4 ± 1.3	0.219
Lipids ($g.kcal^{-1}$)	0.8 ± 0.3	0.7 ± 0.4	0.660
Data are show in mean and ± SD. *P* = < 0.05 vs placebo condition.			

Body composition and anthropometry

All the procedures were performed by the same person in an acclimatized room. Body mass was measured on an electronic scale (Filizzola PL 150, Filizzola® Ltda, Brazil). Body height was measured with a wall-mounted stadiometer (Sanny®, São Paulo, Brazil). Fat-free mass and fat mass were estimated by bioelectrical impedance following the procedure of the manufacturer (Bia Analyzer TM®,The Nutritional Solutions Corporation, Harrisville, MI, USA).

Statistical analysis

According to several previously studies from others and our research group as well as power analysis (β-1 = 0.85), the sample size in this study was large enough to detect prescribed effects with twenty-one participants. Data normality was verified using the Shapiro-Wilk test. Data are reported as means and ± standard deviation (SD). Paired *t* test was used to compare both conditions (CAP and placebo). Statistical significance was set at $p < 0.05$. The data were analysed using *Statistical Package for the Social Sciences* (SPSS® v.24, Inc., Chicago, IL, USA).

Results

Table 1 shows the participant's general characteristics. Table 2 presents the values for total kilocalorie and total macronutrient intake 24 hours before exercise for each condition. There were no significant differences between trials ($P > 0.05$).

Table 3 presents performance and physiological responses in the 10-km running test under CAP and placebo conditions.

Table 3
Performance and physiological response in 10-km running test at CAP and placebo conditions (n = 21)

	Trial 1 (Blinded)	Trial 2 (Blinded)	*P*-value	Placebo	CAP	*P*-value
Time 10-km (min)	45.1 ± 0.00	45 ± 0.00	0.429	45.2 ± 6.7	44.4 ± 6.3	0.823
Mean velocity (km.h-1)	13.5 ± 1.8	13.6 ± 1.9	0.294	13.5 ± 1.9	13.5 ± 1.8	0.707
Vmax from the incremental test (%)	76.1 ± 100	76.6 ± 103.2	-	76.5 ± 104.2	76,2 ± 98.9	-
HR_{peak} (bpm)	181.0 ± 12.9	181.0 ± 12.1	0. 798	181.0 ± 11.2	180.0 ± 13.5	0.942
RPE_{peak} (AU)	17 ± 2.0	17 ± 2.3	0.550	17 ± 2.3	17 ± 2.0	0.550
$[La^-]$ rest (mmol⁢L^{-1})	0.8 ± 0.3	0.9 ± 0.5	0.457	0.9 ± 0.4	0.8 ± 0.4	0.507
Peak $[La^-]$ (mmol⁢L^{-1})	5.0 ± 1.6	5.5 ± 1.9	0.219	5.2 ± 1.8	5.2 ± 1.8	0.950

Data are presented in mean and SD. *P* = < 0.05 vs placebo condition. HR = Heart Rate; RPE = rate of perceived exertion (6–20 point BORG scale); Lac = lactate concentration; - = data not applicable.

Firstly, we compared the first and the second performed test 2 of the trial in order to identify the influence of learning effects. No significant differences between the first and the second attempt of 10-km runs were found ($P > 0.05$).

In a second attempt we compared the effects of CAP and placebo conditions on 10-km time-trial performance which revealed no significant differences between conditions. Additionally, no statistically significant differences were detected for lactate concentration, HR and RPE between conditions.

Figure 2 shows the pace strategies for the 10-km running time-trial in both conditions, placebo and CAP.

The pacing strategy adopted by the participants was the same in both trials (placebo and CAP), except in (6400 meters), where the participants running time was faster in CAP condition when compared with placebo condition (CAP = 1.49 ± 0.001 min *vs* placebo = 1.52 ± 0.004 min, $P < 0.05$).

Discussion

According to our knowledge, this is the first study to investigate the acute effect of CAP supplementation on 10-km time trial performance and physiological responses in amateur athletes. From our main findings we need to refute our initial hypothesis that CAP supplementation has an ergogenic effect improving performance and physiological responses in this athletes.

Our main findings regarding CAP supplementation effects on performance are in contrast to our previous studies investigating these effects in shorter distances. The study conducted by de Freitas et al., (2018) demonstrated that CAP supplementation was efficient to improve 1500 m time-trial performance with lower RPE but no changes of lactate concentrations between conditions in physically active adults. In addition, acute effects of CAP supplementation were verified to improve performance of short (400 m) and moderate distance (3000 m) running time-trials without changes of HR and RPE in physically active men (Costa et al., 2020).

Interestingly, in these previous studies, CAP reduced 1500-m running time-trial performance by 1.35% (de Freitas et al., 2018), decreased running time by 1.04% in a 400 m running time-trial and 2.32% in a 3000 m running time-trial in physically active men (Costa et al., 2020). From these data we might expect a large effect for the 10-km running time-trial performance as the increase in performance seems to be distance dependent. However, in the current study, there were no significant effect of acute CAP on performance during 10-km running time-trial and physiological responses in amateur athletes. Furthermore, the pacing along the 10-km was the same in both condition, except for the difference in (6400 meters), where the subjects running time was faster in CAP than in placebo. Therefore, these findings suggest that the duration of effort (short, middle and longer distance), as well as training status, since previous studies from our group which demonstrated benefits of acute CAP used physically active but in the current study was amateur athletes may be important factors with regard to the potential ergogenic benefits of CAP supplementation on exercise performance.

Several animal studies showed that acute capsaicin supplementation was efficient to improve endurance capacity (exercises protocols between 30–60 minutes of moderate aerobic exercise) (Kim et al., 2016). It might be related in part to an increase in hepatic glycogen content, being considered an important mechanism for energy homeostasis and via activation of TRPV1 due to capsaicin supplementation and improvements of energy metabolism by increasing lipolysis saving and maintaining muscle glycogen reserves (Kim et al., 2016). Kazuya et al., (2014) demonstrate that 100 mg of CAP improve the control exerted adenosine diphosphate (ADP) on mitochondrial respiration, facilitating the potent CAP-induced activation of mitochondrial decoupling processes, leading to the dissipation of the proton gradient generated throughout the respiratory chain in heat; enhances the oxidative ATP contribution in electrostimulation-induced muscle; and reduced the ATP cost of twitch force generation. In addition, the acute CAP supplementation also enhanced the twitch force-generating capacity. It may be therefore suggested, that acute CAP supplementation can contribute to performance and have an effect of postponing fatigue in resistance exercises (Hsu et al., 2016). Although these studies showed evidence for CAP supplementation effects on endurance performance, we did not find any improvements in our 10-km time-trial.

All subjects were encouraged to run as fast as possible giving their best for an excellent performance, however, it was not an official race where the data were collected and therefore motivation influences cannot be ruled out. As an additional limitation we need to mention, that several related markers such as pH, inorganic phosphate, glycogen depletion, calcium release or catecholamine response have not been measured which need to be included in subsequent studies to increase the understanding about CAP supplementation and endurance running performance.

Conclusions

In conclusion, our study failed to show an ergogenic effect of acute CAP ingestion on time to exhaustion, blood lactate concentration, heart rate response or perceived exertion during 10-km running time-trial in amateur athletes. Being the first to investigate the effects of acute CAP supplementation on 10- km running in humans, highlights the need to investigate the effects of CAP supplementation of various doses on the activation of the TRPV1 receptor and the subsequent effects on human metabolism in endurance exercise.

List Of Abbreviations

ADP Adenosine diphosphate

ATP Adenosine triphosphate

CAP Capsaicin analog

HR Heart rate

RPE Rate of perceived exertion

TRPV1 Transient vanilloid-1 receptor

Vmax Maximum velocity

$\dot{V}O_{2max}$ Maximum oxygen uptake

Declarations

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Authors’ contributions

Study design and organization of the manuscript were performed by AEVAM, VAMS, CSP, FER and FSL. Data analysis, statistical analysis, and the first draft of the manuscript were performed by AEVAM, CSP, FER. The manuscript review was performed by AEVAM, CSP, FER, FAM, PH and FSL. The final approval for publication was performed by FSL.

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Availability of data and materials

Data and publication materials can be provided upon request. Please contact corresponding author for this information.

Ethics approval and consent to participate

Ethics approval for this study was approved by Ethics Research Group of the Federal University of Piauí, Teresina-PI, Brazil (Protocol number: 3.654.560/2019). All participants provided written consent before participating in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Figures

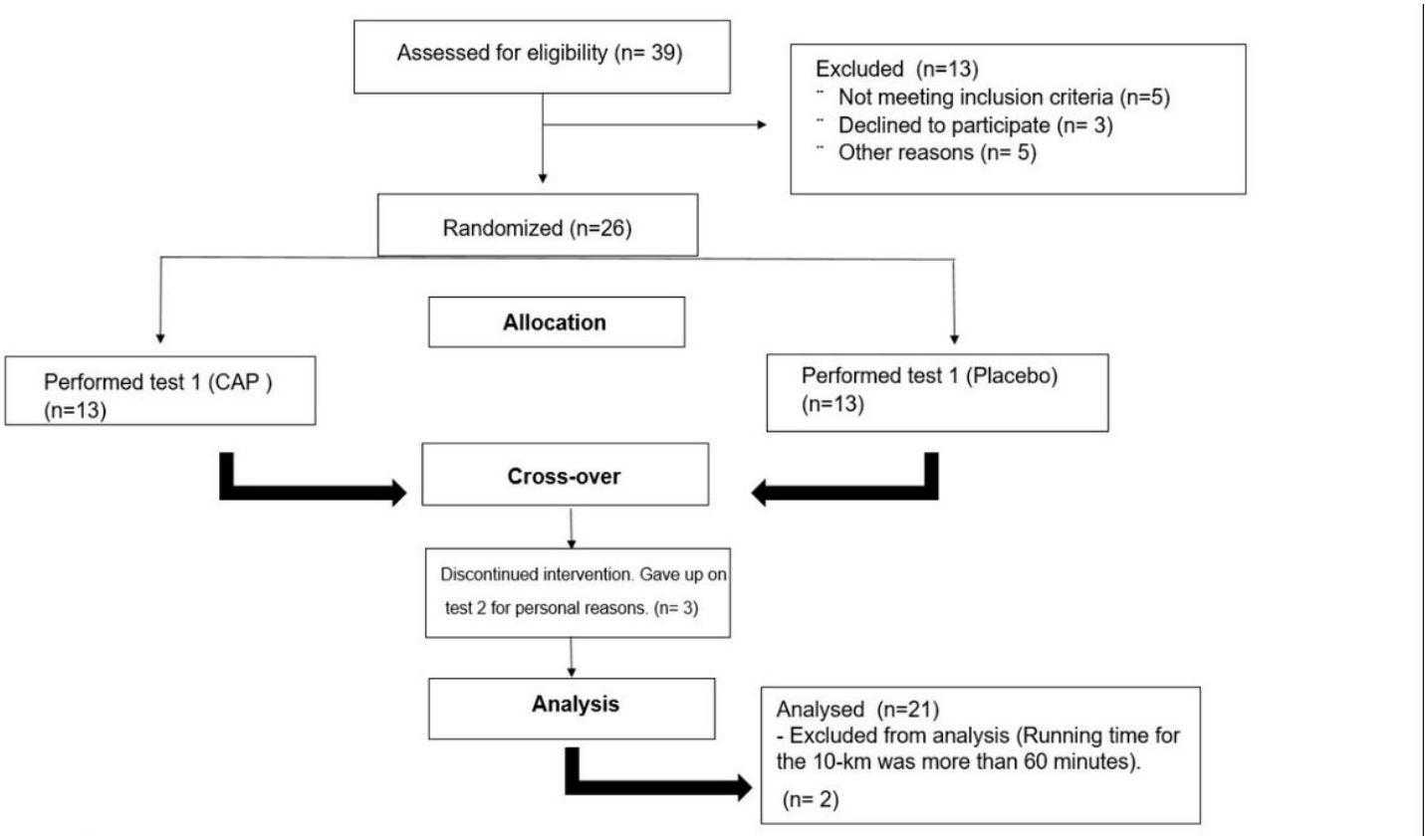

Figure 1

Flow Diagram.

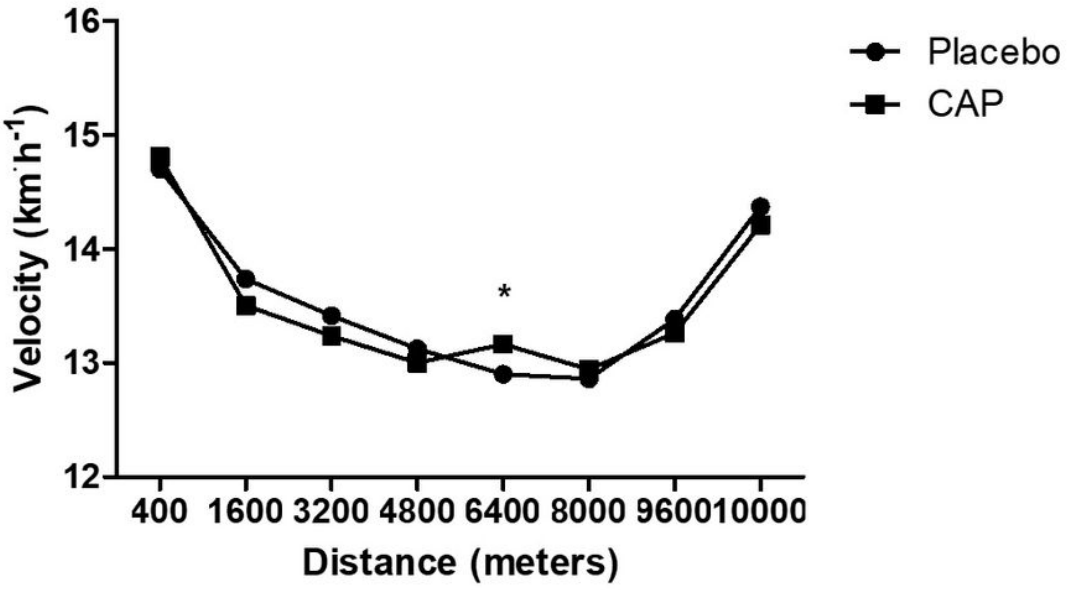

Figure 2

Mean running velocity during a 10-km running time-trial. * p<0.05 CAP vs Placebo in same time.