Effects of Quercetin Supplementation on Endurance Performance and Maximal Oxygen Consumption: A Meta-Analysis

Denis M. Pelletier, Guillaume Lacerte, and Eric D.B. Goulet

Lately, the effect of quercetin supplementation (QS) on endurance performance (EP) and maximal oxygen consumption (VO₂max) has been receiving much scientific and media attention. Therefore, a meta-analysis was performed to determine QS’s ergogenic value on these variables. Studies were located with database searches (PubMed and SPORTDiscus) and cross-referencing. Outcomes represent mean percentage changes in EP (measured via power output) and VO₂max, between QS and placebo. Random-effects model meta-regression, mixed-effects model analog to the ANOVA, random-effects weighted mean effect summary, and magnitude-based inferences analyses were used to delineate the effects of QS. Seven research articles (representing 288 subjects) were included, producing 4 VO₂max and 10 EP effect estimates. Mean QS daily intake and duration were, respectively, 960 ± 127 mg and 26 ± 24 d for the EP outcome and 1,000 ± 0 mg and 8 ± 23 d for the VO₂max outcome. EP was assessed during exercise with a mean duration of 79 ± 82 min. Overall, QS improved EP by 0.74% (95% CI: 0.10–1.39, \( p = .02 \)) compared with placebo. However, only in untrained individuals (0.83% ± 0.78%, \( p = .02 \)) did QS significantly improve EP (trained individuals: 0.09% ± 2.15%, \( p = .92 \)). There was no relationship between QS duration and EP (\( p = .69 \)). Overall, QS increased VO₂max by 1.94% (95% CI: 0.30–3.59, \( p = .02 \)). Magnitude-based inferences suggest that the effect of QS on EP and VO₂max is likely to be trivial for both trained and untrained individuals. In conclusion, this meta-analysis indicates that QS is unlikely to prove ergogenic for aerobic-oriented exercises in trained and untrained individuals.

Keywords: flavonoids, aerobic capacity, exercise capacity, ergogenic aids, sports supplements

Flavonoids are a group of polyphenolic compounds that can be found in significant amounts in many commonly consumed fruits, vegetables, and beverages (Cureton et al., 2009; Harwood et al., 2007). Quercetin is one of the most abundant flavonoids available to humans (Davis, Murphy, & Carmichael, 2009), is found as a nutritional supplement, is highly bioavailable (Jin et al., 2010), and is considered safe and well tolerated by humans (Bischoff, 2008; Cureton et al., 2009; Harwood et al., 2007).

Animal studies suggest that quercetin supplementation (QS) may provide health-related benefits by reducing oxidative stress (Coskun, Kanter, Korkmaz, & Oter, 2005; Duarte et al., 2001), blood pressure (Edwards et al., 2007), and low-grade systemic inflammation (Comalada et al., 2005; Morikawa et al., 2003); improving endothelial function (Rivera, Morón, Sánchez, Zarzuelo, & Galisteo, 2008; Sánchez et al., 2006); and increasing mitochondrial biogenesis (Davis et al., 2009).

Results of human studies are somewhat less promising, showing that in healthy young subjects QS does not decrease inflammation (Nieman, Henson, Davis, Angela Murphy, et al., 2007; Nieman, Henson, Davis, Dumke, et al., 2007) and oxidative stress (McAnulty et al., 2008; Shanely et al., 2010) or improve muscle oxidative capacity (Cureton et al., 2009) and mitochondrial biogenesis (Nieman et al., 2010), but it does enhance endothelial function (Loke et al., 2008).

Several human studies evaluated quercetin’s ergogenic potential on aerobic performance (Bigelman et al., 2010; Cheuvront et al., 2009; Cureton et al., 2009; Davis et al., 2010; Ganio et al., 2010; MacRae & Mefferd, 2006; Nieman et al., 2009; Nieman et al., 2010; Quindry et al., 2008), and recently its effect on endurance exercise capacity has been meta-analyzed (Kressler, Millard-Stafford, & Warren, 2011). Although Kressler et al.’s (2011) meta-analysis helped shed some light on how QS affects maximal oxygen consumption (VO₂max) and endurance performance (EP), it contains several methodological weaknesses that threaten its results and ensuing validity. First, it was concluded that QS “provides a statistically significant benefit in human endurance exercise capacity (VO₂max and endurance exercise performance)” (p. 2396). However, when results are scrutinized, QS only significantly improved EP, not VO₂max. Second, one of the studies included in the meta-analysis evaluated EP using

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fixed-power-output exercise to exhaustion (Davis et al., 2010). Kressler et al. took EP as the percentage change in time to exhaustion between groups, thereby seriously inflating and incorrectly computing the treatment impact on EP (Hopkins, Hawley, & Burke, 1999). Third, a key EP measure from Bigelman et al.’s study (2010) was not included. Finally, results of studies with substantially different and incompatible research designs—field versus laboratory-controlled studies and acute versus prolonged QS—were combined together, which may have acted to confound findings.

The objective of this study was to meta-analyze the effects of prolonged (≥5 days) QS on EP and VO2max. To render results comparable across studies and meaningful for athletes and coaches, all EP outcomes were put on the same scale and converted to mean percentage changes in power output. This computational technique was not used by Kressler et al. (2011). In addition, we determined the odds of QS’s improving EP and VO2max under real-life conditions, something that was not adequately addressed by Kressler et al. We hope our results will provide concrete help for athletes, coaches, and sports scientists using or interested in working with quercetin.

**Methods**

**Search Strategy**

A thorough search of the scientific literature using the PubMed (which includes the new and old MEDLINE) and SPORTDiscus databases was performed. Medical subject headings were quercetin or quercetin supplementation combined with performance, endurance performance, maximal oxygen consumption, endurance capacity, or time-trial performance. The literature search was limited to French- and English-language citations. An extensive manual search of the reference sections of all articles that were found during the electronic search was made. Electronic tables of contents of major exercise- and nutrition-related journals were searched for ahead-of-print articles not yet indexed in databases. Case studies, published abstracts, conference proceedings, or dissertations were not admissible for the review. Abstracts of all potential articles were thoroughly read, and a further evaluation of the Methods sections was performed when it was reported in the abstract that an intervention looking at the effect of QS on exercise capacity, endurance capacity, performance, EP, or VO2max was performed. Otherwise, articles were discarded. We searched the literature back to 1966, with the last day of the literature search being March 11, 2011.

**Inclusion and Exclusion Criteria**

Statistical and meta-analytical computations were made from results of studies that met all of the following criteria: data necessary to compute the effect estimates and variances; controlled supplementation and exercise protocols; with the exception of quercetin and ingredients (other than ergogenic substances) helping quercetin absorption at the intestinal level, no difference in ingredients between the placebo and quercetin group; QS ≥5 days; and exercise protocol duration ≥5 min. Any research conducted in animals was excluded from this meta-analysis.

**Data Extraction**

Coding sheets with operational definitions were developed and used for this investigation. When necessary, authors were contacted and asked to provide key variables (p values, confidence intervals [CI], standard deviations [SD], or standard errors [SE] of the EP or VO2max score changes) needed to precisely calculate their studies’ variances and concomitant weighting factors. Coded variables included study characteristics, subject physical and fitness characteristics, exercise protocol characteristics, supplementation period characteristics, pre- and post supplementation plasma quercetin values, and EP and VO2max outcomes.

**Measurement of Exercise Duration**

Exercise duration represents the mean of the means total exercise time completed in the QS and placebo groups.

**Plasma Quercetin Concentration**

For all studies, pre- to post supplementation percentage changes in plasma quercetin were calculated as follows:

\[
\frac{\text{([postsupplementation QS group value – presupplementation QS group value]) / presupplementation QS group value]}{\times 100}
\]

**Measurement of EP**

All EP outcomes represent percentage changes in power output between QS and placebo and were computed using the following formulas:

- **Exercise test providing mean power-output data:**
  \[
  \frac{\text{((QS group power output – placebo group power output)/placebo group power output})}{\times 100}
  \]

- **Fixed-power-output test to exhaustion:**
  \[
  \frac{\text{[(QS group time to exhaustion – placebo group time to exhaustion)/placebo group time to exhaustion] \times 100/(% VO2max at which the test was performed/6.4)}}{(Hopkins et al., 1999)}
  \]

- **Incremental test to exhaustion:**
  \[
  \frac{\text{[(QS group time to exhaustion – placebo group time to exhaustion)/ placebo group time to exhaustion] \times 100 \times [1 – (%VO2max or peak power output at which the test started/100)]}}{(Hopkins, 2004)}
  \]

According to Hopkins (2004), a 1% change in power output corresponds to a 1% change in running time-trial performance and a 0.4% change in cycling time-trial performance.
Measurement of VO2max

For all studies, relative percentage changes in VO2max were measured with the following formula:

\[
\frac{(\text{QS group relative } \text{VO2max} - \text{placebo group relative } \text{VO2max})}{\text{placebo group relative VO2max}} \times 100
\]

Smallest Worthwhile Effect of QS on EP and VO2max

The relative chances QS’s improving VO2max and trained athletes’ running and cycling EP were determined using Hopkins’s spreadsheet (2002). Based on average typical variations of 2.6% (Hopkins & Hewson, 2001), 1.3% (Paton & Hopkins, 2006), and 5% (Katch, Sady, & Freedson, 1982) for trained athletes’ running times, trained athletes’ cycling times, and trained/untrained individuals’ VO2max, respectively, and a product factor of 0.5, as recommended by Hopkins et al. (1999), the smallest worthwhile percentage changes in running EP, cycling EP, and VO2max were set at 1.3%, 1.6%, and 2.5%, respectively.

Evaluation of Heterogeneity

Between-studies heterogeneity was statistically tested using the Cochrane Q test with \( p \leq 0.01 \) for significance (Borenstein, Hedges, Higgins, & Rothstein, 2009) and quantified using the \( I^2 \) statistic (Higgins & Thompson, 2002).

Publication Bias

Publication bias was not tested because there were fewer than 10 publications that evaluated the effect of quercetin on VO2max or EP (Lau, Ioannidis, Terrin, Schmid, & Olkin, 2006).

Statistical Analyses

Statistical analyses were performed with SPSS version 12.0.0. (Chicago, IL), SPSS macros found in Lipsey and Wilson (2001), and with Comprehensive Meta-Analysis (CMA) version 2.2.048. (Englewood, NJ). A random-effects model was used to derive mean weighted summary estimates for EP and VO2max. A mixed-effects model analysis-of-variance-like procedure was used to determine the influence of training state on EP. Untrained individuals and recreationally active subjects were classified as a group of untrained individuals, and elite athletes, moderately trained athletes, and trained athletes were classified as a group of trained individuals. Random-effects-model metaregressions were performed to evaluate the relationship between QS duration and EP, as well as that between exercise duration and EP. The low number of studies prevented subgroup and meta-regression analyses for the VO2max outcome. The variances and inverse variances were calculated for all performance-related variables. When provided, the \( SE \) of the difference between EP or VO2max scores was used.

When not provided, it was calculated from the exact \( p \) value provided. When only \( p \leq x \) was reported, \( p \) was considered to equal \( x \), where \( x \) is any \( p \) value \( \leq 0.05 \). When only \( p > 0.05 \) was reported, individual variances for net percentage changes in power output were estimated with the following formula:

\[
\sqrt{\frac{A^2 + B^2 - (2 \times R \times A \times B)}{N}}
\]

where \( A \) is the SD of the QS group and \( B \) is the SD of the placebo group. \( R \) was imputed and taken as .50 (Follmann, Elliott, Suh, & Cutler, 1992). A 95% CI was calculated and results were considered significant when it did not include zero. Unless otherwise noted, results are presented as \( M \pm SD \).

Results

Search Results

Ten manuscripts (Abbey & Rankin, 2011; Bigelman et al., 2010; Cheuvront et al., 2009; Cureton et al., 2009; Davis et al., 2010; Ganio et al., 2010; MacRae & Mefferd, 2006; Nieman et al., 2009; Nieman et al., 2010; Quindry et al., 2008) were identified, of which seven (Bigelman et al., 2010; Cureton et al., 2009; Davis et al., 2010; Ganio et al., 2010; MacRae & Mefferd, 2006; Nieman et al., 2009; Nieman et al., 2010) met the inclusion criteria. Altogether, those manuscripts provided 10 and 4 EP and VO2max effect estimates, respectively. Reasons for study exclusion were an exercise protocol duration of \(< 5 \) min (Abbey & Rankin, 2011), QS \(< 5 \) days (Cheuvront et al., 2009), and a noncontrolled exercise protocol (field study; Quindry et al., 2008). All of those studies reported no statistically significant effect of QS on EP.

Study Characteristics

Five research groups published seven research papers in six peer-reviewed journals from 2006 to 2010. All investigations were performed in the United States by researchers from academic institutes. Quercegen Pharma and Nutravail Technologies provided quercetin for five of the seven research investigations (Bigelman et al., 2010; Davis et al., 2010; Ganio et al., 2010; Nieman et al., 2009; Nieman et al., 2010). Nutravail Technologies is closely affiliated with Quercegen Pharma, which manufactures Q-force, a quercetin supplement. MacRae and Mefferd (2006) used quercetin drinks provided by New Sun Nutrition LLC, whose name was changed to the FRS Company, LLC, in 2007. FRS develops and distributes products containing quercetin.

Research Protocol Characteristics

Table 1 describes the key research-protocol characteristics of included studies. All studies used randomized, double-blind, placebo-controlled research protocols, with four using crossover designs (Davis et al., 2010; Ganio et al., 2010; MacRae & Mefferd, 2006; Nieman et al., 2010)
Table 1  Summary of Research Protocol Characteristics of Included Studies That Evaluated the Effectiveness of Quercetin Supplementation (QS) on Endurance Performance (EP) and Maximal Oxygen Consumption (VO$_{2\text{max}}$), M ± SD

<table>
<thead>
<tr>
<th>Reference</th>
<th>N; gender; age, years</th>
<th>Training state, relative VO$_{2\text{max}}$</th>
<th>Exercise protocol</th>
<th>Type of exercise, mean total exercise duration</th>
<th>Supplementation dose</th>
<th>Supplementation duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bigelman et al. (2010)</td>
<td>58; 44 men, 14 women; 21</td>
<td>Moderately trained, 47 ml · kg$^{-1}$ · min$^{-1}$</td>
<td>(1) ITTE to evaluate VO$_{2\text{max}}$ and EC (Study B); (2) 3.2-km TT on an outdoor 400-m oval track (Study A)</td>
<td>(1) Running, 8 min; (2) running; 15 min</td>
<td>1,000 mg/day (500 mg during breakfast and dinner)</td>
<td>52 days</td>
</tr>
<tr>
<td>Cureton et al. (2009)</td>
<td>30; 30 men; 23</td>
<td>Recreationally active but untrained, 42 ml · kg$^{-1}$ · min$^{-1}$</td>
<td>(1) ITTE to evaluate VO$<em>{2\text{max}}$ and EC (Study B); (2) FPOE at 50% VO$</em>{2\text{max}}$ followed by a TT (Study A)</td>
<td>(1) Cycling, 16 min; (2) cycling, 70 min</td>
<td>1,000 mg/day (250 mg during breakfast, lunch, dinner, and before sleep)</td>
<td>VO$_{2\text{max}}$ outcome: 8 days; EP outcome: 13 days</td>
</tr>
<tr>
<td>Davis et al. (2010)</td>
<td>12; 7 men, 5 women; 23 ± 2</td>
<td>Untrained, 46 ± 3 ml · kg$^{-1}$ · min$^{-1}$</td>
<td>(1) ITTE to evaluate VO$<em>{2\text{max}}$; (2) FPOTTE at 75% VO$</em>{2\text{max}}$</td>
<td>(1) Cycling, duration not provided; (2) cycling, 100 min</td>
<td>1,000 mg/day (500 mg before breakfast and dinner)</td>
<td>7 days</td>
</tr>
<tr>
<td>Ganio et al. (2010)</td>
<td>11; 5 men, 6 women; 20 ± 4</td>
<td>Untrained, 44 ml · kg$^{-1}$ · min$^{-1}$</td>
<td>ITTE to evaluate VO$_{2\text{max}}$ and EC</td>
<td>Cycling, 10 min</td>
<td>1,000 mg/day (1,000 mg in the morning)</td>
<td>5 days</td>
</tr>
<tr>
<td>MacRae &amp; Melford (2006)</td>
<td>11; 11 men; no age provided</td>
<td>Elite, 64 ± 10 ml · kg$^{-1}$ · min$^{-1}$</td>
<td>Laboratory-controlled 30-km TT</td>
<td>Cycling, 51 min</td>
<td>600 mg/day (300 mg during breakfast, 300 mg in the afternoon or during dinner)</td>
<td>72 days</td>
</tr>
<tr>
<td>Nieman et al. (2009)</td>
<td>39; 32 men, 7 women; 27</td>
<td>Trained, 61 ml · kg$^{-1}$ · min$^{-1}$</td>
<td>FPOE at 57% of maximal power output followed by a 5 (Day 1), 10 (Day 2) and 20 (Day 3) -km TT with quercetin (Study A) and quercetin + EGCG (Study B)</td>
<td>Cycling, 224 min</td>
<td>1,000 mg/day (500 mg between 7 and 8 a.m., 500 mg at 2 p.m.)</td>
<td>17 days</td>
</tr>
<tr>
<td>Nieman et al. (2010)</td>
<td>26; 26 men; 20 ± 0.4</td>
<td>Untrained, 46 ± 6 ml · kg$^{-1}$ · min$^{-1}$</td>
<td>FPOE at 60% VO$_{2\text{max}}$ and 10% grade followed by a TT at 15% grade</td>
<td>Running, 72 min</td>
<td>1,000 mg/day (500 mg at 8 a.m., 500 mg at 1 p.m.)</td>
<td>14 days</td>
</tr>
</tbody>
</table>

Note. ITTE = Incremental test to exhaustion; EC = endurance capacity; TT = time trial; FPOE = fixed-power-output exercise; FPOTTE = fixed-power-output test to exhaustion.
and three parallel-group designs (Bigelman et al., 2010; Cureton et al., 2009; Nieman et al., 2009). A total of 187 and 111 subjects were represented for the EP and VO$_{2\text{max}}$ outcomes, respectively, with women being 20% and men 80% of subjects. Mean sample size was 29 ± 17 subjects (range 11–58) for the EP outcome and 28 ± 22 subjects (range 11–58) for the VO$_{2\text{max}}$ outcome. A washout period of 0–22 days was used by studies using crossover designs. With the exception of Nieman et al.'s (2009) study, all subjects were familiarized with the EP tests.

**Subjects’ Physical and Fitness Characteristics**

For the EP outcome, untrained individuals, recreationally active individuals, moderately trained athletes, and elite athletes served as participants. Untrained individuals, recreationally active individuals, and moderately trained athletes served as subjects for studies examining the effect of QS on VO$_{2\text{max}}$. Mean age, height, weight, and VO$_{2\text{max}}$ of subjects represented in the EP outcome were, respectively, 23 ± 3 years ($n = 9$), 175 ± 4 cm ($n = 7$), 73 ± 5 kg, and 50 ± 9 ml · kg$^{-1}$ · min$^{-1}$ and for those represented in the VO$_{2\text{max}}$ outcome were 22 ± 2 years, 174 ± 4 cm, 72 ± 6 kg, and 45 ± 2 ml · kg$^{-1}$ · min$^{-1}$.

**Supplementation Period Characteristics**

For the EP outcome, mean daily QS was 960 ± 127 mg (range 600–1,000), with a mean supplementation period of 26 ± 24 days (range 5–72). All studies looking at the effect of QS on VO$_{2\text{max}}$ provided 1,000 mg/day for an average of 8 ± 23 days (range 11–58). As a result of supplementation, plasma quercetin concentration increased 443% ± 5% from a mean presupplementation value of 107 ± 62 μg/L to a mean postsupplementation value of 430 ± 256 μg/L.

**Exercise Protocol Characteristics**

**EP** Performance was evaluated using either cycling (Cureton et al., 2009; Davis et al., 2010; MacRae & Mefferd, 2006; Nieman et al., 2009) or running (Bigelman et al., 2010; Ganio et al., 2010; Nieman et al., 2010) tests. Mean exercise-testing duration was 31 ± 29 min (range 8–100). To test EP, two studies used full-length time-trial exercise (Bigelman et al., 2010; MacRae & Mefferd, 2006), three used incremental tests to exhaustion (Bigelman et al., 2010; Cureton et al., 2009; Ganio et al., 2010), one used a full-length fixed-power-output test to exhaustion (Davis et al., 2010), and three required subjects to perform fixed-power-output preload work immediately before completing a time trial (Cureton et al., 2009; Nieman et al., 2009; Nieman et al., 2010). When these latter exercise bouts are taken into account, mean total exercise time across studies amounted to 79 ± 82 min (range 8–224). Overall, only two studies used ecologically valid research designs (Bigelman et al., 2010; MacRae & Mefferd, 2006) where no fixed-power-output bouts of exercise were conducted.

**VO$_{2\text{max}}$** Aerobic capacity was tested using incremental running (Bigelman et al., 2010; Ganio et al., 2010) and cycling (Cureton et al., 2009; Davis et al., 2010) tests to exhaustion. Mean VO$_{2\text{max}}$ test exercise duration was 14 ± 3 min.

**Figure 1** — Forest plot showing the effect of quercetin supplementation on the percentage changes in endurance performance in each of the included studies. An overall weighted mean summary effect is presented together with subgroup overall weighted mean summary effects for untrained subjects and trained athletes. A mixed-effects model was used. Square sizes are proportional to the study weights. Results are $M$ ± 95% CI.
± 1.04% (95% CI: 0.10–1.39%, \( p = .02 \)), compared with the placebo condition. Using one effect estimate per research investigation to account for independency of studies yielded an overall effect summary of 0.79% ± 1.00% (95% CI: 0.04–1.53%), which was not significantly different from the effect summary derived from all 10 effect estimates (\( p = .93 \)). Moreover, removing findings of the two studies that used ecologically valid research designs did not change the overall summary effect (0.81% ± 0.96%, \( p = .02 \)). However, as clearly demonstrated by the forest plot, the overall positive effect of QS on EP was mainly driven by, and an artifact of, its effect in untrained subjects, which amounted to 0.83% ± 0.78% (95% CI: 0.14–1.51%, \( p = .02 \)), compared with that observed in trained subjects (0.09% ± 2.15%, 95% CI: −1.79% to 1.97%, \( p = .92 \)). The length of QS was 42 ± 24 days for the trained athletes’ group, compared with 9 ± 4 days for the untrained one. As shown in Figure 2, however, there was no relationship between QS duration and the percentage changes in EP between groups (\( p = .69 \)). There was a wide variation in exercise duration between studies, but no significant correlation (\( p = .10 \)) was observed between that variable and the percentage changes in EP between groups (Figure 3). The aforementioned results suggest that the chances of QS altering trained runners’ and cyclists’ EP in an important, trivial, or negative manner under real-world conditions are 9%, 83%, and 8%, respectively. QS is very unlikely to confer any EP advantage in untrained individuals, because their capacity to reproduce a performance is much less reliable than in trained individuals (Hopkins, Schabort & Hawley, 2001).

VO\(_{2}\text{max}\)

Figure 4 presents the effect of QS on VO\(_{2}\text{max}\). When results of all four effect estimates are combined, QS increased aerobic capacity by 1.94% ± 1.68% (95% CI: 0.30–3.59, \( p = .02 \)), compared with the placebo. Three of the four

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure2}
\caption{Meta-regression of the relationship between duration of quercetin supplementation and the percentage changes in endurance performance. Circle diameters are proportional to the study weights.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure3}
\caption{Meta-regression of the relationship between exercise duration and the percentage changes in endurance performance. Circle diameters are proportional to the study weights.}
\end{figure}
Quercetin, VO2\text{max}, and Endurance Performance

Figure 4 — Forest plot showing the effect of quercetin supplementation on the percentage changes in VO2\text{max} in each of the included studies together with an overall weighted mean summary. A random-effects model was used. Results are $M \pm 95\% \ CI$.

studies used in the summary effect computation were conducted in untrained subjects. A fixed-effect-model weighted mean summary effect indicates that in untrained individuals QS would increase VO2\text{max} by 1.96\% (95\% CI: 0.27–3.66\%, $p = .02$). In the only study conducted in trained individuals (Bigelman et al., 2010), QS non-statistically significantly increased VO2\text{max} by 1.62\%. The chances that QS affects VO2\text{max} in a meaningfully important, trivial, or negative manner in untrained individuals are 10\%, 90\%, and 0\%, respectively. In trained subjects, further research is required to evaluate QS’s effect on VO2\text{max}.

Heterogeneity

With respect to the EP outcome, results were homogeneous across studies ($Q = 7.681$, $p = .567$), with an $I^2$ value of 0\% (no heterogeneity). Similarly, results were homogeneous ($Q = 4.295$, $p = .231$) for VO2\text{max}, with an $I^2$ value of 30\% (low heterogeneity).

Discussion

The current meta-analysis adds several novel and important findings to the ergogenic-aid-related scientific literature that will help sport-governing bodies, nutritionists, scientists, coaches, and athletes make evidence-based decisions about QS’s effectiveness. First, it was demonstrated in trained athletes that prolonged QS (i.e., ≥5 days) is unlikely to improve EP in a meaningful way under real-world exercise conditions. Second, whether prolonged QS can alter VO2\text{max} in trained athletes is unclear and deserves to be further investigated. Third, under real-life exercise circumstances, prolonged QS is unlikely to improve untrained individuals’ VO2\text{max} and very unlikely to enhance their capacity to perform prolonged exercise.

Several findings of the current meta-analysis substantially differ from those reported in Kressler et al.’s (2011). From a scientific and practical point of view, the implications of these differences are, we believe, so important that they cannot be discarded and need to be disseminated to the scientific and athletic community. First, Kressler et al. reported that QS significantly improved EP by 3\% (see Kressler et al.’s erratum), independent of fitness level. Such an ergogenic effect has the potential to confer a meaningful increase in EP under real-world exercise conditions. On the other hand, we demonstrated that the effect of QS on EP is training-state-dependent, 4- (untrained subjects) to 33-fold (trained individuals) less important than in Kressler et al.’s study, and only statistically significant in untrained individuals. Moreover, we concluded that QS is unlikely to improve EP, independent of training state. Second, Kressler et al. reported that QS did not significantly improve VO2\text{max} in trained and untrained individuals. In the current meta-analysis, we did show that QS significantly ($p = .02$) increases VO2\text{max} in untrained individuals; in trained athletes, its effect is unclear.

Trained cyclists or runners may hope to benefit from the use of a sports nutrition supplement during out-of-doors, real-world exercise conditions if it produces an effect under laboratory-controlled exercise conditions that is 1.3–1.6\% (Hopkins et al., 1999; Hopkins & Hewson, 2001; Paton & Hopkins, 2006) greater than the effect of the placebo. In this meta-analysis, it was demonstrated that QS confers an increase in EP that is much less than this efficacy threshold, thereby indicating that it is unlikely to confer any worthwhile ergogenic value, at least within the length of supplementation used and quercetin doses provided by the actual studies. Further studies are required to determine the effect of higher daily quercetin doses on EP. It is unclear whether increasing QS durations beyond those studied could alter QS’s effect, because meta-regression analysis showed no relationship between QS duration and EP within the range of 5–72 days.

In line with the observations made in athletes, in untrained individuals it is very unlikely that QS will improve EP in a worthwhile manner. The direct implication of this finding is not clear or may even be seen
as irrelevant for some, because untrained individuals would not be expected to take part in competitive events without any prior physical preparation. Or if they would, it is unlikely that their interest to perform would be such that they would think of using prior QS. However, what this result suggests is that daily quercetin intake is unlikely to induce physiological adaptations helping untrained subjects’ physical exercise capacity in the early stages of a training program or decreasing fatigue during an acute bout of exercise. It would not be trivial if a nutritional supplement could meaningfully increase sedentary individuals’ physical exercise capacity, as it could presumably decrease recovery time, reduce fatigue, and potentially encourage adherence and maintain long-term exercise participation.

The fact that QS did not improve untrained subjects’ VO$_{2\text{max}}$, in a valuable way gives credence to and supports the previously proposed idea that in these individuals quercetin likely does not produce favorable health- and exercise-related physiological and biological adaptations. This assertion makes sense, given that it has been demonstrated in humans that QS does not increase mitochondrial biogenesis (Nieman et al., 2010), decrease inflammation (Nieman, Henson, Davis, Angela Murphy, et al., 2007; Nieman, Henson, Davis, Dumke, et al., 2007b) and oxidative stress (McAnulty et al., 2008; Shanely et al., 2010), or improve muscle oxidative capacity (Cureton et al., 2009). The fact that QS does not induce meaningful changes in aerobic capacity and exercise capacity indicates that this supplement should not be promoted as such for untrained, sedentary individuals.

It is unclear whether QS could improve trained athletes’ aerobic capacity. In fact, of the four studies used to derive the overall treatment effect, three were conducted in untrained subjects. Moreover, the result observed in the single study conducted in trained individuals was not significant. Because QS did not improve trained athletes’ EP, it is reasonable to put forward the idea that in aerobically trained subjects it may not confer a VO$_{2\text{max}}$ improvement, although we acknowledge that a disconnect between these variables cannot be ruled out. More studies are required before a definitive statement about QS’s effect on VO$_{2\text{max}}$ in trained athletes can be made. This meta-analysis has some limitations that are worth mentioning. Results of studies using radically different exercise protocols (time trial vs. fixed-power-output exercises) and exercise durations (8–224 min) were combined to derive an overall treatment effect. However, removing the two studies (Bigelman et al., 2010; MacRae & Mefferd, 2006) that used time trials did not change the overall outcome. In addition, no relationship was observed between the percentage changes in EP and exercise duration. These observations suggest that it was technically reasonable to combine all research findings together. Some comparisons were made where the quercetin supplements contained ingredients not found in the placebos (i.e., epigallocatechin 3-gallate, N$_2$-PUFA, vitamin C, and folic acid), which prevented completely isolating the effect of quercetin. Although those compounds are not known to provide any ergogenic benefit

In conclusion, results of the current meta-analysis can be summarized as follows: (a) Daily quercetin intake of 600–1,000 mg for 5–72 days improves trained athletes’ EP capacity by 0.09%, which is unlikely to be sufficient to affect EP in a worthwhile fashion under real exercise circumstances; (b) whether QS may improve aerobic capacity in trained athletes is unclear and deserves further investigation; (c) QS does not modulate EP in a dose-dependent manner; and (d), in untrained individuals, daily quercetin intake of 1,000 mg for 5–13 days improves VO$_{2\text{max}}$ and EP by 1.96% and 0.83%, respectively, which, however, is unlikely to translate into an improvement of these parameters under real-life exercise circumstances.

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References


