Minerva Medica 2018 August;109(4):285-9
DOI: 10.23736/S0026-4806.18.05681-1

ORIGINAL ARTICLE

Quercetin phytosome® in triathlon athletes: a pilot registry study

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ABSTRACT

BACKGROUND: Oxidative stress is associated with delayed recovery and higher risk of post-training pain in triathlon athletes. Therefore, supplementation with antioxidant compounds may have a role in enhancing recovery. Quercetin presents marked antioxidant activity. In this pilot registry study, we evaluated the effects of the supplementation with a novel proprietary delivery form (phytosome®) of quercetin in amateur triathlon athletes.

METHODS: We employed a specific study model of triathlon according to the "Sprint" distance. The individual triathlon training included repetition of the run 8 times in 14 days. A group of athletes used quercetin phytosome® supplementation (one tablet of 250 mg quercetin phytosome® twice daily). A control group did not use supplementation. All subjects attended a baseline measurement run and a second final measurement run at day 14. At the end of the study, subjective performance, post-training pain, cramps, time to full recovery and oxidative stress were measured.

RESULTS: In total, 23 subjects used the supplement and 25 did not. No side effects were reported. The improvement of time to complete the run was greater in subjects on quercetin supplementation compared with the control group (-11.3% *vs.* -3.9%; $P<0.05$). Training was considered more valuable in the quercetin group compared with controls ($P<0.05$). Similarly, post-run muscular pain, cramps, localized pain and the post-exercise recovery time were all considered better with the supplementation ($P<0.05$). Oxidative stress was also reduced ($P<0.05$).

CONCLUSIONS: This pilot study suggests that the oral supplementation with quercetin phytosome® may result in improved training and performance in amateur triathlon athletes.

(*Cite this article as:* Riva A, Vitale JA, Belcaro G, Hu S, Feragalli B, Vinciguerra G, *et al*. Quercetin phytosome® in triathlon athletes: a pilot registry study. Minerva Med 2018;109:285-9. DOI: 10.23736/S0026-4806.18.05681-1)

KEY WORDS: Quercetin - Dietary supplement - Physical endurance - Phytosome®.

Endurance is defined as the ability of strength to continue or last, despite fatigue, stress or other adverse conditions.[1] Triathlon athletes require high endurance levels to complete their competition, and prompt recovery from training is crucial to achieve higher endurance.[1, 2]

Oxidative stress has been associated with delayed recovery and higher risk of post-training pain in triathlon athletes.[2-4] To this end, supplementation with anti-oxidant compounds in the training and post-competition phases may have a role in enhancing recovery.[4]

Quercetin is one of the most abundant polyphenol compounds, commonly found in fruits and vegetables.[5] This flavonoid is endowed with marked antioxidant activity, as well as with anti-inflammatory properties.[6] Furthermore, quercetin acts as a strong scavenger of reactive oxygen

species, chelates transition metals and exerts a protective effect against lipid peroxidation.[6] In prior studies, quercetin showed skin protective effect by reducing signs of inflammation of damaged skin.[6, 7]

In this pilot registry study, we evaluated the effects of the supplementation with a novel proprietary delivery form (phytosome®) of quercetin (Indena S.p.A., Milan, Italy), in amateur triathlon athletes.

Materials and methods

Study setting and design

The registry included non-professional triathlon athletes. In our study, we have employed a specific study model of triathlon according to the 'Sprint' distance: 1) a swim distance in open seawater of 750 m; 2) a cycling distance of 20 km (12 miles); and 3) a 5-km run, as applied in other studies.[2, 3] The training was conducted at the beachside of Pescara, Italy.

To keep conditions as standard as possible, the period of registry training was organized in July when the average temperature at the beachside in Pescara, Italy around 7 pm is approximately 21-28 °C. The average running times for each of these three events was approximately 12-15 minutes, 40 minutes and 25 minutes, respectively, with a total intended average of about 100 minutes. Amateur athletes able to perform the triathlon in about 100±15 minutes were considered for inclusion.

The study was conducted according to the Declaration of Helsinki. The local Ethical Committee has approved the study design, and all subjects signed an informed consent before inclusion; however, the supplementation was given in a purely "field-practice" setting.

Training

The individual triathlon training included repetition of the defined distances 8 times in 14 days in the same environment. Diet was completely free, but advice from the investigators was given. A mineral over-the-counter supplementation (Polase®) was allowed, but no other supplementations were permitted.

A group of athletes used quercetin phytosome® supplementation (one tablet of 250 mg quercetin phytosome® twice a day, with breakfast and dinner). Quercetin phytosome® is a novel stable optimized solid dispersion of quercetin, meant to allow a higher absorption. Its composition is the following: anhydrous quercetin (34-42%), sunflower lecithin (40%), other food grade excipients (20%).

A control group did not use quercetin containing supplement; however, they followed the same training and nutritional plans. Athletes were free to decide whether or not take the quercetin supplementation.

Evaluations

To assess performance, all subjects attended a baseline measurement "Sprint" run and a second final measurement "Sprint" run at day 14. These run measurements were not competitive but rather chronometric; the final time to complete each run was recorded for each participant. At the end of the study period, a Visual Analogue Scale line (range: 0-10) was used to evaluate the subjective performance, post-training pain and cramps. Time to full recovery was measured. In addition, oxidative stress was measured by testing plasma free radicals using the d-ROMS test.[8] Routine laboratory evaluations were performed at baseline and just before the last measurement run.

Statistical analysis

A total of 16 registry subjects in each group (control or supplement) were considered necessary to highlight differences after a 2-week training on the basis of observations from previous studies.[2, 3] The two-way ANOVA test was used to compare the differences in performance prevalence in the two groups. The normalization of total triathlon times in seconds was used as the final evaluation target to measure the percent decrease in time. All measurements were considered non-parametric and evaluated with non-parametric tests (Mann-Whitney).

A Sigma plot (Systat Software Inc.) program was used to perform all statistical analyses. A P value of <0.05 was considered statistically significant.

TABLE I.—*Results of the 100-minute triathlon, at baseline and after 2-week training.*

100-min triathlon	Quercetin (N.=23)		Control (N.=25)	
	Baseline	2 weeks	Baseline	2 weeks
Swim, s	856±227	728±273*	858±237	794±216
Bike, s	2315±490	2047±428*	2240±482	2127±515
Run, s	1560±314	1423±288*	1535±333	1489±365
Total (includes transition phases and rest), s	6113±424	5425±380*	6033±470	5797±499

Comparison between 2-week values and those reported at baseline were significant in both groups (P<0.05).
*P<0.05 *vs.* controls.

Results

In total, 48 subjects were enrolled (age range: 30-40 years). Of them, 23 subjects used the supplement and 25 did not. The two groups were comparable in terms of gender (males/females: 16/7 *vs.* 16/9) and age (mean: 33 years in each group). No side effects or tolerance problems were reported; compliance to the supplement was 100%.

All subjects completed the baseline and the measurement runs. All subjects improved with training, in the total time and in all the three single events of the triathlon race, with respect to baseline (Table I). Remarkably, the improvement was greater in subjects on quercetin supplementation compared with the control group. The final variation in time (expressed in seconds, including transitions) was -11.3% with quercetin in comparison with a variation of -3.9% in the non-supplemented group.

Table II and Figure 1, 2, 3 show the subjective parameters and plasma-free radicals. Overall, training was considered more valuable in the quercetin group compared with controls (P<0.05). Similarly, post-run muscular pain, cramps, localized pain and straining, and the post-exercise recovery time were all considered better with the supplementation (P<0.05). Oxidative stress was also reduced with quercetin phytosome® compared with controls (P<0.05).

TABLE II.—*Other parameters at 2 weeks.*

Parameters	Quercetin (N.=23)	Controls (N.=25)
Training efficacy (VAS score)	8.6±1.1	7.1±1.4
Post-run diffuse muscular pain (VAS score)	3.4±1.0	6.0±1.3
Cramps and localized pain (VAS score)	3.1±1.3	4.0±1.2
Time to full recovery, hours	18.1±1.3	20.4±2.2
PFR, Carr units	392±31	431±22

P<0.05 for quercetin *vs.* control for all comparisons.
PFR: plasma-free radical; VAS: Visual Analogue Scale.

At the end of the study, subjects on supplementation displayed lower levels of unconjugated bilirubin compared with controls (0.68±0.3 *vs.* 0.89±0.3 mg/dL; +15.0% from baseline in the quercetin group and +43.5% in the control

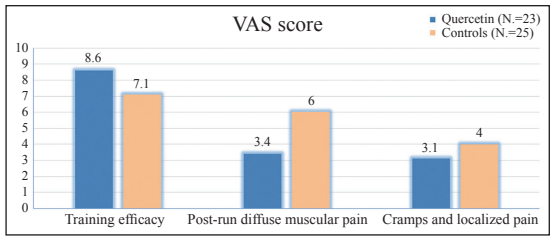

Figure 1.—Perceived training efficacy, diffuse and localized pain in the quercetin and the control group. P<0.05 for quercetin *vs.* control for all comparisons.

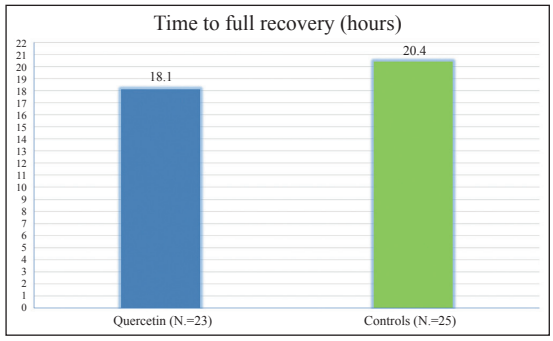

Figure 2.—Time to full recovery pain in the quercetin and the control group. P<0.05 for quercetin *vs.* controls.

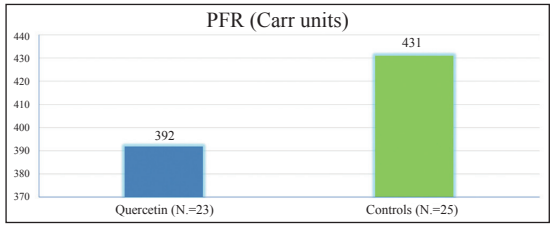

Figure 3.—Plasma-free radical in the quercetin and the control group. P<0.05 for quercetin *vs.* controls.

group; P<0.05) and lower level of lactate dehydrogenase (343±38 *vs.* 411±24; +11.4% from baseline in the quercetin group and +33.9% in the control group; P<0.05). No other relevant alterations of laboratory parameters were reported.

Discussion

The use of quercetin as such has been limited so far by its low bioavailability, which is determined by a poor gastrointestinal absorption.[9] On the other hand, the phytosome® technology is a well-established approach able to guarantee high absorption rates of desired compounds. Basically, the phytosome® technology allows to achieve a stable optimized solid dispersion of otherwise poorly soluble compounds with the use of the dietary surfactant lecithin and other food grade excipients. A human pharmacokinetic study, currently under publication, has demonstrated a 20-fold absorption improvement for quercetin phytosome® *versus* regular quercetin (on a weight equivalence basis, *i.e.* 500 mg of quercetin phytosome®, containing 200 mg of pure quercetin, *vs.* 500 mg of pure quercetin).

In this pilot, registry study, supplementation with quercetin phytosome® was associated with improved performance and endurance compared with lack of supplementation, in amateur triathlon athletes. This advantage was particularly evident in terms of reduction of the time necessary to complete a validated model of triathlon race.[2, 3] More specifically, subjects on quercetin were able to reduce their time to complete the race by about 10%, with respect to baseline, after a 2-week intensive training. As a mean of comparison, according to our experience, a variation around 5% in a similar competition enrolling 1000 participants may allow a subject to get from the 800th place to around 700th. This remarkable advantage may be due to improved training efficacy and reduced pain after training, as suggested by the own personal evaluation of the involved athletes. Indeed, better training, a lower level of fatigue, a better rest, easier efforts and improved quality of performance may result in a more pleasant and less stressful experience with triathlon, ultimately leading to improve performance.

Currently, there is considerable confusion on the role of "antioxidant" supplementation in exercise. Supplementation with vitamin C has been shown to reduce the development of endurance capacity[10] and the view that exercise and antioxidants may work against each other was also suggested by studies showing that antioxidant supplementation abrogates the beneficial effects of exercise on insulin resistance.[11] Since exercise increases consumption of oxygen and mitochondrial activity, reactive oxygen species might, paradoxically, mediate not only cellular damage associated to exercise, but also its beneficial effect. Direct anti-oxidants such as vitamin C and vitamin E were used in these "negative" antioxidant studies. These compounds are direct antioxidants – that is, they directly react and quench free radicals and reactive oxygen species, while quercetin and polyphenols are essentially boosters of the body's endogenous antioxidant response and exert "antioxidant" activity indirectly, by Nrf2-mediated stimulation of the cellular antioxidant system and the expression of cytoprotective genes.

Importantly, in our study subjects on quercetin supplementation showed a reduced oxidative stress, with respect to controls. Reduction of oxidative stress by oral supplementation results in improved performance in triathlon.[4] Given the well-established anti-oxidant and anti-inflammatory activity of quercetin,[6, 7] it is possible to conceive that this supplementation has contributed to improve performance and endurance in the evaluated subjects, without any adverse event. Noteworthy, in the present study, an oral supplementation with quercetin phytosome® was used. The phytosome® technology allows improved pharmacokinetics of the active compound, thus further enhancing product delivery and bioavailability.[12, 13]

Interestingly, quercetin phytosome® supplementation resulted in reduced unconjugated bilirubin and lactate dehydrogenase (an enzyme abundant in red blood cells and released into the bloodstream after their breakdown) compared to control group. Although this finding does require further validation in dedicated studies, it may suggest the association between quercetin phytosome® supplementation and improved metabolism, especially of the liver. Moreover, uncon-

jugated bilirubin is considered a marker of hemolysis:[14] therefore, it is possible to speculate a protective effect of quercetin on red blood cells, to be investigated in dedicated studies.

Conclusions

Although with all the inherent limitations of any registry study, the results of this pilot analysis suggest that the oral supplementation with quercetin phytosome® may result in improved training and performance in amateur triathlon athletes.

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Conflicts of interest.—Stefano Togni and Antonella Riva are employees of Indena S.p.A. Luca Giacomelli is a consultant for Indena S.p.A. Editorial assistance was provided by Aashni Shah; this assistance was supported by internal funds.

Manuscript accepted: May 8, 2018. - Manuscript received: April 26, 2018.