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Evaluation of the effects of supplementation with Pycnogenol® on fitness in normal subjects with the Army Physical Fitness Test and in performances of athletes in the 100-minute triathlon

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Aim. The aim of this registry study was to evaluate the effects of Pycnogenol® (French pine bark extract) on improving physical fitness (PF) in normal individuals using the Army Physical Fitness Test (APFT). The study evaluated the efficacy of Pycnogenol, used as a supplement, in improving training, exercise, recovery and oxidative stress.

Methods. The study was divided into 2 parts. In PART 1 (Pycnogenol 100 mg/day), the APFT was used to assess an improvement in PF during an 8-week preparation and training program. In PART 2 (Pycnogenol 150 mg/day), the study evaluated the effects of Pycnogenol supplementation in athletes in training for a triathlon.

Results. PART 1. There was a significant improvement in both males and females in the 2-mile running time within both groups, but the group using Pycnogenol (74 subjects) performed statistically better than controls (73 subjects). The number of push-ups was improved, with Pycnogenol subjects performing better. Sit-ups also improved in the Pycnogenol group. Oxidative stress decreased with exercise in all subjects; in Pycnogenol subjects the results were significantly better. PART 2. In the Pycnogenol group 32 males (37.9; SD 4.4 years) were compliant with the training plan at 4 weeks. In controls there were 22 subjects (37.2;3.5) completing the training plans. The swimming, biking and running scores in both groups improved with training. The Pycnogenol group had more benefits in comparison with controls. The total triathlon time was 89 min 44 s in Pycnogenol subjects *versus* 96 min 5 s in controls. Controls improved their performing time on average 4.6 minutes in comparison with an improvement of 10.8 minutes in Pycnogenol subjects. A significant decrease in cramps and running and post-running pain was seen in the Pycnogenol group; there were no significant differences in controls. There was an important, significant post-triathlon decrease of PFR one hour after the end of the triathlon with an average of -26.7,

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whereas PFR in controls increased. In Pycnogenol subjects there was a lower increase on oxidative stress with a faster recovery to almost normal levels (<330 for these subjects). These variations in PFR values were interpreted as a faster metabolic recovery in subjects using Pycnogenol.

Conclusion. This study opens an interesting new application of the natural supplementation with Pycnogenol that, with proper hydration, good training and nutritional attention may improve training and performances both in normal subjects and in semi-professional athletes performing at high levels in difficult, high-stress sports such as the triathlon.

KEY WORDS: Fitness - Oxidative stress - Dietary supplements.

Physical fitness (PF) includes two concepts: general fitness (a state of health and well-being); and specific task-oriented or sport-oriented fitness (a task-oriented definition based on the ability to perform specific skills in defined sports). PF is considered a measure of the individual ability to function efficiently and effectively in work and sport activities and to meet both external (*i.e.*, an unexpected need to perform an unusual effort) and internal (*i.e.*, the ability to fight an infection)¹⁻³ emergency situations. Although the President's Council on Physical Fitness and Sports could not offer a simple, general definition of physical fitness,⁴ it is generally achieved through a combination of several factors including correct nutrition, exercise, and enough rest. PF can

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also be defined as the full capacity to carry out the normal day's activities without undue fatigue.¹⁻⁴

Several factors considered in PF are shown in Table I. A comprehensive fitness program should be individual and may focus on one or more specific needs and skills, on specific age groups or on health-related needs such as bone and cardiac health.⁴⁻⁷

While in the past PF was considered and pursued mainly for healthy individuals, now even subjects with defined clinical or risk conditions (*i.e.*, diabetes, metabolic syndrome or even oncological problems) may look for fitness standards for their specific condition.⁵⁻¹⁰ PF improvements may actually enhance body resistance to infections and improve the response to disease-related stress.¹¹⁻¹³

A combination of mental, social and emotional health have significant roles in creating fitness status. PF may also prevent, control or even treat many chronic health conditions brought on by unhealthy lifestyle or aging¹⁰⁻¹² and fight the effects of handicaps.

Specific or task-oriented fitness allows specific activities to be performed with efficiency, *i.e.*, in sports or military service. Specific training prepares athletes to perform well in their sport. In sprint/fast runs (*i.e.*, 400 m) the athletes should be trained mainly to improve their fitness working anaerobically throughout the race. In long distance running (marathons, triathlons) athletes are trained to work aerobically and psychologically to improve their endurance.

In jobs related to security, policing and protection such as firefighters, policemen and military staff, PF is essential to operate in safety. In many countries regular fitness tests are used to evaluate capability in tasks requiring fitness or strength. In the USA soldiers must be able to pass the Army Physical Fitness Test (APFT) designed to test muscular strength, endurance, and cardiovascular respiratory fitness.¹³⁻¹⁹ Soldiers are scored on the basis on their performance in three events (push-ups, sit-ups and a two-

mile run) ranging from 0 to 100 points in each event. A minimum score of 60 in each event is required to pass the test. The soldier's overall score is the sum of the points from the three events. To pass the test the total may range from 180 to 300. Active soldiers are required to take an official record APFT at least twice a year; reserve soldiers take one record APFT per year.^{18, 19}

Comparable guidelines could be considered for non-military personnel^{19, 20} because of the close association between fitness and good health for the prevention of most significant clinical problems. In addition, improving fitness may have a positive impact on aging and on the problems associated with aging.²¹

Fitness and oxidative stress have an interesting but not completely understood relationship; but generally, improving fitness may reduce oxidative stress associated with many conditions.²² When PF decreases, plasma free radicals (PFR) may be increased²²⁻²⁴ due to a more sedentary lifestyle. Several nutritional and food supplements have been tested in healthy subjects and in patients with the aim of improving fitness and controlling oxidative stress.²²⁻²⁸

Pycnogenol®, the standardized extract from the bark of a specific French pine (Horphag Research Ltd.), has shown remarkable characteristics in controlling oxidative stress and in improving training both in healthy athletes and in patients.²⁷⁻²⁹ Its effects are superior to other products used in exercising subjects to control oxidative stress and improve muscular performances.²⁹⁻³²

The main aim of this registry study was to evaluate the effects of Pycnogenol used as a supplement on improving PF in normal individuals, using the APFT testing system. The registry study was also planned to evaluate the efficacy of Pycnogenol, used as a supplement, in improving training, exercise, recovery from fatigue and in controlling oxidative stress. The study was comprised of two parts: Part 1 stud-

TABLE I.—Factors considered in physical fitness.

	Health related	Skill related	Sports
Metabolic	Body composition	Agility	Team sport
Morphological	Cardiovascular fitness	Balance	Individual sport
Bone integrity	Flexibility	Coordination	Lifetime
Other	Muscular endurance	Power	Other
	Muscle strength	Speed	
		Reaction time	
		Other	

ied fitness in normal, healthy subjects tested for PF improvements with the APFT test; and Part 2, was a more advanced evaluation that included the study of improvement in performances in triathlon amateur athletes.

Materials and methods

PART 1: Fitness study in normal subjects

In this open experience, the APFT was used to assess an improvement in PF during an 8-week preparation and training program.

After full informed consent, 150 normal subjects ages 35-55 were screened for any hidden pathology, metabolic problems or cardiovascular condition. A resulting registry group of subjects ages 32-36 was included. At inclusion, all subjects were able to perform the three exercises (push-ups, sit-ups and a two-mile run) within the APFT standards for their age and sex. The relative standards for the APFT performance for this category of subjects are shown in Table II. No clinical condition was present; subjects were not allowed to use any drug or other nutritional food or supplement during the study.

Of these, 80 subjects used Pycnogenol (100 mg, equivalent to two tablets/day), and at least 60 comparable controls were included into the 8-week registry study. Subjects were evaluated with the APFT at inclusion and at 8 weeks. After careful briefing, subjects were trained by repeating in sequence the three APFT tests at least 5 times per week during the 8 weeks of the study. A diet excluding excess salt, sugar and fat was suggested, and the consumption of alcohol, soda drinks, salt (NaCl) and caffeine-including products was limited (maximum one glass/cup/day), self-controlled. Also “sport drinks” and “energy drinks” were not allowed.

The BMI at inclusion for all subjects was on average 23.5; 0.6 becoming 23.4;0.3 at 8 weeks. The

subjects were basically fit, and the exercise was not meant to reduce weight but to increase the muscular mass, efficiency and PF within the same weight range. Also weight lifting and other exercise, *i.e.*, including walking and stair climbing instead of using cars or transports or lifts, were suggested in an accessory plan adapted to the daily activity of the subjects but left to personal initiative.

The Pycnogenol dose was fixed at 100 mg/day for subjects weighing between 55 and 80 kg. Heavier or smaller subjects were excluded.

OTHER EVALUATIONS

Routine blood tests (including thyroid functional tests) were evaluated at inclusion to exclude any clinical or risk condition (*i.e.*, hyperlipidemia, hypertension, diabetes) or metabolic problems. Oxidative stress was evaluated at inclusion and at 8 weeks measuring plasma free radicals with FRAS equipment (Corcon, Parma, Italy). Subjects’ activity and working conditions were unchanged and not limited or altered.

SUPPLEMENT STUDIES

Supplement studies^{33, 34} are aimed to define the field of activity of supplements and possible preventive applications. The best field of application for supplements are preclinical, borderline applications or the supplementary management of risk conditions. Supplements - unless there are specific claims - are not generally used for treatment of signs/symptoms or clinical conditions. Generally, the aim of supplement studies is to produce supplementary data to be compared to background historical data (*i.e.*, based on the best available management for comparable subjects) or to other management plans.

Pycnogenol in tablet form was used at a dosage of two 50 mg tablets daily for an average of 8 weeks. After this period all subjects using Pycnogenol de-

TABLE II.—Standards for subjects (age 32-36 years).

Test	Females	minimum	Males	minimum
2 MILES	15 min. 54 sec	21.42	13.18	17.42
PUSH UPS	45	15	75	34
SIT UP*	76	42	76	42

* Males and female: same standards.

cided whether to carry on with the supplement up to 12 months.

Pycnogenol is a standardized extract from a French pine bark used in the recent past for several vascular studies^{35, 36} and in venous microangiopathy. The product is very powerful as 100 mgs of Pycnogenol produces significant effects in several pre-clinical or clinical conditions.³⁵⁻⁴¹ Pycnogenol is very effective in acute models of edema^{37, 38} with a selective action on lower limb swelling and edema. Pycnogenol may also improve the healing of venous ulcers in severe models of chronic venous insufficiency by controlling edema;³⁹ it is also very effective after deep venous thrombosis in post-thrombotic limbs³⁹⁻⁴¹ as seen in a recent study.

In this study supplementation with Pycnogenol was used according to the following rules:

1. supplementation was SUGGESTED to the evaluation subjects as an option that would possibly improve the management of the condition;
2. the supplementation was used in association with what was considered at the time the 'standard or best-management' available for that condition according to international guidelines, if available;
3. the use of Pycnogenol should not have interfered with other treatments or preventive measures;
4. the periods of follow-up were considered variable (ideally 8 weeks);
5. the type of non-clinical evaluation was a registry.
6. the supplement was available in the market and voluntarily acquired by the registry subjects. A quantity of product was made freely available.

The evaluation of the compliance concerning the use of the supplement was of significant value in indicating how many subjects were willing to use the product. Accessory information in this type of evaluation included: how many subjects were willing to initiate supplementation after briefing and how many subjects would continue with the use of the supplement as they observed benefits or good tolerability. There was no defined group allocation and no randomization organized by the investigators. Subjects decided - on the basis of the preliminary briefing - the group they would join. No placebo was used. Patients were informed about the supplement or the other possible option. Possible placebo effect was also explained and considered. Data were analyzed after a period of study of at least 4 weeks.

The analysis of data was managed by a group of external reviewers not in contact with the registry subjects. Commercial sponsorship from the producers of the tested supplement was not available.

PART 2: Higher level fitness study: the 100-min triathlon

The aim of this study was to evaluate the effects of Pycnogenol supplementation in athletes in training. The registry included triathlon athletes.

Triathlon races may vary in distance. The main international race distances are reported in Table III according to international standards (International Triathlon Union, and USA Triathlon). In our study, however, we developed a specific model of triathlon including:

- a swim distance in open sea water of 750 metres (0.47 miles);
- a cycling distance of 20 km (12 miles); and
- a 5 km run.

To keep conditions as standard as possible, the period of registry training was between May 15 and June 20 when the average temperature at beachside in Pescara, Italy at 2 pm is about 21-25 °C. The average running times for these three events was, ideally, around 12-15 minutes, 40 minutes and 25 minutes with a total intended average around 100 min that is relatively easy to evaluate and can be performed by many non-professional or semiprofessional athletes.

Transition areas/points between the swim and bike segments (T1) and between the bike and run segments (T2) were used to switch from swimming to cycling and cycling to running. The time spent in T1 and T2 is included in the overall time of the race. The nature of this sport focuses on persistent and periodic training in each of the three disciplines, general psychological and physical strength and nutritional conditioning. The evaluation of the single distances and of the global time for the triathlon were considered as the targets to improve in 4 weeks of training.

Initially, the registry included 80 amateur athletes able to perform the triathlon in about 100 minutes (with a variation of plus/minus 15 minutes). An analogue scale line (range 0-10) was used to evaluate the subjective performance, post-training pain, cramps and generally negative effects of training

TABLE III.—Main international race distances.

Definitions: triathlon races vary in distance.
According to the International Triathlon Union, and USA Triathlon, the main international race distances are:

Sprint distance	750 m (0.47 mi) swim, 20 km (12 mi) cycling; 5 km (3.1 mi) run;	12-15 40 min 25 min
Intermediate (or standard) distance, commonly referred to as “Olympic distance”	1.5 km (0.93 mi) swim 40 km (25 mi) bike 10 km (6.2 mi) run	
Long Course	1.2 miles (1.9 km) swim, 56 miles (90 km) ride, 1 3.1 miles (21.1 km) run, such as the Half Ironman	
Ultra Distance	2.4 miles (3.9 km) swim 112 miles (180 km) ride full marathon: 26.2 miles (42.2 km run);	

The most recognized branded Ultra Distance is the “Ironman” triathlon. Transition areas/points are positioned both between the swim and bike segments (T1), and between the bike and run segments (T2) and are where the switches from swimming to cycling and cycling to running occur. These areas are used to store bicycles, performance apparel, and any other accessories needed for preparing for the next stage of the race. The time spent in T1 and T2 is included in the overall time of the race.

on muscles. Also oxidative stress was measured by testing PFR.

STUDY TRAINING

The triathlon was performed at least 10 times in 30 days (on average every 3 days). A group of amateur athletes used 150 mg of Pycnogenol (one 50 mg tablet three times a day at breakfast, lunch and dinner). A control group did not use any supplement but followed the training and nutritional plans. Females were excluded from this part of the study for variability problems (*i.e.*, in the plasma free radicals evaluation) including the use of hormonal treatments. Results include only male, protocol-compliant subjects.

OXIDATIVE STRESS MEASUREMENTS

Postexercise levels of oxidative stress (value one hour after the end of triathlon) were measured. The evaluation of PFR⁴²⁻⁴⁴ was made with FRAS equipment (Diacron, Parma, Italy) supplied by Corcon, Milan. The FRAS 4 system is a photometric analytical system developed for the global assessment of oxidative stress. The equipment measured PFR by measuring reactive oxygen metabolites (using the d-ROMS test) and biological antioxidant potential (using the PAT test) in whole plasma samples. FRAS measures PFR with a single drop of peripheral (fin-

ger) blood by the absorbance measurement of a sample solution through a monochromatic light beam. The centrifuge and the aluminum case with the photometric unit are temperature-controlled (37 °C).⁴⁵⁻⁴⁸ This method has been validated and has been used in several preventive, epidemiological and clinical studies showing good reproducibility and low intra-individual and inter-individual variability even in tests repeated in different days. PFR and oxidative stress tend to be increased in several clinical conditions and in risk conditions (*i.e.*, hypertension, diabetes, hyperlipidemia).⁴²⁻⁴⁸ After strenuous exercise PFR tend to increase in most subjects, and the persistence of higher levels of PFR has been associated with recovery from exercise-induced fatigue.⁴²⁻⁴⁵

In a randomly selected subgroup of subjects (10 from each group) PFR was measured at the start and finish line (at 60 minutes) and at the transition points during the final triathlon-test.

Statistical analysis

At least 25 registry subjects in each group (control or Pycnogenol) were considered necessary to evaluate differences at 8 weeks in the registry, on the basis of observations from previous studies. The ANOVA was used to compare the differences in performance prevalence in the two groups.

A Sigma plot (Systat Software Inc.) program was used to perform all statistical analyses.⁴⁹ All meas-

urements were considered non-parametric and evaluated with non-parametric tests (Mann-Whitney).

Results

PART I

The two resulting registry groups (Table IV) were comparable for age and sex distribution: 38 males and 36 females using Pycnogenol completed the training protocol without significant variation (less than one missed training session in a month). In controls 36 males and 37 females completed the registry. All dropouts were due to logistical prob-

lems of training not performed according to the registry.

Table V shows the results (divided into males and females) for the 2-mile run, push-ups and sit-ups. There was a significant improvement in the 2-mile running time for males and females ($P < 0.05$) within both groups. The improvement was statistically better in the group using Pycnogenol ($P < 0.05$) both in males and females. The number of push-ups was also significantly improved in males and females in all subjects completing the registry ($P < 0.05$). Pycnogenol subjects performed significantly better ($P < 0.05$). Sit-ups also improved in all subjects; the improvement in performance was significantly better in the Pycnogenol group ($P < 0.05$).

TABLE IV.—Subjects within age range: 32-36 completing the study (first part).

	Pycnogenol subjects	MEAN AGE	LOST
TOTAL INCLUDED	80		
COMPLETING			
MALES	38	34.5;1.4	2
FEMALES	36	33.5;1.6	4
	CONTROLS	MEAN AGE	LOST
TOTAL INCLUDED	77		
COMPLETING			
MALES	36	35.1;1.2	1
FEMALES	37	33.6;1.5	3

TABLE V.—Tests and oxidative stress results at 8 weeks (first part).

Test	Females		Males	
	incl.	8 weeks	incl.	8 weeks
2 MILES				
PYCNO	18 min 2 s	16 min 3 s*#	16 min 8 s	14 min 11 s*#
CONTR	17 min 20s	17 min 3 s*	16 min 6 s	15 min 34 s*
PUSH UPS				
PYCNO	31.2 (3.1)	39 (2.1)*#	56 (3.2)	69 (3.1)*#
CONTR	31 (2.2)	34.1 (1.1)*	58.2 (2)	62.2 (2.2)*
SIT UP*				
PYCNO	61.2 (2.2)	67 (1.3)*#	63.2 (3)	73.2 (2.2)*#
CONTR	61.2 (2.1)	64.2 (2.2)*	63.2 (1.1)	67.3 (2.2)*

* = $P < 0.05$ (before-after); # = $P < 0.05$ between groups.

OXIDATIVE STRESS (carr units)		Males	Females
PYCNO	inclusion	335.3;32	339.4;27.5
	8 weeks	318.2;19.4*#	311.3;24.3*#
CONTR	inclusion	310;22.4	332.3;21.6
	8 weeks	344.4;25.3*	356.2;29.1*

Normal values: males <330 Carr Units; females <335

Generally, with exercise, oxidative stress tends to increase. *: statistical difference compared to baseline; #: significant difference between Pycnogenol and controls.

TABLE VI.—Details of triathlon subjects (32 male athletes, mean age 37.9; SD 4.4).

		Inclusion (min sec SD)	4 weeks (min sec SD)	Diff.
A. Swim	Pycno	13 min 28 s; 2.2	12 min 34 s; 2.1	*#
		13 min 36 s; 2.5	13 min 38 s; 1.9	*
B. Bike	Pycno	39 min 21 s; 2.7	35 min 7 s; 1.9	*#
		38 min 29 s; 2.8	37 min 39 s; 2.6	ns
C. Run	Pycno	25 min 4 s; 1.9	22 min 31 s; 2.4	*#
		26 min 21 s; 1.9	24 min 31 s; 2.9	*
+2 transition times	Pycno	22 min 31 s; 4.5	20 min 2 s; 4.2	*#
		22 min 5 s; 4.9	21 min 17 s; 4.1	ns
TOTAL	Pycno	100 min 24 s; 3.2	89 min 44 s; 4.5*#	10 min 48 s
		101 min 1 s; 3.9	96 min 5 s; 3.2*	4 min 36 s
Difference				6 min 12 s

* difference before-after; # difference between groups; values in minutes. SD is expressed in seconds.

Oxidative stress was significantly decreased with exercise (improved; $P < 0.05$); in Pycnogenol subjects the results were significantly better ($P < 0.05$) both in males and females.

No side effects for the use of Pycnogenol were observed. All subjects using Pycnogenol reported a good tolerability and compliance (none was forced to stop the supplementation).

PART 2

At 4 weeks in the Pycnogenol registry group there were 32 male athletes (mean age 37.9; SD 4.4) correctly compliant with the training plan. The standards for triathlon are shown in Table VI. In the control group there were 22 subjects (mean age 37.2; 3.5) correctly completing the registry training plans. Dropouts were due mainly to logistical problems or to missed training sessions for working or personal problems or for minor, sport-related injuries delaying training or altering training plans.

For swim, bike and run (Table VI), both Pycnogenol subjects and controls improved with training ($P < 0.05$). The Pycnogenol group had more significant benefits ($P < 0.05$) in comparison with controls. The total triathlon time was 89 min 44 s in Pycnogenol in comparison with 96 min 5 s in controls ($P < 0.05$). Control subjects improved their performing time on average 4.6 minutes (4 min 36 s) in comparison with the average improvement of 10.8 minutes (10 min 48 s) observed in Pycnogenol subjects. The average difference of 6.2 min (6 min 12 s) is particularly important with a subgroup of 12 subjects improving more than 7 minutes in the Pyc-

nogenol group versus only one in controls. The improvements in performance are also shown graphically in Figure 1.

Table VII shows the changes in the visual analogue scale line and in oxidative stress. There was an improvement in subjective performance evaluation ($P < 0.05$), and a decrease in post-training pain and fatigue ($P < 0.05$). A significant decrease in cramps and running and post-running pain was seen in the Pycnogenol group ($P < 0.05$) while there were no significant differences in controls. Finally, there was an important, significantly lower post-triathlon value of PFR one hour after the end of the triathlon (with an average of -26.7%; $P < 0.05$). Variations were higher in PFR in controls. Figure 2 shows the variations in PFR at inclusion (1 indicated the average value before the start of the test-triathlon), after the first part (column 2), the second part (column 3) and the third part (column 4). The final evaluation (1 hour after the race, column 5) is also shown.

In Pycnogenol subjects there was a significantly lower increase of oxidative stress with a faster recovery ($P < 0.05$) to almost normal levels (< 330 for these subjects).

The variations in PFR values may be interpreted as a faster metabolic recovery in subjects using Pycnogenol. The exponential trends are also shown; the differences in trends is significant ($P < 0.05$).

Discussion

This preliminary registry study indicates that Pycnogenol may help to improve fitness both in normal

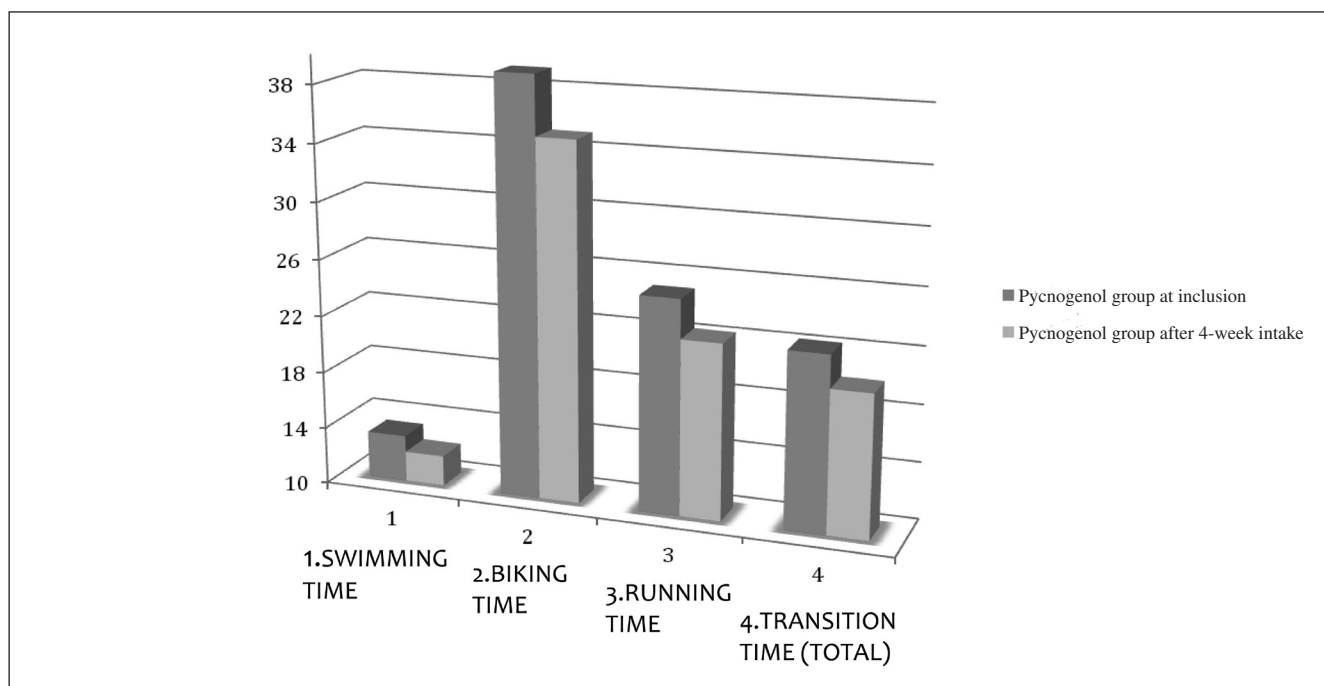


Figure 1.—Results, in minutes, before and after 4 weeks of training with 150 mg Pycnogenol/day.

TABLE VII.—The Visual Analogue Scale Line (range 0-5) and the post-exercise PFR (Carr Units): average and SD are shown.

		Inclusion	4 weeks
1. Subjective performance evaluation	Pyc	3.4;0.5	4.3;0.2*#
	Cont	3.5;0.2	3.5;0.4 ns
2. Post-training pain/fatigue	Pyc	4.3;0.3	2.6;0.5 *#
	Cont	4.1;0.2	4.3;0.2 ns
3. Cramps and negative effects of running	Pyc	3.7;0.2	1.6;0.3 *#
	Cont	3.6;0.3	3.4;0.3 ns
4. PFR in blood (one finger drop): post-exercise levels of oxidative stress (value 1 h after end of triathlon)	Pyc	543;65	398;23 *#
	Cont	573;44	582;32 ns

subjects and in athletes. The improvement was observed when training and improving fitness for simpler tasks (as seen with the AFPT), or for more definite, demanding, specific sport events (the 100 min triathlon).

In previous studies we have observed that Pycnogenol supplementation reduced training and post-training muscular pain,²⁸ reduces cramps during/after exercise²⁸ and has a significant effect on oxidative stress and PFR that are generally increased during and after training. These effects have been seen in both studies including normal, healthy subjects and in clinical studies including patients with diabetes and vascular problems.

There are several possible positive effects of Pycnogenol on training. It may act in most subjects as an anti-inflammatory agent (by reducing cramps and muscular pain associated with training, exercise and recovery), making training more effective and recovery shorter. Controlling pain and intramuscular edema (an immediate consequence of exercise) allows a better post-training rest and recovery. The performances and subsequent training sessions are more effective and tolerable, allowing a better exercise compliance.

An outstanding result of this study is the fact that athletes achieved better results under Pycnogenol

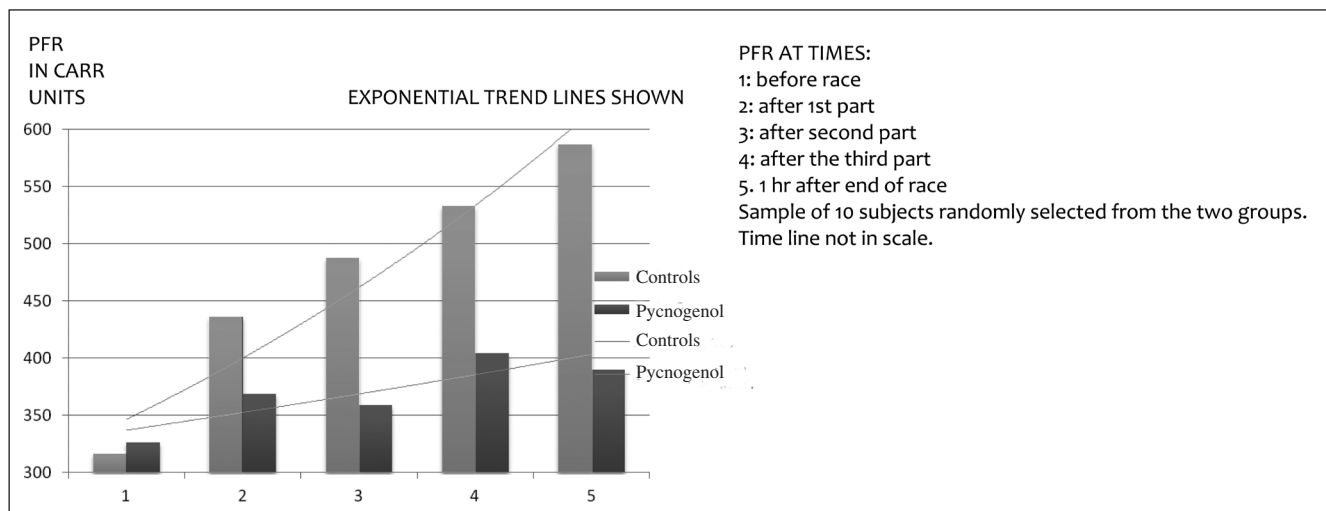


Figure 2.—Final test (triathlon at day 28).

compared to control, but suffered less from oxidative stress. Normally, a more intense physical activity should produce more oxidative stress. The control group presented exactly this expected increase of free radicals during exercising. But, on the contrary, the members of the Pycnogenol group had not only no increase of oxidative stress compared to start, they had less free radicals compared to start. It is really remarkable that even when the athletes in the Pycnogenol group outperformed the control group, they were better protected in triathlon and the other test against free radicals than the athletes in the control group.

This points to a great benefit of Pycnogenol for hard training athletes: Complete protection against oxidative stress. It is uncertain whether this elimination of free radicals during exercise enables the athlete to a better performance. However, we have to report that the supplementation with Pycnogenol inhibited the circulation of free radicals and we measured better results regarding physical fitness under Pycnogenol.

This APFT is a simple, cheap test that measures aerobic capacity and muscular strength and endurance. The combination of two-mile run, push-ups and sit-ups may not be complete or ideal to assess PT, but it is an important expression of fitness and it is widely understood and considered. The two-mile run is a true measure of aerobic strength, well correlated with maximal oxygen uptake (VO_{2max}). Most

subjects that perform within range for age in this test have a normal cardiovascular system, and a cardiac stress test could be completely negative in some 90% of them (aging >50 years). Muscular strength and absolute muscular endurance are highly correlated so that measurements of a single test (APFT) can be effective to verify different aspects of fitness. Studies using factor analysis have indicated that push-ups and sit-ups may have moderate to high factor loadings on various muscular strength/endurance factors. However, there are relative methodological problems in relating different type of muscular strength to a single, simplified, multiple test. Making the tests for fitness more complex is beyond the scope of the APFT, which is meant to be simple, repeatable and indicative and can be performed without specific equipment.

Several nutritional and food supplements have been tested with the aim of controlling oxidative stress in healthy subjects and in patients with the aim of improving fitness and controlling oxidative .²²⁻²⁸ Pycnogenol has shown remarkable characteristics in reducing oxidative stress and in improving training both in healthy athletes and in patients.²⁷⁻²⁹ Its effect appears to be superior to other products used in exercising subjects to control oxidative stress and legally improve performances.²⁹⁻³² In respect to safety, Pycnogenol has shown remarkable safety and tolerability both in normal subjects and in patients with severe clinical or metabolic alterations (*i.e.*, in kidney failure).

Conclusions

This study opens an interesting new application of supplementation with Pycnogenol that, with correct hydration, good training and nutritional attention may improve training and performances both in normal subjects and in semi-professional athletes performing at high levels in difficult, high-stress sports such as triathlon.

References

- Morrow JR Jr, Tucker JS, Jackson AW, Martin SB, Greenleaf CA, Petrie TA. Meeting physical activity guidelines and health-related fitness in youth. *Am J Prev Med* 2013;44:439-44.
- Jiménez-Pavón D, Sesé MA, Huybrechts I, Cuenca-García M, Palacios G, Ruiz JR *et al.* Dietary and lifestyle quality indices with/without physical activity and markers of insulin resistance in European adolescents: the HELENA study. *Br J Nutr* 2013;1-7.
- Sekulic D, Males B, Miletic D. Navy recruits: fitness measuring, validation, and norming. *Mil Med* 2006;171:749-52.
- “President’s Council on Physical Fitness and Sports Definitions for Health, Fitness, and Physical Activity”. Archived from the original on August 25, 2012.
- Kim BR, Han EY, Joo SJ, Kim SY, Yoon HM. Cardiovascular fitness as a predictor of functional recovery in subacute stroke patients. *Disabil Rehabil* 2013 [Epub ahead of print].
- Mirandola D, Miccinesi G, Muraca MG, Sgambati E, Monaci M, Marini M. Evidence for adapted physical activity as an effective intervention for upper limb mobility and quality of life in breast cancer survivors. *J Phys Act Health* 2013 [Epub ahead of print].
- Coombes JS, Law J, Lancashire B, Fassett RG. “Exercise is medicine”: curbing the burden of chronic disease and physical inactivity. *Asia Pac J Public Health* 2013 [Epub ahead of print].
- “US Department of Health and Human Services Presentation: Physical Activity Fundamental to Preventing Disease [Internet]. [cited 2013 July 3]. Available at: <http://aspe.hhs.gov/health/reports/physicalactivity/June 2002>
- Exercise also help people to rest and sleep better. Several studies indicate that to stay healthy it is important to engage in regular physical activity.
- “How much physical activity do adults need? 2008 Physical Activity 10. Shrestha M, Combest T, Fonda SJ, Alfonso A, Guerrero A. Effect of an accelerometer on body weight and fitness in overweight and obese active duty soldiers. *Mil Med* 2013;178:82-7.
- Nikolaïdis PT. Physical fitness is inversely related with body mass index and body fat percentage in soccer players aged 16-18 years. *Med Pregl* 2012;65:470-5.
- Heinrich KM, Spencer V, Fehl N, Poston WS. Mission essential fitness: comparison of functional circuit training to traditional Army physical training for active duty military. *Mil Med* 2012;177:1125-30.
- Wyss T, Von Vigier RO, Frey F, Mäder U. The Swiss Army physical fitness test battery predicts risk of overuse injuries among recruits. *J Sports Med Phys Fitness* 2012;52:513-21.
- Sharp MA, Knapik JJ, Walker LA, Burrell L, Frykman PN, Darakjy SS *et al.* Physical fitness and body composition after a 9-month deployment to Afghanistan. *Med Sci Sports Exerc* 2008;40:1687-92.
- Vanderburgh PM. Occupational relevance and body mass bias in military physical fitness tests. *Med Sci Sports Exerc* 2008;40:1538-45.
- Thomas DQ, Lumpp SA, Schreiber JA, Keith JA. Physical fitness profile of Army ROTC cadets. *J Strength Cond Res* 2004;18:904-7.
- Zivotic-Vanović M, Dimitrijević B, Zivanić S, Mijić R. Evaluation of physical fitness in military personnel using the 1600 meter running test]. *Vojnosanit Pregl* 1995;52:443-9
- O’Connor JS, Bahrke MS, Tetu RG. 1988 Active Army Physical Fitness Survey. *Mil Med* 1990;155:579-85.
- Knapik J. The Army Physical Fitness Test (APFT): a review of the literature. *Mil Med* 1989;154:326-9.
- Guidelines for Americans [Internet]. Available at: <http://www.cdc.gov/physicalactivity/everyone/guidelines/adults.html>
- Kawano H, Iemitsu M, Gando Y, Ishijima T, Asaka M, Aoyama T *et al.* Habitual rowing exercise is associated with high physical fitness without affecting arterial stiffness in older men. *J Sports Sci* 2012;30:241-6.
- Traustadóttir T, Davies SS, Su Y, Choi L, Brown-Borg HM, Roberts LJ 2nd *et al.* Oxidative stress in older adults: effects of physical fitness. *Age (Dordr)* 2012;34:969-82.
- Silva LA, Tromm CB, Da Rosa G, Bom K, Luciano TF, Tuon T *et al.* Creatine supplementation does not decrease oxidative stress and inflammation in skeletal muscle after eccentric exercise. *J Sports Sci* 2013 [Epub ahead of print].
- Jendzjowsky NG, Delorey DS. Acute superoxide scavenging reduces sympathetic vasoconstrictor responsiveness in short-term exercise trained rats. *J Appl Physiol* 2013 [Epub ahead of print].
- Gąsiorowski A, Dutkiewicz J. Weight training and appropriate nutrient supplementation as an alternative method to pharmacological treatment in rehabilitation of post-myocardial infarction patients. *Ann Agric Environ Med* 2012;19:333-8.
- Bentley DJ, Dank S, Coupland R, Midgley A, Spence I. Acute antioxidant supplementation improves endurance performance in trained athletes. *Res Sports Med* 2012;20:1-12.
- Belcaro G, Cesarone MR, Dugall M, Hosoi M, Ippolito E, Bavera P *et al.* Investigation of Pycnogenol® in combination with coenzyme Q10 in heart failure patients (NYHA II/III). *Panminerva Med* 2010;52(2 Suppl 1):21-5.
- Vinciguerra G, Belcaro G, Cesarone MR, Rohdewald P, Stuard S, Ricci A *et al.* Cramps and muscular pain: prevention with pycnogenol in normal subjects, venous patients, athletes, claudicants and in diabetic microangiopathy. *Angiology* 2006;57:331-9.
- Belcaro G, Cesarone MR, Rohdewald P, Ricci A, Ippolito E, Dugall M *et al.* Prevention of venous thrombosis and thrombophlebitis in long-haul flights with pycnogenol. *Clin Appl Thromb Hemost* 2004;10:373-7.
- Tarnopolsky MA, Safdar A. The potential benefits of creatine and conjugated linoleic acid as adjuncts to resistance training in older adults. *Appl Physiol Nutr Metab* 2008;33:213-27.
- Galán AI, Palacios E, Ruiz F, Díez A, Arji M, Almar M *et al.* Exercise, oxidative stress and risk of cardiovascular disease in the elderly. Protective role of antioxidant functional foods. *Biofactors* 2006;27:167-83.
- McAnulty SR, McAnulty LS, Nieman DC, Morrow JD, Shooter LA, Holmes S *et al.* Effect of alpha-tocopherol supplementation on plasma homocysteine and oxidative stress in highly trained athletes before and after exhaustive exercise. *J Nutr Biochem* 2005;16:530-7.
- Belcaro G, Cornelli U, Dugall M, Luzzi R, Hosoi M, Ledda A *et al.* Panel 2013 supplements and greendrugs studies; new rules 2013. London and Annecy Panel; 2013.
- Belcaro G, Nicolaides AN. A new role for natural drugs in cardiovascular medicine. *Angiology* 2001;52(Suppl 2):S1.
- Cesarone MR, Belcaro G, Rohdewald P, Pellegrini L, Ledda A, Vinciguerra G *et al.* Improvement of signs and symptoms of chronic venous insufficiency and microangiopathy with Pycnogenol: a prospective, controlled study. *Phytomedicine* 2010;17:835-9.
- Cesarone MR, Belcaro G, Rohdewald P, Pellegrini L, Ledda A, Vinciguerra G *et al.* Rapid relief of signs/symptoms in chronic

- venous microangiopathy with Pycnogenol: a prospective, controlled study. *Angiology* 2006;57:569-76. Erratum in: *Angiology* 2008;59:385.
37. Belcaro G, Cesarone MR, Ricci A, Cornelli U, Rohdewald P, Ledda A *et al.* Control of edema in hypertensive subjects treated with calcium antagonist (nifedipine) or angiotensin-converting enzyme inhibitors with Pycnogenol. *Clin Appl Thromb Hemost* 2006;12:440.
 38. Cesarone MR, Belcaro G, Nicolaidis AN, Ricci A, Geroulakos G, Ippolito E *et al.* Prevention of venous thrombosis in long-haul flights with Flite Tabs: the LONFLIT-FLITE randomized, controlled trial. *Angiology* 2003;54:531-9.
 39. Belcaro G, Cesarone MR, Errichi BM, Ledda A, Di Renzo A, Stuard S *et al.* Venous ulcers: microcirculatory improvement and faster healing with local use of Pycnogenol. *Angiology* 2005;56: 699-705.
 40. Errichi BM, Belcaro G, Hosoi M, Cesarone MR, Dugall M, Feragalli B *et al.* Prevention of post thrombotic syndrome with Pycnogenol® in a twelve month study. *Panminerva Med* 2011;53(3 Suppl 1):21-7.
 41. Nuzum DS, Gebru TT, Kouzi SA. Pycnogenol for chronic venous insufficiency. *Am J Health Syst Pharm* 2011;68:1589-90, 1599-601.
 42. Cornelli U, Belcaro G, Ledda A, Feragalli B. Activity of some physiological modulators in reducing the side effects of levothyroxine in patients suffering from primary hypothyroidism. *Panminerva Med* 2011;53(3 Suppl 1):99-103.
 43. Cornelli U, Belcaro G, Ledda A, Feragalli B. Oxidative stress following administration of levothyroxine in subjects suffering from primary hypothyroidism. *Panminerva Med* 2011;53(3 Suppl 1):95-8.
 44. Cesarone MR, Belcaro G, Carratelli M, Cornelli U, De Sanctis MT, Incandela L *et al.* A simple test to monitor oxidative stress. *Int Angiol* 1999;18:127-30.
 45. Cornelli U. Treatment of Alzheimer's disease with a cholinesterase inhibitor combined with antioxidants. *Neurodegener Dis* 2010;7:193-202.
 46. Campise M, Bamonti F, Novembrino C, Ippolito S, Tarantino A, Cornelli U *et al.* Oxidative stress in kidney transplant patients. *Transplantation* 2003;76:1474-8.
 47. Incandela L, Belcaro G, Cesarone MR, De Sanctis MT, Griffin M, Cacchio M *et al.* Oxygen-free radical decrease in hypertensive patients treated with lercanidipine. *Int Angiol* 2001;20:136-40.
 48. Cornelli U. Antioxidant use in nutraceuticals. *Clin Dermatol* 2009;27:175-94.
 49. Freedman A. *Statistical models, theory and practice.* Cambridge: Cambridge University Press; 2009.
 50. Bottari A, Belcaro G, Ledda A, Cesarone MR, Vinciguerra G, Di Renzo A *et al.* Kidney function in metabolic syndrome may be improved with Pycnogenol®. *Panminerva Med* 2010;52(2 Suppl 1):27-32.
 51. Cesarone MR, Belcaro G, Stuart S. Kidney flow and function in hypertension: Protective effects of Pycnogenol in hypertensive subjects – A controlled study. *J. of cardiovascular pharmacology & Therapeutics* 2010;15:41-46.
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