WETLANDS

Volume 35 · Number 6 · December 2015

ORIGINAL RESEARCH

Instructions for Authors for *Wetlands* are available at http://www.springer.com/13157.

JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY

J. Agric. Food Chem. 2006, 54, 2891−2896 2891

Salicylic Acid Content of Spices and Its Implications

JOHN R. PATERSON,[†,⊥] RAJEEV SRIVASTAVA,[†,§] GWEN J. BAXTER,*[,†] ALAN B. GRAHAM,[#] AND JAMES R. LAWRENCE[†]

Dumfries and Galloway Royal Infirmary, Dumfries DG1 4AP, Scotland, U.K., and University of Strathclyde, Glasgow G4 0NR, Scotland, U.K.

This work was done to determine the salicylate content of a variety of commonly used spices and to assess whether this potential dietary source of salicylate was bioavailable. Spices, Indian cooked dishes, and blood and urine samples taken after ingestion of a test meal were investigated for their salicylate content using high-performance liquid chromatography with electrochemical detection. The serum salicylic acid concentrations in samples from villagers in southern India were also measured and have been compared with typical European values. Salicylic acid was determined in all spices (up to 1.5 wt %) and cooked dishes. The salicylate content of blood and urine was shown to increase following consumption of the meal, indicating that this dietary source of salicylic acid was bioavailable. Salicylic acid levels in the serum from rural Indians were significantly (median almost 3-fold) higher than values previously measured in Western vegetarians. Chemoprotective aspirin is rapidly hydrolyzed to salicylic acid, and this phytochemical may contribute to the low cancer incidence in rural India.

KEYWORDS: Salicylic acid; spices; salicylates; chemoprotection; colorectal cancer

INTRODUCTION

Many investigations of the relationships among health, disease, and dietary factors have indicated that diets containing a substantial proportion of foodstuffs derived from plants may provide protection against a variety of cancers (*1*). Eastwood (*2*) speculated that secondary metabolites of plants, such as alkaloids and phenolic substances, may contribute to this benefit. Aspirin is used widely to treat cardiovascular disease, and it is manufactured, sold, and taken on a massive scale for the analgesic, antipyretic, and anti-inflammatory actions that its consumption produces (*3*). After ingestion, aspirin undergoes extremely rapid hydrolysis ($t_{1/2}$ = 20 min) to generate salicylic acid ($t_{1/2}$ = 2−4 h), and it is this phenolic acid that brings about its persistent anti-inflammatory effect (*4*). People who had taken aspirin regularly over long periods and who, therefore, have been exposed chronically to the effects of salicylic acid experienced a greatly reduced risk of developing atherosclerosis and colorectal and other soft tissue cancers (*5*−*7*). Moreover, several randomized controlled trials (*8*−*10*) have now shown that regular intake of low-dose aspirin decreases the risk of recurrent colonic adenoma formation in predisposed patients.

Salicylic acid and two of its hydroxylated metabolites were found in the serum of people who had not taken salicylate drugs (*11*). Salicylic acid and, in much higher concentration, its metabolite, salicyluric acid, were also present in the urine of these people, and it was suggested that these compounds are of dietary origin (*12*). Significantly higher concentrations of salicylic acid were found in the serum of vegetarians who had not taken salicylate drugs than in the serum of the people with an unrestricted diet, and the range of concentrations observed in the serum of vegetarians overlapped with that of patients receiving 75 mg of aspirin (acetylsalicylic acid) daily. In addition, larger amounts of salicyluric acid were excreted in the urine of vegetarians than in that of nonvegetarians (*13*). Although the amount of salicylic acid in foodstuffs is controversial (*14*−*17*; see also the Discussion), these findings strongly suggest that foodstuffs derived from plants are major dietary sources of this phenolic acid.

Colorectal cancer is a leading cause of death due to cancer in Western populations (*18*). However, the incidence of this form of cancer is very low in India, particularly in rural parts of the country (*19*, *20*). The population of rural India, with an incidence of colorectal cancer which is one of the lowest in the world (*21*), has a diet that could be extremely rich in salicylic acid. It contains substantial amounts of fruits, vegetables, and cereals flavored with large quantities of herbs and spices. Swain et al. (*14*) have reported that certain herbs and spices are rich in salicylic acid and other salicylates. Most of the foodstuffs consumed in rural India are, moreover, likely to have been prepared from plants that were reared without protection from pesticides, herbicides, and fungicides. Because salicylic acid is a defense hormone of plants, the concentration of which is increased when plants become stressed or infected (*22*−*24*), the plants from which this population's foodstuffs were prepared may have higher contents of salicylic acid than those cultivated

* Author to whom correspondence should be addressed [telephone +44-(0)1387241165; fax +44(0)1387241825; e-mail gwen.baxter@nhs.net].
† Dumfries and Galloway Royal Infirmary.
⊥ Deceased.
§ Present address: Ninewells Hospital and Medical School, Dundee DD1 9SY, Scotland.
# Univerisity of Strathclyde (retired).

10.1021/jf058158w CCC: $33.50
Published on Web 03/21/2006

in the West. This proposition is supported by the observation that soups prepared from vegetables that had been grown "organically" had significantly higher contents of salicylic acid than soups prepared from conventially grown ingredients (*25*).

A substantial intake of salicylic acid by rural Indians might account for their very low incidence of colorectal cancer. To examine this hypothesis we set out to (a) establish whether salicylic acid was present in a variety of spices that are used frequently and in considerable amounts in Indian cookery, (b) determine the content of salicylates in these materials, (c) determine the content of salicylates in three prepared Indian cooked dishes, (d) investigate, in a pilot study, whether the salicylates present in the cooked food became bioavailable to man and were absorbed, and (e) determine the concentrations of salicylic acid present in the serum of native Indians who live in a rural area near Chennai (Madras).

MATERIALS AND METHODS

Spice samples were purchased from a retailer of foodstuffs supplying the Indian/Pakistani community in Glasgow or imported directly from Dehli, donated by Dr. R. Srivastava. Samples of a few spices were also purchased from a "health food" retailer in Glasgow. Cooked vegetable dishes that had been prepared according to typical Indian recipes were purchased from a local restaurant. Additional ethical approval was obtained to examine samples of blood that had been obtained from 21 native Indians who had not taken salicylate drugs (10 males, 11 females; median age = 32 years). These volunteers live in a rural area near Chennai and have a diet of locally grown vegetables, grains, and pulses flavored with spices and herbs; they were originally recruited for another study in India (*26*) as representative of that community for health, lifestyle, and nutritional status.

Determination of Salicylic Acid. The content of salicylic acid in spices, cooked vegetable dishes, and serum was determined by using the method of Paterson et al. (*11*). The concentrations of the phenolic acid and salicyluric acid in urine were determined according to the method of Baxter et al. (*12*). For the determination of "free" salicylic acid the following process of extraction was employed. Finely powdered spices (50 mg) and portions of urine (0.5 mL) and serum (0.5 mL) were acidified with 1 mol/L HCl so that they contained finally a concentration of 0.1 mol/L. The acidified mixtures were extracted immediately with two 2 mL volumes of ethyl acetate.

Salicylates in plants are present in three principal forms, the "free" phenolic acid and its carboxylic esters and phenolic glycosides (*22*). For the determination of "total" salicylates in food and spices, the salicylic acid extracted from the materials after their treatment with alkali was determined. Powdered spices (50 mg) were suspended in 2 mL of 2.5 mol/L NaOH. To 1 g of homogenized cooked food was added 2 mL of 2.5 mol/L NaOH. After 24 h at room temperature, 1 mL of 5.3 mol/L HCl was added to the alkaline mixtures so that they contained finally a concentration of HCl of 0.1 mol/L. The acidified mixtures then were extracted with two 3 mL portions of ethyl acetate.

Confirmation of the Identity of Salicylic Acid. After treatment of powdered cumin, paprika, and turmeric (50 mg) with alkali (2 mL of 2.5 mol/L NaOH), acidification of the mixtures, and extraction with ethyl acetate, the acidic and neutral hydrophobic substances removed were separated by HPLC, as described by Paterson et al. (*11*), but with the detector switched off. The compound eluted at the retention time of salicylic acid was removed from the eluates, treated with a solution of acetyl chloride in methanol to achieve methylation, and examined by using gas chromatography–mass spectrometry (GC-MS) (*27*).

Assessment of Bioavailability. Blood and urine samples were obtained from a human volunteer (Caucasian male, aged 46 years) who had not taken salicylate drugs and who had fasted for 10 h. The volunteer then consumed 545.3 g of a cooked vegetable dish that the aliquot assay showed to contain 94.03 mg of total salicylates. At intervals of 1 h, blood was removed, and the urine he excreted was collected at ~2 hourly intervals over the next 6.5 h. The concentrations of salicylic acid in the blood and of salicylic acid and salicyluric acid in the urine were determined as described above.

Table 1. GC-MS of Salicylic Acid Treated with Acetyl Chloride in Methanol and a Compound Extracted from Cumin, Paprika, and Turmeric Isolated by HPLC and Treated with Acetyl Chloride in Methanol

		principal ions in spectrum	
compound	t_R (min)	mass[a]	relative abundance
salicylic acid	7.35	65	39
		92	82
		120	100
		152*	36
substance extracted from cumin	7.45	65	36
		92	82
		120	100
		152*	37
substance extracted from paprika	7.48	65	36
		92	82
		120	100
		152*	35
substance extracted from turmeric	7.45	65	38
		92	81
		120	100
		152*	36

[a] Asterisks indicate the molecular ion. The molecular mass of methyl salicylate is 152.1.

RESULTS

Our methods for the electrochemical (oxidative) determination of salicylic acid in urine (*12*) and in food, spices, and blood (*11*) rely upon separating by HPLC (with programs of stepwise elution) the hydrophobic substances that were extracted into ethyl acetate from strongly acidic aqueous phases. The substance extracted from cumin, paprika, and turmeric that was eluted at the retention time of salicylic acid was removed from the eluates, treated with an esterifying reagent, and examined by using GC-MS. The derivative formed had a gas chromatographic retention time and a mass spectrum identical to those of the methyl ester of salicylic acid (**Table 1**).

The contents of total salicylates and salicylic acid in the spices examined are shown in **Table 2**. For comparison, the contents of these substances reported by previous authors are also included. Our results are distinctly different from most of those reported in the past, and they show very clearly that the typical diet of a rural Indian potentially contains a very large amount of salicylates which could be converted into salicylic acid in vivo. Red chilli powder, paprika, and turmeric contained total salicylates in excess of 0.1% (by weight), and cumin, an ingredient used in very large amounts in Indian cookery, had a content of >1.5% (by weight), most of which was the phenolic acid itself. In addition, the contents of salicylic acid in several batches of cumin, also obtained from the retailer supplying the Glasgow Asian community, were estimated by using a much less sensitive and less specific colorimetric procedure following thin-layer chromatography (TLC) separation. The substances extracted into ethyl acetate from TLC-separated suspensions of cumin (100 mg) in 1 mol/L HCl were redissolved in 1 mL of 1% $NaHCO_3$, and portions of these solutions were treated with a reagent containing Fe(III) in dilute HCl. The absorbance of the colored solutions produced was measured at 527 nm [λ_{max} of the Fe(III)/salicylic acid complex]. These contents ranged from 1084 to 1521 mg of salicylic acid/100 g of cumin.

The contents of total salicylates in three conventionally prepared vegetable dishes were determined. One dish (500 g of food) that was prepared according to a Madras style contained 20.3 mg; another (549 g of food), cooked according to a spicier

Table 2. Content of Total Salicylates (TS) and Salicylic Acid (SA) in Various Spices (Milligrams per 100 g)

	source 1[a]		source 2[b]		reported previously[c]	reported previously[d]		reported previously[e]	reported previously[f]
spice	TS	SA	TS	SA	TS	TS	SA	TS	TS
asafoetida	3.8	0.5							
cardamom (black)	27.0	<0.1							
cardamom (green)	13.2	<0.1							
chilli powder (red)	146.6	3.0							
cinnamon	64.2	4.7	12.0	2.9	15.20	1.0		12.20	2.4
cloves	2.5	0.4			5.74	2.0		trace	
coriander	2.7	0.8			0.20	0.1	trace		
cumin	1629.4	1474.7	980.0	744.9	45.00				
fennel	2.0	<0.1			0.80			0.048	
fenugreek	0.1	<0.1			12.20			0.298	
garlic	5.6	<0.1			0.10			0.305	
ginger	3.5	0.1			4.50				
mustard	26.2	5.2			26.00	0.4	0.2		trace
paprika	104.3	3.0	104.7	10.8	203.00	0.7			0.3
pepper seeds (black)	9.0	7.3			6.20	0.3			0.3
tamarind	9.6	1.1							
turmeric	350.5	23.3	288.9	15.3	76.40	1.7			

[a] Source 1, retailer supplying the Indian/Pakistani community in Glasgow; asafoetida, fennel, and tamarind were imported from India. [b] Source 2, health food shop. [c] Swain et al. (*14*). [d] Herrmann (*33*). [e] Variyar and Bandyopadhyay (*16*). [f] Venema et al. (*15*).

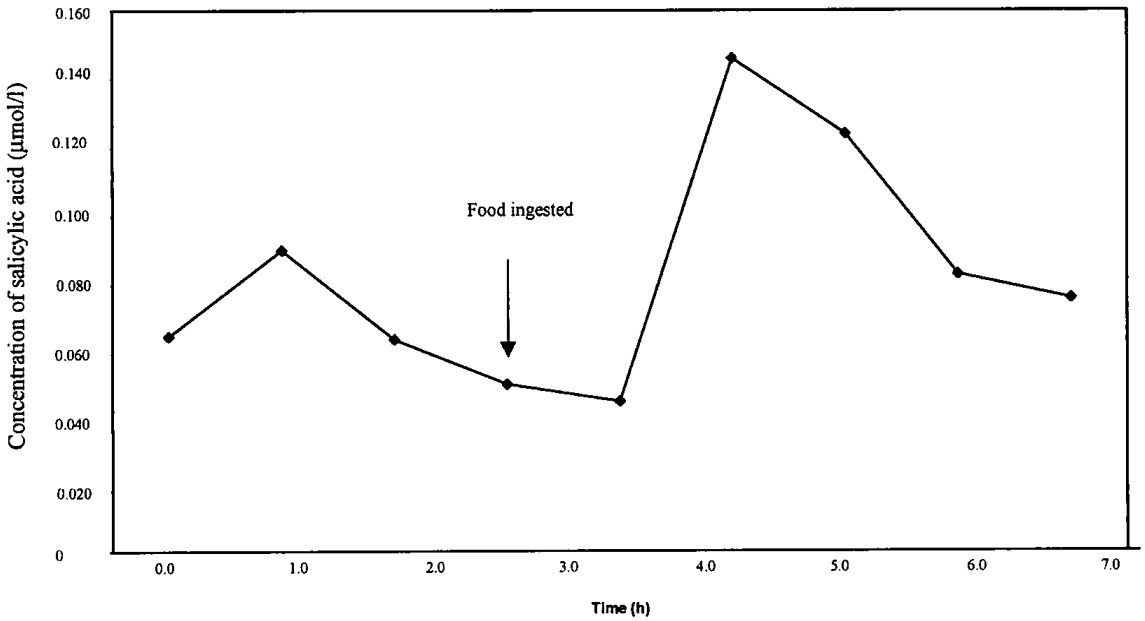

Figure 1. Concentration of salicylic acid in the serum of a volunteer before and after consumption of food rich in salicylates.

Vindaloo recipe, contained 85.9 mg. To determine if the salicylates in this type of cooked food were bioavailable, a volunteer consumed 545.3 g of vegetable Vindaloo in a meal that contained 94.03 mg of total salicylates. Within 1 h of consuming the food, the concentration of salicylic acid in the volunteer's serum increased rapidly and reached a maximum value after ~1.5 h (**Figure 1**). During the following 1.5 h the concentration of salicylic acid in the serum declined steeply and returned to the range of concentrations encountered prior to dietary exposure to the salicylates ~5 h after consumption of the food (**Figure 1**). Within 1.5 h of consumption of the food, when the concentration of salicylic acid in serum was near its maximum, salicyluric acid, derived from the salicylates in the food, began to appear in the urine (**Figure 2**). During the following 4 h the amount of the conjugated metabolite excreted increased steadily, and the rate of its excretion had not returned to the value observed prior to consumption of the food even after 6.5 h. Salicylic acid derived from the food ingested appeared in the urine when the rate of excretion of salicyluric acid was at its highest, and it was elevated above the rate of excretion prior to exposure even after 6.5 h. From the cumulative amounts of salicylic and salicyluric acids excreted that were in excess of those predicted from the rates of excretion prior to the test meal, it was calculated that at least 3% of the salicylates in the food had become bioavailable and been absorbed.

The concentrations of salicylic acid found in the serum of individual native rural Indians were not distributed normally; the median values and the ranges found are displayed in **Table 3**. Included, for comparison, are the median concentrations and ranges of the phenolic acid present in the serum of a group of vegetarians of predominantly European descent living in Dumfries and Galloway and a group of nonvegetarians from Dumfries we reported earlier (*28*). The median concentration in the serum of the Indians was significantly higher (~2.5–3.5-fold higher) than those found in the sera of the other groups ($p < 0.001$ against the vegetarians and $p < 0.001$ against the nonvegetarians; Mann–Whitney U tests).

DISCUSSION

In recent years claims have been made for many components of plant cells as being primarily responsible for the health-giving properties of a diet rich in plant foods. The evidence presented

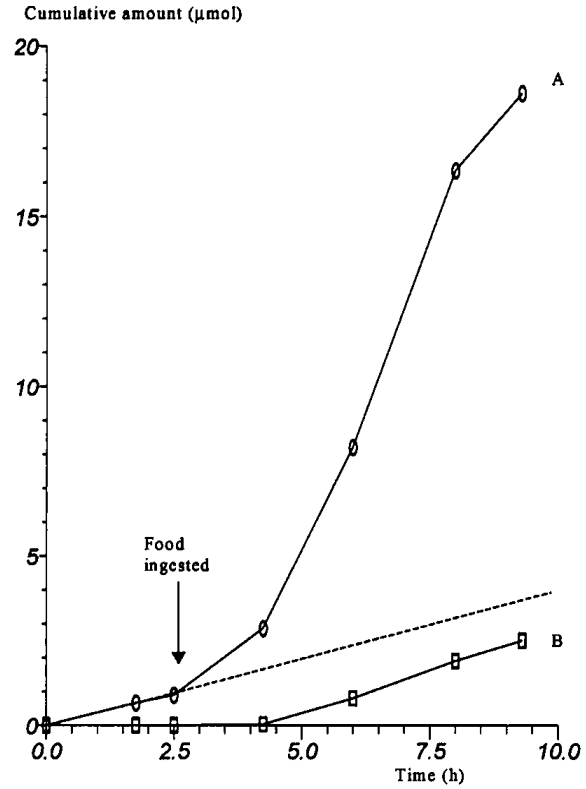

Figure 2. Amount of salicylic and salicyluric acids excreted in the urine of a volunteer before and after consumption of food rich in salicylates.

Table 3. Concentration of Salicylic Acid in the Serum of Various Groups of People[a]

group	no. in group	concn of SA (μmol/L) median	concn of SA (μmol/L) range
South Indians[b]	21	0.263	0.05–0.64
vegetarians[c]	37	0.110	0.04–2.47
nonvegetarians[d]	39	0.070	0.02–0.20
aspirin takers[e] (75 mg/day)	14	10.030	0.23–25.40

[a] The values observed for comparison vegetarians, nonvegetarians, and the people receiving aspirin were determined by Blacklock et al. (*28*). Concentration in the serum of vegetarians was significantly higher than that in serum of nonvegetarians ($p < 0.0001$). [b] Native rural Indians, non-aspirin takers, traditional Indian diet (10 males, 11 females, median age = 32 years). [c] Buddist monks in retreat at Samye Ling Monastry, Eskdalemuir, southwestern Scotland, non-aspirin takers, strict vegetarian diet (24 males, 13 females, median age = 41.7 years). [d] General population of southwestern Scotland, non-aspirin takers, unrestricted diet (21 males, 18 females, median age = 40.5 years). [e] Patients, taking aspirin, drawn from General Practitioner's lists in southwestern Scotland, unrestricted diet (7 males, 7 females, median age = 58.9 years).

in this paper does, taken together with the published efficacy and accepted lability (*29*) of its acetyl ester, aspirin, lay the foundation for salicylic acid as an important phytochemical. We suggest it may well contribute to the low incidence of colon cancer in subjects with a predominantly vegetarian diet flavored with regularly used spices.

Our results confirm the presence of, and enhance prior estimates of, salicylic acid content in a variety of frequently, often copiously, used spices. Sampled cooked dishes were shown to contain pharmacological amounts of salicylic acid, a proportion of which was bioavailable as shown by the significant rise in serum concentration (peak concentration more than double baseline) and the increased cumulative urinary metabolite excretion (~20-fold increase) in the hours after a test meal.

Most suggestive, in relation to results of prospective intervention studies using low-dose aspirin (*5*−*7*), is the significantly higher median serum salicylic acid concentration in the small group of rural Indians compared with published results in subjects *not* taking aspirin. The median level determined was more than double that observed in a Western vegetarian population whose results, we have previously shown (*28*), overlapped significantly with those from patients on low-dose aspirin.

The major strength of the work presented here is the robustness of the extraction processes and assays (*11*, *12*, *25*) used to measure salicylic acid and its metabolites. One potential weakness is that only three cooked meals were analyzed and that salicylic acid levels after only one test meal are shown. However, published results show salicylic acid absorption from other food sources with known salicylic acid content (*30*, *31*), albeit with the anticipated low bioavailability from a mixed diet (*31*).

Our results on the salicylic acid content of spices are comparable, where comparison is possible, with those of Swain et al. (*14*) save in the cases of cumin and turmeric. Different species of the plants might help to explain the very high content of salicylic acid in our cumin and turmeric, but the enhanced recovery of total salicylate from the spice by our methodology is the likely major reason for the discrepancy in the case of turmeric. The acknowledged (*14*) possible imperfect separation in Swain's chromatography system should, in theory, have enhanced their estimate for cumin given the use of a relatively nonspecific UV detector. Although it might appear to be unlikely that the difference in estimates for cumin could arise from extraction (as 80% efficiency was reported for added salicylic acid in both methods), Swain used 50 g of material and 200 mL of diethyl ether for the extraction step. Therefore, the >30-fold amount of material versus organic solvent may well be a factor in explaining the different estimates. The entirely different separation/detection system also reported here—using TLC and colorimetric detection—gave a salicylic acid content result for cumin in agreement with our more sensitive and specific assay, which was itself corroborated by the GC-MS data. Another factor that may contribute to the difference between Swain's and our own estimate for cumin is the likelihood of interbatch variability in the salicylic acid content of the spice.

Whereas our results for spices are, cumin apart, compatible with those reported by Swain (*14*), they are, where comparison is possible, considerably higher than reported by other workers (*15*−*17*) who used fluorescence detection after HPLC based on the method of Venema (*15*). That method should, from published details, achieve reasonably satisfactory chromatographic separation of salicylic acid, but we suspect the isocratic elution used led to potential coelution of compounds that interfered by quenching to decrease the intensity of fluorescence emission with the sensitivity of the fluoresence detector used. It is revealing that Janssen's (*31*) estimate of dietary salicylate intake from salicyluric acid excretion was compatible only with Swain's (*14*) data on food content. Although Janssen emphasizes, in discussion, the low overall bioavailability set against the total estimated salicylate content of diet, that finding is not unexpected from whole food with the salicylic acid contained in complex matrices. There is, it is well recognized (*29*), great variability in the extent to which aspirin is absorbed: the bioavailability of salicylic acid from food sources is likely to be much more variable still.

We have established that salicylic acid is present in spices and in a cooked meal prepared using a mixture of the same and that this salicylic acid is absorbed, but the question arises whether the extent of its bioavailability is sufficent to provide a chemoprotective effect against colorectal cancer. Giovannucci

(*32*) concluded low-dose (81 mg/day) aspirin taken over one or two decades was sufficient, and chronic exposure to aspirin 75 mg per day [containing 56 mg of salicylic acid at ~60% bioavailability (*29*)] has been shown to provide protection against colorectal cancer. More recently, reported prospective intervention studies using aspirin (*8*−*10*) at 81−325 mg/day showed efficacy in the prevention of colonic adenoma recurrence. The threshold dose for efficacy is not yet known, but in vitro very low concentrations of salicylic acid suppressed Cox 2 transcription (*4*) and there was a distinct overlap in serum salicylic acid levels from patients on 75 mg of aspirin/day and vegetarians (*28*). Approximately a fourth of the vegetarians in that study had serum salicylic acid concentrations above the lowest level observed in the aspirin-taking patients. In keeping with the saturable conjugation of salicylic acid, there were comparable urine levels of that compound in aspirin takers and vegetarians (*13*). The absence of a dose−response correlation in one prospective study using aspirin (*8*) led to the suggestion that a low threshold dose may be required for chemoprotection. It is not inconceivable, moreover, that luminal concentrations of salicylic acid pertaining during food digestion/absorption will be relevant to the chemoprotective action of salicylic acid in colon cancer.

It is, we think, increasingly unlikely that salicylic acid levels are simply a marker for plant food intake. Two major pieces of work are required to further advance our hypothesis that salicylic acid is the link between aspirin, diet, and the prevention of colorectal cancer (*34*). The efficacy of feeding salicylic acid to animals at risk of colon cancer and related pathology needs to be established; preliminary results of this approach are encouraging. Finally, it is necessary to show that in individuals salicylic acid exposure predetermines their future risk of colon cancer.

LITERATURE CITED

(1) Schrienmachers, D. M.; Everson, R. B. Aspirin use and lung, colon, and breast cancer incidence in a prospective study. *Epidemiology* **1994**, *5*, 138−146.

(2) Eastwood, M. A. A molecular biological basis for the nutritional and pharmacological benefits of dietary plants. *Q. J. Med.* **2001**, *94*, 45−48.

(3) Sneader, W. The discovery of aspirin. *Pharm. J.* **1997**, *259*, 614−617.

(4) Xu, X.-M.; Sansores-Garcia, L.; Chen, X.-M.; et al. Suppression of inducible cyclooxygenase gene transcription by aspirin and sodium salicylate. *Proc. Natl. Acad. Sci. U.S.A.* **1999**, *96*, 5292−5297.

(5) Hass, W. K.; Easton, J. D.; Adams, H. P.; et al. A randomised trial of ticlopidine hydrochloride with aspirin for the prevention of stroke in high-risk patients. *New Engl. J. Med.* **1989**, *321*, 501−507.

(6) Ridker, P. M.; Cushman, M.; Stamper, M. J.; et al. Inflammation, aspirin and the risk of cardiovascular disease in apparently healthy men. *New Engl. J. Med.* **1997**, *336*, 973−979.

(7) The Multicenter Salsalate/Aspirin Comparison Study Group. Does the acetyl group of aspirin contribute to the anti-inflammatory efficacy of salicylic acid in the treatment of rheumatoid arthritis? *J. Rheumatol.* **1989**, *16*, 321−327.

(8) Baron, J. A.; Cole, B. F.; Sandler, R. S.; et al. A randomised trial of aspirin to prevent colorectal adenomas. *New Engl. J. Med.* **2003**, *348*, 891−899.

(9) Sandler, R. F.; Halabi, S.; Baron, J. A.; et al. A randomised trial of aspirin to prevent colorectal adenomas in patients with previous colorectal cancer. *New Engl. J. Med.* **2003**, *348*, 883−889.

(10) Benamouzig, R.; Deyra, J.; Martin, A.; et al. Daily soluble aspirin and prevention of colorectal adenoma recurrence: one year results of the APACC trial. *Gastroenterology* **2003**, *125*, 328−336.

(11) Paterson, J. R.; Blacklock, C.; Campbell, G.; et al. The identification of salicylates as normal constituents of serum: a link between diet and health? *J. Clin. Pathol.* **1998**, *51*, 501−505.

(12) Baxter, G. J.; Lawrence, J. R.; Graham, A. B.; et al. Identification and determination of salicylic acid and salicyluric acid in urine of people not taking salicylate drugs. *Ann. Clin. Biochem.* **2002**, *39*, 50−55.

(13) Lawrence, J. R.; Peter, R.; Baxter, G. J.; et al. Urinary excretion of salicyluric and salicylic acids by non-vegetarians, vegetarians and patients taking low dose aspirin. *J. Clin. Pathol.* **2003**, *56*, 651−653.

(14) Swain, R.; Dutton, S. P.; Truswell, A. S. Salicylates in foods *J. Am. Diet. Assoc.* **1985**, *85*, 950−960.

(15) Venema, D. P.; Hollman, P. C. H.; Janssen, P. L. T. M. K.; et al. Determination of acetylsalicylic and salicylic acid in foods, using HPLC with fluorescence detection. *J. Agric. Food Chem.* **1996**, *44*, 1762−1767.

(16) Variyar, P. S.; Bandyopadhyay, C. Estimation of phenolic acids in cinnamon, clove, cardamon, nutmeg and mace by high performance liquid chromatography. *J. Spices Aromatic Crops* **1995**, *4*, 129−134.

(17) Robertson, G. I.; Kermode, W. J. Salicylic acid in fresh and canned fruit and vegetables. *J. Sci. Food Agric.* **1981**, 833−836.

(18) World Health Organisation. *The World Health Report; Health Education: a Programme Review*; report by the Director-General to the 53rd session of the Executive Board; WHO: Geneva, Switzerland, 1997.

(19) Jussawala, D. J.; Desphande, V. A.; Haenszel, W.; et al. Differences observed in the site incidence of cancer between the Parsi community and the total population of Greater Bombay: a typical appraisal. *Br. J. Cancer* **1997**, *24*, 56−66.

(20) Mohandas, K. M.; Desai, D. Epidemiology of digestive tract cancers in India V. Large and small bowel. *Indian J. Gastroenterol.* **1999**, *18*, 118−121.

(21) World Cancer Research Fund in association with the American Institute for Cancer Research. *Cancers, Nutrition and Food: Colon and Rectum. Food, Nutrition and the Prevention of Cancer: A Global Perspective*; 1997; pp 218−251.

(22) Chadha, K. C.; Brown, S. A. Biosynthesis of phenolic acids in tomato infected with *Agrobacterium tumefaciens*. *Can. J. Bot.* **1974**, *52*, 2041−2046.

(23) Dangi, J. Plants just say NO to pathogens. *Nature* **1998**, *394*, 525−527.

(24) Matsuki, M. Regulation of plant phenolic synthesis: from biochemistry to ecology and evolution. *Aust. J. Bot.* **1996**, *44*, 613−634.

(25) Baxter, G. J.; Graham, A. B.; Lawrence, J. R.; et al. Salicylic acid in soups prepared from organically and non-organically grown vegetables. *Eur. J. Nutr.* **2001**, *40*, 289−292.

(26) McCreadie, R. G.; Thara, R.; Srinivasan, T. N.; et al. Spontaneous dyskinesia in first-degree relatives of chronically ill, never-treated people with schizophrenia. *Br. J. Psychiatry* **2003**, *183*, 45−49.

(27) Pfleger, K.; Mauer, H. H.; Weber, A. In *Mass-Spectral and Gas-Chromatography Data of Drugs, Poisons, Pesticides, Pollutants and Their Metabolites*, 2nd rev. ed.; Cambridge, Weinheim Publishing: 1992; Vol. I, pp 19−20, Vol. II, pp 536−917.

(28) Blacklock, C. J.; Lawrence, J. R.; Wiles, D.; et al. Salicylic acid in the serum of patients not taking aspirin.Comparisons of salicylic acid concentrations in the serum of vegetarians, non-vegetarians, and patients taking low dose aspirin. *J. Clin. Pathol.* **2001**, *54*, 553−555.

(29) Needs, C. J.; Brooks, P. M. Clinical pharmacology of the salicylates. *Clin. Pharmacokin.* **1985**, *10*, 164−177.

(30) Duthie, G. G.; Kyle, J. A. M.; Jenkinson, A. McE.; Increased salicylate concentrations in urine of human volunteers after consumption of cranberry juice. *J. Agric. Food Chem.* **2005**, *53*, 2897−2990.

(31) Janssen, P. L. T. M. K.; Hollman, P. C. H.; Reichman, E.; et al. Urinary salicylate excretion in subjects eating a variety of diets shows that amounts of bioavailable salicylates in foods are low. *Am. J. Clin. Nutr.* **1996**, *64*, 743−747.

(32) Giovannucci, E.; Rimm, E. B.; Stampfer, M. J.; et al. Aspirin use and the risk for colorectal cancer and adenoma in male health professionals. *Ann. Intern. Med.* **1994**, *121*, 241−246.

(33) Herrmann, K. Occurrence and content of hydroxycinnamic and hydroxybenzoic acid compounds in foods. *Crit. Rev. Food Sci. Nutr.* **1989**, *28*, 315−336.

(34) Paterson, J. R.; Lawrence, J. R. Salicylic acid: a link between aspirin, diet and the prevention of colorectal cancer. *Q. J. Med.* **2001**, *94*, 445−448.

Received for review October 11, 2005. Accepted January 24, 2006.

JF058158W

INTERNATIONAL JOURNAL OF FOOD SCIENCES and NUTRITION

http://informahealthcare.com/ijf
ISSN: 0963-7486 (print), 1465-3478 (electronic)

Int J Food Sci Nutr, 2014; 65(2): 151–163
 DOI: 10.3109/09637486.2013.849662

informa
healthcare

COMPREHENSIVE REVIEW

Dietary strategies to recover from exercise-induced muscle damage

Mónica Sousa[1], Vítor H. Teixeira[2,3], and José Soares[1]

[1]*Faculdade de Desporto, Centro de Investigação, Formação, Intervenção e Inovação em Desporto (CIFI2D),* [2]*Faculdade de Ciências da Nutrição e Alimentação, and* [3]*Faculdade de Desporto, Centro de Investigação em Actividade Física, Saúde e Lazer (CIAFEL), Universidade do Porto, Porto, Portugal*

Abstract

Exhaustive or unaccustomed intense exercise can cause exercise-induced muscle damage (EIMD) and its undesirable consequences may decrease the ability to exercise and to adhere to a training programme. This review briefly summarises the muscle damage process, focusing predominantly on oxidative stress and inflammation as contributing factors, and describes how nutrition may be positively used to recover from EIMD. The combined intake of carbohydrates and proteins and the use of antioxidants and/or anti-inflammatory nutrients within physiological ranges are interventions that may assist the recovery process. Although the works studying food instead of nutritional supplements are very scarce, their results seem to indicate that food might be a favourable option as a recovery strategy. To date, the only tested foods were milk, cherries, blueberries and pomegranate with promising results. Other potential solutions are foods rich in protein, carbohydrates, antioxidants and/or anti-inflammatory nutrients.

Keywords

Food, inflammation, nutrients, oxidative stress

History

Received 10 May 2013
Revised 10 September 2013
Accepted 25 September 2013
Published online 31 October 2013

Introduction

Exhaustive or unaccustomed intense exercise can cause muscle damage, which results in muscle soreness, temporary decrease in muscle force, oedema, inflammation and an increase of intramuscular proteins in blood (Howatson & Van Someren, 2008; Smith et al., 2008). It has been described that the combination of a novel type of exercise with eccentric contractions leads to the occurrence of a higher degree of damage (Howatson & Van Someren, 2008), and its severity is influenced by the type, intensity and duration of training (Schoenfeld, 2012). Although the energy cost is lower for eccentric contractions compared with concentric ones, for the same power output, the former can cause a large degree of muscle damage (Evans, 2000; Newham et al., 1983). Eccentric contractions have also been considered more damaging than isometric ones (Clarkson & Hubal, 2002). It is believed that this is due to the increased generation of tension as muscle lengthens, resulting in a higher load distributed amongst the same number of fibres that causes a higher load per fibre ratio (Clarkson & Hubal, 2002; Enoka, 1996).

One of the most undesirable consequences of exercise-induced muscle damage (EIMD), especially in practical athletic terms, is its negative impact on muscle function, namely the decrease in muscle force-generating capacity, which is seen particularly after exercises involving eccentric contractions (Cheung et al., 2003; McGinley et al., 2009). Injury-induced strength loss, due to eccentric contractions, starts immediately after the end of the exercise and, depending on the severity of damage, it may persist from several days (McGinley et al., 2009) to 5–6 weeks (Howell et al., 1993). Muscle strength may decline up to 40%–50% after the exercise (Howell et al., 1993; Ingalls et al., 1998), leading to a large deleterious impact on athletic performance. On the other hand, pain, tenderness, swelling and stiffness, typically appear only within the first 24–48 h after eccentric exercise, being its duration also related to the extent of the damage (Allen, 2001; McGinley et al., 2009). Given the delayed nature of these symptoms, they are altogether often called "delayed onset muscle soreness" (DOMS) (Allen, 2001). Although EIMD can have detrimental effects, it has also been proposed that the associated inflammation and increased protein turnover are essential for hypertrophic adaptation (Evans & Cannon, 1991). Schoenfeld (2012), in his recent review, concluded that there is theoretical rationale supporting that EIMD may enhance the accretion of muscle proteins, although it seems that muscle growth can also occur in the relative absence of muscle damage. Furthermore, there may be a threshold beyond which damage does not have further effect on hypertrophy (Komulainen et al., 2000), and that excessive damage, particularly due to its induced force loss, can impair athletes' ability to train, which would consequently have an detrimental impact on muscle growth (Schoenfeld, 2012).

Nevertheless, due to its consequences, EIMD can hinder the adherence to an exercise training programme (Howatson & Van Someren, 2008). So, the study of interventions that may help to reduce the negative impact of EIMD, in order to accelerate the recovery process, may play a significant role for the sports population. The most common strategies used to prevent and treat EIMD are nutritional, pharmacological, stretching, massage, electrical therapy, cryotherapy and exercise (Howatson &

Correspondence: Vítor Hugo Teixeira, PhD, Faculdade de Ciências da Nutrição e Alimentação, Universidade do Porto, Rua Dr. Roberto Frias, 4200-465 Porto, Portugal. Tel: +351 225074320. Fax: +351 225074329. E-mail: vhugoteixeira@fcna.up.pt

Van Someren, 2008). Regarding the nutritional approach, the existing review literature is almost null and not focused on practical recommendations.

Thus, the aims of this review are to briefly summarise the muscle damage process, focusing on oxidative stress and inflammation, and to describe how nutrition may be positively used to help recovering from EIMD. Although nutrition is believed to provide prophylactic and therapeutic effect in reducing EIMD (Howatson & Van Someren, 2008), this review will focus especially on its therapeutic effects, particularly during the recovery period. For this review, databases PubMed and Scopus were used and searches were performed up to March 2013. Combinations of the following keywords were used as search terms: "muscle damage", "recovery", "oxidative stress", "inflammation", "exercise", "food", "antioxidants", "proteins", "carbohydrates" and "omega-3 fatty acids". References of retrieved articles were used whenever they were considered relevant. Additionally, the book Nutrition (Insel et al., 2007) was used to search nutritional contents of food.

Muscle damage

Although the exact mechanisms responsible for muscle damage remain unclear, it is believed that both mechanical and metabolic pathways are involved (Torres et al., 2012) and that the magnitude of damage is influenced by the mode, intensity and duration of exercise (Bowtell et al., 2011). A damage model, divided into two general phases, has been proposed: (i) a primary damage that occurs during the exercise, involving mechanical and metabolic alterations (Ebbeling & Clarkson, 1989; Tee et al., 2007); and (ii) a secondary damage associated with the inflammatory response (Howatson & Van Someren, 2008). EIMD involves, therefore, a complex interaction of events (Trombold et al., 2011), which seems to include sarcomere disruption due to the high mechanical tension on the myofibril (Proske & Morgan, 2001), impaired excitation–contraction coupling related to altered intracellular calcium homeostasis (Warren et al., 2001), oxidative stress (Favero, 1999) and inflammation (Peake et al., 2005). These events will lead to structural damage of the skeletal muscle cells and degradation of cell membrane, resulting in fibre necrosis and, ultimately, in fibre remodelling (Howatson & Van Someren, 2008). The possible sources of oxidants and the inflammatory process associated with EIMD will be further developed in the next sections.

Oxidative stress

It is largely accepted that exercise can create an imbalance between oxidant and antioxidant levels, known as oxidative stress (Leeuwenburgh & Heinecke, 2001). This phenomenon is caused by the production of reactive oxygen species (ROS) both acutely, i.e. during exercise, and throughout the long-term response to the EIMD (Powers & Jackson, 2008). ROS play an important role as mediators of EIMD (Finaud et al., 2006; Sacheck & Blumberg, 2001). Although it is widely recognized that ROS lead to the increment of markers of lipid, protein and DNA oxidation, ROS actions regarding EIMD seem to be associated with the oxidation of critical redox-sensitive sites within skeletal muscle – see Powers & Jackson (2008) for comprehensive review. Beyond their negative impact, ROS can also lead to positive outcomes, as contraction-induced adaptive responses of muscle fibres and regulation of gene expression (Powers & Jackson, 2008; Powers et al., 2011b).

Several mechanisms have been proposed as potentially liable parties of ROS increment during exercise. The electron transport associated with the mitochondrial respiratory chain has been considered one of the major intracellular source of ROS during exercise (Di Meo & Venditti, 2001). It is known that around 0.15% of the consumed oxygen is not completely reduced to water in the respiratory chain (St-Pierre et al., 2002), being converted into superoxide ion ($O_2^{\bullet -}$) (Boveris et al., 1972) primarily in complexes I and III of the mitochondrial electron transport chain (Finaud et al., 2006). Another alternative cause for ROS production could be ischemia-reperfusion (Finaud et al., 2006). During exhaustive exercise, working muscles are the primary tissue to be supplied with blood, while other tissues may undergo partial ischemia due to the reduced blood flow (Vollaard et al., 2005). Additionally, during exercise performed at intensities at or above maximal oxygen consumption ($\dot{V}O_{2max}$), muscle fibres may experience hypoxia since oxygen supply is beneath the energy demand (Packer, 1997). The ischemia conditions trigger the conversion of xanthine dehydrogenase to xanthine oxidase, which upon reoxygenation of the hypoxic tissue produces $O_2^{\bullet -}$ (Gomes et al., 2012). However, this mechanism has been shown to happen only in few studies (Gomes et al., 2012). Other processes that may be involved in ROS production during exercise include: (i) auto-oxidation of haem proteins, namely haemoglobin and myoglobin (Mb) (Finaud et al., 2006), (ii) the activity of the enzyme nicotinamide adenine dinucleotide phosphate oxidase (NADPH oxidase) (Powers & Jackson, 2008), (iii) the phospholipase A_2-dependent processes (Powers & Jackson, 2008; Powers et al., 2011b), and (iv) nitric oxide (NO) synthase (Powers & Jackson, 2008). Additional exercise-related changes that might be involved in ROS production are: (i) the increase in catecholamines which can lead to ROS release during their metabolic inactivation (Clarkson & Thompson, 2000), (ii) the production of lactic acid that is able to convert $O_2^{\bullet -}$ into hydroxyl radical ($OH^{\bullet}$) (Clarkson & Thompson, 2000), (iii) the rise in muscle temperature and (iv) the increase in carbon dioxide (CO_2) (Arbogast & Reid, 2004).

Although ROS may mediate cell damage, exercise-induced cell damage can also stimulate ROS production, since during the inflammatory response to EIMD the infiltrated leukocytes (neutrophils and macrophages) can release ROS (Leeuwenburgh & Heinecke, 2001). Their oxidative burst involves the production of $O_2^{\bullet -}$ that can be rapidly removed by reaction with other free radicals or due to conversion to hydrogen peroxide (H_2O_2) by superoxide dismutase (SOD) (Hampton et al., 1998). Furthermore, neutrophils can convert H_2O_2 into hypochlorous acid, a highly potent oxidant, via myeloperoxidase (Vollaard et al., 2005). Myeloperoxidase, an enzyme expressed primarily by neutrophils, has been shown to increase following exercise, and may remain elevated for days (Childs et al., 2001). Additionally, it was demonstrated that the level of myeloperoxidase activity per neutrophil is increased by exercise (Suzuki et al., 1996). Moreover, activated macrophages are a rich source of nitric oxide (NO) and they can lyse muscle cells *in vitro* through nitric-oxide-dependent mechanisms (Nguyen & Tidball, 2003). In addition, the presence of muscle cells seems to induce a higher NO production by macrophages and their cytolytic capacity appears to be increased by the presence of neutrophils (Nguyen & Tidball, 2003). Similar to neutrophils, macrophages are also thought to play a major role in promoting muscle damage after muscle injury (Tidball, 2005). However, recent findings demonstrated that macrophages recruited by damaged skeletal cells exhibit a phagocytic and pro-inflammatory profile, which is rapidly converted to an anti-inflammatory phenotype (Arnold et al., 2007). This phenotype is associated with myogenesis and muscle growth (Arnold et al., 2007), suggesting that macrophages do not contribute to secondary damage. Other aspects of the inflammatory phenomenon resultant from EIMD will be developed in the subsequent section.

Inflammation

Intense physical exercise, especially eccentric exercise, triggers a rapid and sequential invasion of muscle by inflammatory cells which can persist for days to weeks (Leeuwenburgh & Heinecke, 2001; Tidball, 2005). White blood cells (WBC) are the major cellular mediators of inflammation (Cannon & St. Pierre, 1998) and their increased concentrations after EIMD are believed to be mainly due to the rise of neutrophils and monocytes/macrophages (Evans, 2000; Malm et al., 1999; Sacheck & Blumberg, 2001; Urso & Clarkson, 2003). Lymphocytes are also recruited during strenuous exercise but their count declines immediately after the end of the exercise (Pendersen & Toft, 2000). The inflammatory process is believed to be mediated (i) by neuroendocrinological factors, such as adrenaline, noradrenaline, growth hormone and cortisol (Pendersen & Toft, 2000) and (ii) by cytokines, namely pro-inflammatory cytokines as tumour necrosis factor-alpha (TNF-α) and interleukin-1 beta (IL-1β), and the inflammation-responsive cytokine IL-6 (Pedersen & Hoffman-Goetz, 2000). Although it is generally accepted that cytokines have a central role in the inflammatory process, the exact mechanism of action of each one remains unclear (Smith et al., 2008) (for detailed review see Cannon & St Pierre (1998)). Endothelial cells also play a significant role in regulating the inflammatory response, namely (i) by expressing leukocyte's adhesion molecules, which are determinant for the influx of neutrophils and monocytes, (ii) possibly by producing NO, which is vasodilator, and (iii) by secreting several cytokines as IL-1α and -1β, IL-6 and IL-8 (Cannon & St. Pierre, 1998). The local inflammatory process is afterwards accompanied by a systemic response known as acute-phase response, similar to what happens in an infection (Evans, 2000; Pedersen & Hoffman-Goetz, 2000).

Eccentric exercise results in a greater rise of neutrophil counts compared with concentric exercise, where both circulating and skeletal muscle neutrophils increase (Evans, 2000). Exercise causes demargination of neutrophils, increasing the circulating populations (Tidball, 2005). Within 1 h of increased muscle loading, neutrophils invasion begins and their concentrations can remain elevated for periods as long as 5 days (Fielding et al., 1993). The mobilization of neutrophils seems to depend on exercise intensity and to be mediated by the secretion of stress hormones, such as catecholamines, cortisol and growth hormone (Pendersen & Toft, 2000; Sacheck & Blumberg, 2001). Their function after infiltration in the damaged muscle is to phagocytise the necrotic myofibers and help to degrade cellular debris (Cannon & St. Pierre, 1998), by releasing proteases and oxygen radicals, as explained in the previous section, which can damage muscle even further and also other healthy surrounding tissues (Evans & Cannon, 1991; Leeuwenburgh & Heinecke, 2001; Tidball, 2005). This process is known as secondary damage (Smith et al., 2008). In fact, evidence has shown that administration of an antibody that blocks the respiratory burst and degranulation of neutrophils prior to a single eccentric contraction, led to a significant decrease in muscle damage (Brickson et al., 2003). Moreover, neutrophils are thought to be one of the most important players in the secondary damage since they are the immune cells that predominate in the injured tissue at the time when secondary damage occurs (Smith et al., 2008). Neutrophils may also magnify the inflammatory process via the release of inflammatory cytokines as IL-6 (Smith et al., 2008), IL-1β and TNF-α (Cannon & St. Pierre, 1998).

The inflammatory cell pattern changes within the first 24 h, with the number of neutrophils starting to decrease and the macrophages count beginning to increase (Smith et al., 2008). Thus, macrophages are evident in the damaged muscle around 1 day after exercise and their counts may remain high up to 7–14 days post-exercise (Round et al., 1987). There is a poor understanding of macrophages' functions during exercise-induced inflammation and their role in muscle damage is complex, since they secrete various growth factors, cytokines and free radicals, and act as antigen-presenting cells, regulating the cellular immune response (Tidball, 2005). Some of the cytokines released by macrophages include IL-1β, TNF-α and IL-6, which magnify the inflammatory process and coordinate the various elements of the systemic acute-phase response (Sacheck & Blumberg, 2001; Smith et al., 2008). As neutrophils, they also have the ability to phagocytize damaged tissue and both seem to play a key role in muscle repair and remodelling (Tidball, 2005). The discussion of the mechanisms by which these inflammatory cells contribute to muscle repair and remodelling is beyond the scope of this review; for that, other review papers (Smith et al., 2008; Tidball, 2005) are suggested.

Nutritional strategies

Due to the heavy sport's schedule of athletes, training or competing more than once within a single day is oftentimes their routine. Therefore, maximising and accelerating the recovery processes is crucial to potentiate their performance (Betts & Williams, 2010). Some interventions have been proposed to reduce the negative effects associated with EIMD, like nutrition, pharmacological strategies, electrical and manual therapies, cryotherapy and active exercise (Howatson & Van Someren, 2008; Torres et al., 2012). With training programmes becoming more demanding any possible help should be considered, and nutrition is an area that obviously can make a difference (Maughan et al., 2004). Given the fact that feeding is a mandatory physiological demand, it is of countless interest to potentiate the athletes' food intake in order to maximise their training programme. Recovering faster and more efficiently will allow athletes to train more and to respond to training more positively, leading to the expected performance improvements. It has been widely stated that during post-exercise recovery, optimal nutritional intake is essential to facilitate muscle repair and regeneration (Beelen et al., 2010). Some nutrition interventions have been considered capable of assisting recovery after EIMD.

Proteins

Proteins alone

Few studies have been conducted that have examined the role of protein supplementation in preventing or alleviating symptoms associated with EIMD (Howatson et al., 2012; Jackman et al., 2010; Matsumoto et al., 2009; Nosaka et al., 2006; Shimomura et al., 2006), with the majority of them using branched chain amino acids (BCAA). It has been concluded that the ingestion of amino acids seem to be able to reduce muscle damage – measured by creatine kinase (CK) (Howatson et al., 2012; Matsumoto et al., 2009; Nosaka et al., 2006), aldolase (Nosaka et al., 2006), Mb (Nosaka et al., 2006), lactate dehydrogenase (LDH) (Matsumoto et al., 2009), granulocyte elastase (Matsumoto et al., 2009) or muscle soreness (Howatson et al., 2012; Jackman et al., 2010; Matsumoto et al., 2009; Nosaka et al., 2006; Shimomura et al., 2006) – decrease sensation of fatigue (Matsumoto et al., 2009; Shimomura et al., 2006), and accelerate the functional recovery process (Howatson et al., 2012). However, in one study (Jackman et al., 2010), no differences were found for CK, Mb, IL-6, maximal isometric strength and low-frequency fatigue compared with placebo.

It is widely accepted that a positive muscle protein balance is necessary to facilitate the muscle repair and adaptation from EIMD (Hawley et al., 2006). Regarding muscle protein synthesis

(MPS) and net protein accretion, it has been concluded that they can be promoted by an early post-exercise protein consumption (Phillips, 2011). For optimal stimulation of muscle protein synthesis, recent data suggest an intake of 20–25 g protein following resistance exercise (Moore et al., 2009; Phillips, 2011). Essential amino acids (EAA) seem to be the primarily responsible for the stimulation of muscle protein synthesis (Volpi et al., 2003) and leucine seems to be a key metabolic regulator of MPS (Crozier et al., 2005). The amount of protein mentioned above (≈20 g) corresponds approximately to 8.5 g of EAA or 1.5 g leucine (Phillips, 2011), which is approximately the amount shown to maximally stimulate protein synthesis (Cuthbertson et al., 2005). Considering this, Phillips (2011) in his recent review suggests an ingestion of at least 25 g high-quality protein containing not less than 8–10 g EAA, delivered as soon as possible post-exercise, for maximal stimulation of MPS.

Proteins plus carbohydrates

Although it has been demonstrated that the administration of CHO alone has little or no effect in attenuating signs and symptoms of muscle damage (Howatson & Van Someren, 2008), the combined intake of CHO with proteins seems to be beneficial. There is already a strong body of scientific evidence showing that the simultaneous ingestion of CHO and protein may attenuate muscle damage (Baty et al., 2007; Bird et al., 2006; Cockburn et al., 2008, 2010; Doyle et al., 1993; Luden et al., 2007; Pritchett et al., 2009; Romano-Ely et al., 2006; Samadi et al., 2012; Saunders et al., 2004, 2007, 2009; Skillen et al., 2008; Valentine et al., 2008), suggesting that the combination of these two macronutrients can be a valuable strategy. However, some studies (Breen et al., 2010; Green et al., 2008; White et al., 2008; Wojcik et al., 2001) do no support these findings. The possible reasons for these discrepancies are (i) the inherent inter-individual variability for indirect systemic markers of muscle damage, namely CK (Betts & Williams, 2010), which was the only blood parameter used to assess muscle damage in the four studies that did not find positive results, and (ii) the different exercise protocols applied.

CHO ingestion after exercise has been shown to improve net protein balance by attenuating the exercise-induced increment in muscle protein breakdown, which has been attributed to a rise in plasma insulin (Beelen et al., 2010; Børsheim et al., 2004). However, when an ample dose of protein was administrated, the co-ingestion of CHO and proteins did not seem to further improve protein synthesis and protein breakdown (Koopman et al., 2007; Staples et al., 2011). Still, it is important to note that the amount of CHO used in those studies was considerably low: 0.15 or 0.6 g/kg/h (Koopman et al., 2007) and 50 g (Staples et al., 2011). Although conflicting data still exists regarding whether or not the ingestion of CHO plus proteins has an undoubtedly advantage versus protein alone, it seems clear that it is not a disadvantage combining these two macronutrients during the recovery time. Additionally, the palatability of a CHO-protein solution has usually a better acceptance than one with proteins only. Moreover, low glycogen levels have been shown to possibly have a negative impact on MPS (Churchley et al., 2007; Creer et al., 2005; Wojtaszewski et al., 2003) and to promote muscle protein breakdown (Lemon & Mullin, 1980). It is important to note that a high volume of resistance exercise can lead to a decrease in muscle glycogen stores (MacDougall et al., 1999; Robergs et al., 1991) and that muscle glycogen re-synthesis is impaired by EIMD (Costill et al., 1990; O'Reilly et al., 1987; Seifert et al., 2005). It is known that CHO feeding during the recovery period can stimulate greater rates of muscle glycogen re-synthesis than when no CHO are ingested at all (Betts & Williams, 2010). Furthermore, it has already been shown that a high CHO intake (8.5 g CHO/kg/d) after an eccentric exercise leads to a higher increase in intramuscular CHO storage compared to a lower amount (4.25 g CHO/kg/d) (Costill et al., 1990). Moreover, a recent review paper (Beelen et al., 2010) suggested that the co-ingestion of 0.2–0.4 g/kg/h protein with 0.8 g/kg/h CHO (compared to the recommended amount of 1.2 g/kg/h CHO alone), in addition to provide proteins that are essential to stimulate MPS, seems to result in optimal muscle glycogen-repletion rate (Beelen et al., 2010; Van Loon et al., 2000). This phenomenon may be due to the synergetic influence of CHO and protein on insulin secretion (Van Loon et al., 2000).

Therefore, and regarding the existing evidence, it seems that ingesting 0.8–1.2 g CHO/kg/h and 0.2–0.4 g protein/kg/h, preferably in the early recovery period, with a minimum content of 20 g high-quality protein, may enhance the recovery after EIMD. Some discussions have been raised recently regarding the importance of nutrient timing consumption (Aragon & Schoenfeld, 2013) and if CHO and proteins really need to be consumed as soon as possible after the exercise. Even though it is not yet certain that a real advantage for the early feeding after exercise exists, certainly a quick nutrient delivery after a demanding effort will not be a disadvantage. Furthermore, from a practical point of view, the promotion of an early nutritional recovery strategy, preferably carried out within the sports context, may enhance the adherence to that strategy and ensures a correct and proportional feeding.

Antioxidant supplementation

Whether or not athletes benefit from the use of antioxidant supplements remains a hot topic and it is still controversial. Powers and collaborators, in a recent review about this topic (Powers et al., 2011a), highlighted the arguments that have been used for and against antioxidant supplementation. Briefly, the most commonly used arguments to support antioxidant supplementation are: (i) the fact that exercise leads to an increase in ROS production and that increased levels of antioxidants could counteract the ROS, preventing or reducing damage and, therefore, muscle pain (Urso & Clarkson, 2003), (ii) that some antioxidants shown to improve endurance performance (Kelly et al., 2009) and to delay fatigue, and (iii) that some athletes may not achieve the nutritional recommendations for antioxidant intake just with food (Machefer et al., 2007; Palazzetti et al., 2004; Rankinen et al., 1998). On the other hand, some arguments have been used against antioxidant supplementation, namely: (i) the fact that regular exercise leads to an increase in enzymatic and non-enzymatic antioxidants in muscle fibres (Powers et al., 2011b), (ii) that antioxidant supplementation may impair muscle function or delay some adaptations induced by exercise (Coombes et al., 2001; Teixeira et al., 2009), by interfering with cell signalling functions of ROS, affecting muscular performance (McGinley et al., 2009), (iii) that antioxidant supplementation does not seem to lead to better outcomes, compared with placebo, regarding muscle function, inflammation (Beaton et al., 2002) and redox status (Theodorou et al., 2011) after eccentric exercise; (iv) that antioxidant supplementation may contribute to increase muscle damage and oxidative stress (Childs et al., 2001), and (v) that some studies do not support the concept that antioxidant supplementation is beneficial to human health (Bjelakovic et al., 2007) and doubts have been placed about the long-term effects of antioxidant supplementation in high doses (McGinley et al., 2009). Moreover, it has been reported that the protective effect of a diet, with natural sources of antioxidants, is not equivalent to the protective effect of supplementation (Halliwell, 2000). Given these facts, it is currently suggested (Peternelj & Coombes,

2011; Powers et al., 2011a) that due to the limited evidence to recommend antioxidant supplements, athletes should rather focus on consuming a well-balanced and energetically adequate diet, which can provide antioxidant-rich foods.

Antioxidant and/or anti-inflammatory nutrients in food

Keeping in mind that high doses of antioxidants seem to have detrimental consequences, the use of antioxidant-rich foods seems to be the best option. These foods can provide an amount of antioxidant within the physiological range, while nutritional supplements usually provide supra-physiological doses. Therefore, this review will only focus on the key antioxidants found in food and a brief explanation of their main mechanisms will be given below. Some of these compounds also seem to have an anti-inflammatory action, which may have further benefits on the recovery from EIMD. Given that, most studies regarding muscle damage used nutritional supplements rather than food, reference will be made not only to the studies that used nutrient-dense foods but also to those that utilized the isolate substances in humans. It is important to mention that the level of evidence regarding the cause and health effect relationship, for the majority of these substances, is not yet sufficient for the European Food Safety Authority (EFSA) to consider making health claims. Therefore, more research in this area, especially clinical trials with human beings, will help to understand the possible relationship between the intake of these substances and their possible effects.

Vitamin C and/or vitamin E

Vitamin C, or ascorbic acid, is a potent water soluble vitamin, present in the cytosolic compartment of the cells (Evans, 2000). It is found mainly in citrus fruits, with sweet peppers, strawberries, cruciferous and leafy vegetables, being also good sources (Gerber, 2003). This vitamin exerts its functions by scavenging ROS and reactive nitrogen species, as well as regenerating other antioxidant molecules from their radical species, namely vitamin E, β-carotene and glutathione (Carr & Frei, 1999).

Vitamin E is the most important lipid-soluble antioxidant vitamin and it is virtually found in all cell membranes (Evans, 2000). Its main sources are vegetable oils, especially sunflower, safflower and nuts (Gerber, 2003). It exists in eight different isomers: α-, β-, γ- and δ-tocopherol and α-, β-, γ- and δ-tocotrienol (Gülçin, 2012), being the α-tocopherol the most important biologically active form (McGinley et al., 2009). Vitamin E is known for its ability for stopping the progression of the lipid peroxidation chain reaction and also for acting as a scavenger of superoxide, hydroxyl and lipid peroxyl radicals (McGinley et al., 2009).

An exhaustive review (McGinley et al., 2009) about the effects of supplementation with these two antioxidants, alone or combined, concluded that there is little evidence to support its protection against muscle damage, although there is evidence showing that both can reduce indices of oxidative stress. Moreover, the typical large supplementation dosages can even has a detrimental effect on the adaptive and recovery processes since it may interfere with the signalling functions of ROS (McGinley et al., 2009). Studies after that review continue to show contradictory results, (i) some showing positive outcomes of supplementation concerning muscle soreness (Silva et al., 2010), muscle damage (measured trough LDH (Silva et al., 2010) and CK (Nakhostin-Roohi et al., 2008)), oxidative status (Nakhostin-Roohi et al., 2008; Silva et al., 2010) and inflammation (Silva et al., 2010), (ii) and others showing no effect on muscle damage using CK (Theodorou et al., 2011), muscle soreness (Theodorou et al., 2011), muscle function by isometric peak torque (Theodorou et al., 2011), inflammation (Nakhostin-Roohi et al., 2008; Silva et al., 2010), and oxidative status (Theodorou et al., 2011).

Polyphenols

Polyphenols are the biggest group of phytochemicals and are known for being strong antioxidants (Tsao, 2010). Flavonoids are the largest group of polyphenolic compounds with more than 4000 identified varieties distributed among fruits, vegetables, nuts, tea and wine (Cabrera et al., 2006; González-Gallego et al., 2010; Marzocchella et al., 2011). It has been suggested by a large number of publications that these compounds have immunomodulatory, antioxidant and anti-inflammatory properties (González-Gallego et al., 2010; Marzocchella et al., 2011). Flavonoids seem to exert their antioxidant activity by scavenging ROS (García-Lafuente et al., 2009) and by impairing ROS production by inhibiting NADPH oxidase, xanthine oxidase and myeloperoxidase (Cotelle, 2001). In addition, they also have the ability to inhibit lipid peroxidation, chelating redox-active metals, activating antioxidant enzymes and reducing α-tocopherol radicals (Heim et al., 2002). Some mechanisms have been proposed in order to explain the anti-inflammatory effects of flavonoids, as the reduction of the activities of the arachidonic acid metabolizing enzymes (phospholipase A2, cyclooxygenase, lipoxygenase), inhibition of NO synthase, inhibition of pro-inflammatory molecules (IL-1β, IL-2, IL-6, TNF-α, among others), and modulation of pro-inflammatory gene expression (Marzocchella et al., 2011).

The flavonoid quercetin has been used in some studies (Nieman et al., 2007a,b; O'Fallon et al., 2012) in the context of EIMD. Apart from a diminished post-exercise expression of leukocyte IL-8 and IL-10 mRNA in one of the studies (Nieman et al., 2007b), quercetin, contrary to the expected, failed to positively influence muscle strength, muscle damage, inflammation and plasma cytokine, and hormone levels. Another flavonoid, the epigallocatechin gallate (EGCG) that is a catechin found in high concentrations in green tea, was also investigated along with muscle damage (Kerksick et al., 2010). Its supplementation resulted in reduced muscle soreness compared to placebo. No differences were seen for the other tested parameters (peak torque production, LDH, CK, serum cortisol, neutrophil counts, neutrophil:lymphocyte ratio and markers of apoptosis). Regarding food, cherries and berries, known to be rich in various polyphenol compounds especially in anthocyanins (another class of flavonoids) and the flavonol quercetin (McCune et al., 2011; Szajdek & Borowska, 2008), have been used as treatment in studies related to EIMD (Bowtell et al., 2011; Connolly et al., 2006; Howatson et al., 2010; McLeay et al., 2012). Impressively, all studies showed positive results for muscle force recovery; regarding markers of muscle damage, most of the studies did not found any differences between the tested groups and the results for oxidative stress and inflammation markers varied among the studies (Table 1). Pomegranate and the respective extract are especially rich in the polyphenols ellagitannins (Medjakovic & Jungbauer, 2013), and have also been used in research concerning muscle damage. In a study (Trombold et al., 2010), pomegranate extract showed to reduce muscle force loss but had no impact on CK, Mb, IL-6 and CRP. The same research group conducted another study (Trombold et al., 2011) with pomegranate juice in which they concluded that the supplementation attenuated the force loss and reduced soreness of the elbow flexor muscles; however, no differences from placebo were found for the knee extensor muscles. The general positive results in these studies using food as the supplementation, strengthens the possible positive effect

Table 1. Studies that used food as the strategy to recover from EIMD in humans.

		Food			Muscle damage		Oxidative stress		Inflammation marker		Force/Performance recovery	
Study	Subjects	Dosage	Duration	Exercise protocol	Marker	Treatment effect	Marker	Treatment effect	Marker	Treatment effect	Test	Treatment effect (speed)
(Connolly et al., 2006)	14 males college students	2 × 355 mL cherry juice[a]	3 d pre-ex	2 × 20 single-elbow ECC flexion	Muscle soreness	↓					Isometric	↑
(Cockburn et al., 2008)	24 active males	500 mL semi-skimmed milk[b]	Immediately and 2 h after ex	6 × 10 ECC-CON actions knee flexors 1.05 rad.s^{-1}	CK DOMS Mb	↔ ↔ ↔					PT Total work	↔ Non-dominant leg ↑ Dominant leg ↔ Non-dominant leg ↑ Dominant leg
(Pritchett et al., 2009)	10 males regional-level cyclists and triathletes	Low-fat chocolate milk to achieve 1.0 g/kg[a]	Immediately and 2 h after ex	6 × (5 min cycling at 60% $\dot{V}O_2$ max + 3 × 10 s Wingate sprints)	CK Muscle soreness	↔ ↔					Cycling time at 85% $\dot{V}O_2$ max to exhaustion	↔
(Bowtell et al., 2011)	10 well-trained males	2 × 30 mL cherry juice[a]	7 d pre-ex	10 × 10 single-knee extension 80% 1RM	CK Nitrotyrosine PPT	↔ ↔ ↔	TAS PC	↔ ↓	hsCRP	↔	MVC	↑
(Howatson et al., 2010)	20 (13 male) recreational marathon runners	2 × 237 mL cherry juice[a]	5 d pre-ex	marathon run	CK LDH DOMS	↔ ↔ ↔	TAS TBARS PC	↑ ↓ ↔	CRP IL-6 Uric acid	↓ ↓ ↓	MVIC	↑
(Trombold et al., 2011)	17 trained males	2 × 250 mL pomegranate juice[a]	7 d pre-ex	3 × 20 single-elbow ECC flexion 0.7 rad.s^{-1} + 6 × 10 single-knee extension 110% 1RM	Muscle soreness	↓ Elbow flexors ↔ Knee extensor					Isometric	↑ Elbow flexor ↔ Knee extensor
(McLeay et al., 2012)	10 healthy females	1 blueberry smoothie: 200 g blueberries, 1 banana, 200 mL apple juice[a]	5 and 10 h pre-ex, immediately, 12 and 36 h after ex	3 × 100 single-knee ECC flexion 30°.s^{-1}	CK Muscle soreness	↔ ↔	PC ROS-GC FRAP	↔ ↓ ↑	IL-6	↔	Isometric ECC CON	↑ ↔ ↔
(Cockburn et al., 2013)	14 healthy males	500 mL semi-skimmed milk[a]	Immediately after ex	6 × 10 ECC-CON knee flexion 1.05 rad.s^{-1}	Passive DOMS Active DOMS CK Mb	Unclear Unclear Unclear Unclear					CMJ height Reactive strength index 5 m sprint 10 m sprint 15 m sprint Agility LIST	Unclear Unclear Unclear ↓ ↓ ↓ Unclear

Abbreviations: Pre-ex, pre-exercise; ECC, eccentric; ex, exercise; ECC-CON, eccentric-concentric; CK, creatine kinase; DOMS, delayed onset muscle soreness; Mb, myoblobin; PT, peak torque; $\dot{V}O_2$ max, maximal oxygen uptake; RM, repetition maximum; PPT, pressure pain threshold; TAS, total antioxidant status; PC, protein carbonyls; hsCRP, high-sensitivity C-reactive protein; MVC, maximum voluntary contraction; LDH, lactate dehydrogenase; TBARS, thiobarbituric acid reactive species; CRP, C-reactive protein; IL, interleukin; MVIC, maximum voluntary isometric contraction; ROS-GC, radical oxygen species-generating capacity; FRAP, ferric reducing anti-oxidant power; CMJ, countermovement jump; LIST, Loughborough Intermittent Shuttle Test.

↓, significant decrease; ↑, significant increase; ↔, no significant change.

[a]Comparison with a placebo/control group;

[b]The study has four groups: milk, milk-based carbohydrate-protein supplement, sports drink and water (control). The results are expressed for milk versus control.

of physiological ranges of antioxidants over the typically used supra-physiological doses.

Carotenoids

Carotenoids are present in plants, algae and microorganisms, and they are divided into two classes: carotenes and xanthophylls (Riccioni, 2009). The major dietary sources of carotenoids are fruits and vegetables (Semba et al., 2007), in which they are the principal pigments responsible for their colour (Gülçin, 2012). The most abundant carotenes in the diet are the β-carotene and lycopene while lutein, β-cryptoxanthin, zeaxanthin and astaxanthin, are the most common xanthophylls (Riccioni, 2009). Carotenoids are efficient antioxidants and comprise an important component of the antioxidant defence system in humans by protecting against oxidative stress, scavenging singlet molecular oxygen and free radicals, and inhibiting lipid peroxidation (Semba et al., 2007).

To date, there is only one study in humans (Djordjevic et al., 2012) using only carotenoids (astaxanthin) as the anti-oxidant supplementation treatment. This study showed a positive effect of the supplementation on CK and on the total antioxidant status (TAS), but not on SOD.

α-Lipoic acid

Dietary α-lipoic acid (LA) can be obtained from both animal and plant sources, but is primarily found in animal-derived foods, namely red meat, liver, heart and kidney (Gorąca et al., 2011). Humans can also obtain LA by *de novo* synthesis from fatty acids and cysteine (Biewenga et al., 1997). The reduced form of LA is known as dihydrolipoic acid (DHLA) and it is this form that predominantly interacts with ROS, although the oxidized form of LA can also inactivate free radicals (Packer et al., 2001). Furthermore, both forms may exhibit antioxidant activity by metal chelating (Packer et al., 2001). DHLA has also the capacity to reduce the oxidized forms of several important antioxidants, such as vitamin C and E, co-enzyme Q_{10}, and glutathione (Bilska & Włodek, 2005; Gorąca et al., 2011; Kozlov et al., 1999). For these reasons, the LA/DHLA redox couple is now being recognized as one of the most powerful biologic antioxidant systems (Gorąca et al., 2011).

Regarding LA, one study (Zembron-Lacny et al., 2009b) showed no differences on muscle damage markers CK and LDH between treatments. LA supplementation, on the other hand, influenced the levels of glutathione (GSH), glutathione reductase (GR) and glutathione peroxidase (GPx), after exercise; although the levels of total thiols, TBARS and protein carbonyls (PC), were positively changed throughout the trial compared with the control group, no different kinetics were seen between conditions with exercise. Moreover, no changes were seen after LA supplementation on the exercise parameters measured by the isokinetic device, namely peak torque, time to reach peak torque, total work, average power and maximal average peak torque. In another study (Zembron-Lacny et al., 2009a) by the same research group, similar outcomes were found: no differences in CK levels compared to control but positive results regarding TAS, total thiols, TBARS, PC and uric acid. In a third study (Fogarty et al., 2013), there was also an increase in blood total antioxidant capacity as a result of LA supplementation while DNA damage, lipid peroxidation and hydrogen peroxide, increased following exercise only in the non-supplemented group.

Co-enzyme Q10

Co-enzyme Q, also called ubiquinones, is a natural lipophilic compound found in every living cell (Pravst et al., 2010). Co-enzyme Q10 (CoQ_{10}) is the most abundant form in humans and most animals (Pravst et al., 2010). In addition to endogenous synthesis, food is also a source of CoQ_{10}, with meat, fish, nuts and certain vegetable oils, being the richest nutritional sources (Pravst et al., 2010). However, its dietary uptake is limited to only a few percentage (Bentinger et al., 2010). CoQ_{10} is a key component of the mitochondrial respiratory chain but it is also known for its antioxidant properties (Littarru & Tiano, 2010). Mostly in its reduced form, CoQ_{10} is an effective antioxidant with capacity to protect against lipid peroxidation, DNA and protein oxidation, and to regenerate vitamin C and E as well (Finaud et al., 2006; Pravst et al., 2010).

In one study (Díaz-Castro et al., 2012), the CoQ_{10} supplementation decreased oxidative markers, increased antioxidant markers and also had a positive effect on inflammatory markers. However, no markers of muscle damage or muscle performance were measured. In another study (Östman et al., 2012), the supplementation with CoQ_{10} had no effect on markers of oxidative stress and CK compared with placebo. In a third one (Kon et al., 2008), supplementation with CoQ_{10} decreased CK, Mb and lipid peroxide (LPO), and had no influence on changes in neutrophil counts after exercise. In a last one (Malm et al., 1996), anaerobic work capacity was impaired and CK levels were increased at various points in the CoQ_{10} group whereas during placebo trial there were no changes. It is worth mentioning that the American College of Sports Medicine (Rodriguez et al., 2009) classified CoQ_{10} as an ergogenic aid that does not perform as claimed.

n-3 Polyunsaturated fatty acids

The *n*-3 polyunsaturated fatty acids (PUFAs), namely the long-chain *n*-3 PUFA eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are extensively associated with anti-inflammatory and immunomodulatory properties (Galli & Calder, 2009). Rich sources of PUFA include fatty fish, such as salmon, tuna and mackerel, fish oil and nuts (Insel et al., 2007; Ros & Mataix, 2006).

Typically, the phospholipids of immune cells contain proportionally more arachidonic acid (AA), an *n*-6 PUFA, than other long-chain fatty acids, including *n*-3 PUFAs (Calder et al., 1994; Kew et al., 2004). Therefore, AA is usually the major substrate for eicosanoids synthesis, which is a key mediator and regulator of inflammation (Calder, 2009). The AA-derived eicosanoids, namely prostaglandin (PG) E_2 and 4-series of leukotrienes (LTs), are generally assumed to be pro-inflammatory, although it has been recently discovered that PGE_2 can also have anti-inflammatory actions (Calder, 2009). Nevertheless, it has been shown that the EPA and DHA content of the immune cells membrane can be altered through oral administration of these fatty acids (Calder, 2007). This manipulation results in a decreased production of AA-derived eicosanoids, a rise in alternative substances, such as PGE_3 (less potent then PGE_2) and resolvins (potent anti-inflammatory mediators), and also in an altered gene expression by a direct effect of *n*-3 fatty acids on signalling pathways (Calder, 2009). Through these mechanisms, *n*-3 PUFAs intake seems to have the ability to affect phagocytosis, T-cell signalling and antigen presentation capability (Calder, 2007) and to lead to a decrease in cytokines and ROS production, and in the expression of adhesion molecules (Calder, 2006).

For these reasons, *n*-3 PUFAs may be of a useful nutritional help to modulate the exercise-induced inflammation and immune dysfunction resultant from EIMD. A recent review about *n*-3 fatty acids and physical performance (Mickleborough, 2013) concluded that supplementation with *n*-3 PUFAs may help to alleviate DOMS resulting from muscle damage, possibly due to the ability

of these fatty acids to increase blood flow. However, the author concluded that the evidence from human data is inconclusive to show a beneficial effect of *n*-3 PUFA in attenuating the inflammatory and immunomodulatory response to exercise.

Can food be an adequate alternative to supplements?

Most work, in the area of nutritional recovery from exercise, focus on the use of nutritional supplements rather than on foods. The few studies done using food – milk, cherries, blueberry or pomegranate – to recover from EIMD are described in Table 1. Although the number of studies is scarce and they used different methodologies, their results seem to indicate that food might be a favourable option as a recovery strategy. Moreover, given the issues related to potential contamination resulting in inadvertent doping (Burke et al., 2009), it is a safer option for athletes if they rely on food rather than on nutritional supplements.

Milk

Cow's milk and its derivatives represent a very good source of protein, lipids, amino acids, vitamins and minerals (Roy, 2008). Milk has several characteristics that make it an interesting recovery drink. One of its advantages is that it contains both casein and whey proteins in a ratio of approximately 3:1, which results in sustained elevations of blood amino acid concentrations (Bos et al., 2003; Roy, 2008). Therefore, milk has both fast dietary proteins (whey) that stimulate protein synthesis, and slowly absorbed ones (casein) which suppress muscle protein breakdown (Boirie et al., 1997; Dangin et al., 2003). Another advantage is that whey proteins contain a large proportion of BCAA, which are important in muscle metabolism and protein synthesis (Roy, 2008).

Milk was used in three (Cockburn et al., 2008, 2013; Pritchett et al., 2009) of the eight studies mentioned in Table 1. Essentially, the positive results were found regarding force/performance recovery: one study (Cockburn et al., 2008) found a positive effect of semi-skimmed milk on force recovery and total work for the dominant leg, and the second one (Cockburn et al., 2013) found a positive effect of the same type of milk on limiting increases in sprint time and agility. However, the third study (Pritchett et al., 2009), found no differences on the measured recovery parameters between low-fat chocolate milk and a carbohydrate replacement beverage, despite the previously published data suggesting it has an effective recovery aid (Karp et al., 2006). The three studies found no differences between the milk group and the respective comparison group for the muscle damaged markers, namely CK (Cockburn et al., 2008, 2013; Pritchett et al., 2009), DOMS (Cockburn et al., 2008, 2013; Pritchett et al., 2009) and Mb (Cockburn et al., 2008, 2013).

Cherries

Cherries are known to have a high content in numerous phytochemicals possessing antioxidant properties, with anthocyanins and quercetin playing a special role (McCune et al., 2011). These fruits also contain vitamins C and E and some carotenoids, especially β-carotene (Ferretti et al., 2010). In addition to the antioxidants effects, the consumption of cherries has also been associated with anti-inflammatory effects, namely through inhibition of the activity of the cyclooxygenase II (Ferretti et al., 2010; Seeram et al., 2001), and with pain inhibition (in animal studies) (Tall et al., 2004).

Three (Bowtell et al., 2011; Connolly et al., 2006; Howatson et al., 2010) of the eight studies using food as the intervention to attenuate the consequences associated with muscle damage, used cherries as the treatment. The results seen in these studies (Table 1) are, as a whole, positive and promising. For all the three studies, the cherry supplementation enhanced the performance recovery. One of the studies (Connolly et al., 2006) showed a decrease in DOMS, while the other two did not find any difference in the muscle damage markers. Howatson & collaborators (2010) found a positive outcome for inflammation (CRP, IL-6 and uric acid) and oxidative stress (TAS and TBARS) markers except PC, whereas Bowtell et al. (2011) only found a positive effect for PC (and not for TAS or high-sensitivity CRP).

Berries

Berries, specifically blueberries, are fruits particularly rich in antioxidants (Ehlenfeldt & Prior, 2001; Proteggente et al., 2002; Wang et al., 1996). It is believed that the phenolic compounds – including phenolic acids, tannins, namely ellagitannins and flavonoids as anthocyanins, flavonols and flavanols – are mainly responsible for their antioxidant properties (Basu et al., 2010; Szajdek & Borowska, 2008). Other substances, as β-carotene and other carotenoids and ascorbic acid, may also contribute to these properties but in smaller proportions (Szajdek & Borowska, 2008). Similar to cherries, berries also seem to have anti-inflammatory properties. They have been shown to reduced TNF-α induced up-regulation of inflammatory mediators in human micro-vascular endothelial cells (Youdim et al., 2002), to attenuate inflammatory gene expression in mice (DeFuria et al., 2009), and also to positively influence the NO metabolism (Basu et al., 2010; Pergola et al., 2006).

The only study (McLeay et al., 2012) in the context of EIMD that used blueberries as treatment showed positive results regarding oxidative stress and force recovery, but not for the muscle damaged parameters (CK and muscle soreness).

Pomegranate

Pomegranate was also studied (Trombold et al., 2011) with interesting and positive results. In this study, the ingestion of pomegranate juice was associated with the attenuation of weakness and reduction of soreness in the elbow flexor muscles. Pomegranate is considered a potent and unique polyphenol-rich food, containing mainly ellagitannins and their derived metabolites, which can protect against most types of free radical oxidants (Visioli et al., 2011).

To date, pomegranate's capacity to inhibit oxidative processes, and to accelerate the breakdown and the removal of oxidized lipids, has still been more studied in the health field, namely regarding atherosclerosis development and its consequent cardiovascular events (Aviram et al., 2000, 2004; Visioli et al., 2011).

Other potential solutions

Taking into account the evidence discussed throughout this review, there are some other foods that, although not studied yet, might also have the potential to be considered as an effective solution for EIMD recovery. Therefore, the following examples were chosen due to their nutritional characteristics and may be considered in future investigations.

Meat and fish, although may not be considered as conventional as liquid options, can also be a valuable alternative not only due to their content in proteins with high-biological value (Guigoz, 2011), but also because they are one of the richest sources of some compounds mentioned above, namely LA, CoQ_{10} and PUFAs. Moreover, fatty fishes as salmon, tuna and mackerel may also be a good choice due to their high amounts in *n*-3 PUFAs (Insel et al., 2007). Beef has already shown to be capable of stimulating MPS from young to old persons (Robinson et al., 2013; Symons

et al., 2007); however, to date, no studies regarding muscle damage have been conducted.

Egg may also be a valid option since it has a biologic value of 100, meaning that all the absorbed egg protein is retain by the body (Insel et al., 2007). Egg protein was already used to study MPS (Moore et al., 2009); however, to date, no study has used eggs to investigate recovery from EIMD.

In contrast to the other plant foods, the protein isolated from soya beans provides a complete, high-quality protein equal to the animal protein (Young, 1991). Soya protein is considered a fast protein since it is digested rapidly, leading to a large but transient rise in aminoacidemia (Wilkinson et al., 2007). Yet, compared to fluid milk, it seems to lead to a less acute rise in muscle protein synthesis (Wilkinson et al., 2007). This may be due to the fact that the leucinemia is greater and more prolonged with milk consumption than with soya, probably reflecting the higher leucine content of whey proteins (Phillips, 2011). Nevertheless, soya beverages can be used, for example, when there is a contraindication for milk consumption, such as cow's milk-protein allergy or lactose intolerance.

Typical sources of CHO include bread, pasta, rice, potatoes, beans and fruit. Athletes may choose the type of CHO-rich food to consume according to the glycemic index (GI), the individual goals of each athlete and the timing of ingestion (Mondazzi & Arcelli, 2009). Fruit, in addition to have a high content in minerals, vitamins and antioxidants, is also a rich source of CHO, namely fructose and glucose. It has been shown (Jeukendrup, 2010) that when a combination of several CHO, specially glucose and fructose, is used instead of just one, the CHO absorption could be increased. This phenomenon is due to the utilization of different intestinal transporters for absorption (Jeukendrup, 2010). Particularly, the mixture glucose–fructose, namely the one with a 1:1 ratio, seems to produce one of the highest exogenous carbohydrate absorption rates (Jeukendrup, 2010). Therefore, ingesting a mixture of glucose and fructose seems to provide an optimal balance of dietary CHO for both muscle (Wallis et al., 2008) and liver (Casey et al., 2000) glycogen re-synthesis. Regarding the antioxidant potential of fruits, other berries may also be of interest for future studies, e.g. strawberries, raspberries and blackberries.

Tea is also known for its antioxidant content. Tea is originated from the leaves of *Camellia sinensis* L. and, according to the fermentation process, one can obtain green (not fermented), oolong (partially fermented) and black tea (fermented) (Lin et al., 2003). Green tea is considered an important dietary source of polyphenols, particularly flavonoids (Cabrera et al., 2006), being catechins the main flavonoid present (McKay & Blumberg, 2002). Catechins – especially EGCG – which are found in higher amounts in green tea than in black or oolong, are considered to have strong antioxidant potential, extensively demonstrated by *in vitro* and animal studies (Cabrera et al., 2006), and anti-inflammatory properties (Cabrera et al., 2006). Therefore, as the human clinical evidence is still scarce, future studies are needed in order to define the magnitude of the possible benefits and to establish, if it is the case, safe ranges of consumptions related to its benefits (Chacko et al., 2010).

Along with their high content in vitamins and minerals, unsaturated fatty acids and fibre, nuts enclose several phyto-chemicals that have been shown to possess a range of bioactive actions, including antioxidant and anti-inflammatory properties (Bolling et al., 2010; Chen & Blumberg, 2008). In fact, the consumption of nuts has been inversely associated with bio-markers of inflammation (Jiang et al., 2006). Regarding the antioxidant properties, it has been attributed mostly to their phenolic compounds, but a limited number of studies are available (Chen & Blumberg, 2008).

Conclusions

Due to the fact that EIMD can impair athletes' ability to train and perform properly, developing strategies that meliorate and accelerate the recovery process after muscle damage are of huge importance for the athletic population. Accelerating this process will result in shorter recovery periods that will allow athletes to return sooner to their normal training routine.

Although there are few studies that relate food and recovery from EIMD, the results available seem promising. Moreover, it is important to bear in mind the current issues related to the potential contamination of the nutritional supplements that athletes often use as a recovery strategy. Therefore, considering food as a potential mean to recover from muscle damage becomes even more important, since it is not contaminated with prohibitive compounds.

Some foods enclose potential to be considered an effective recovery option, especially if combined to ensure the delivery of protein, carbohydrates, antioxidants and anti-inflammatory nutrients. Beyond milk, cherries, blueberries and pomegranates, that were already successfully tested regarding EIMD, other foods are considered to be possible solutions to help in the recovery process from muscle damage. These foods include protein sources as milk, meat, fish, eggs and soy, carbohydrate-rich foods, for instance bread, pasta, rice, potatoes, beans and fruit, and foods with a high content in antioxidant and/or anti-inflammatory nutrients, such as other berries, tea and nuts.

It is clear, therefore, that more studies in this specific filed are needed. It is fundamental to have scientific evidence about which types or combination of foods can improve the recovery from EIMD.

Declaration of interest

Mónica Sousa acknowledges the Fundação para a Ciência e a Tecnologia (FCT) regarding the grant SFRH/BD/75276/2010. Vítor Hugo Teixeira acknowledges the FCT for the funded project PEst-OE/SAU/UI0617/2011. The authors acknowledge Alessandro Bini for the language revision.

References

Allen DG. 2001. Eccentric muscle damage: mechanisms of early reduction of force. Acta Physiol Scand 171:311–319.

Aragon AA, Schoenfeld BJ. 2013. Nutrient timing revisited: is there a post-exercise anabolic window? J Int Soc Sports Nutr 10:5.

Arbogast S, Reid MB. 2004. Oxidant activity in skeletal muscle fibers is influenced by temperature, CO2 level, and muscle-derived nitric oxide. Am J Physiol Regul Integr Comp Physiol 287:R698–R705.

Arnold L, Henry A, Poron F, Baba-Amer Y, Van Rooijen N, Plonquet A, Gherardi RK, Chazaud B. 2007. Inflammatory monocytes recruited after skeletal muscle injury switch into antiinflammatory macrophages to support myogenesis. J Exp Med 204:1057–1069.

Aviram M, Dornfeld L, Rosenblat M, Volkova N, Kaplan M, Coleman R, Hayek T, et al. 2000. Pomegranate juice consumption reduces oxidative stress, atherogenic modifications to LDL, and platelet aggregation: studies in humans and in atherosclerotic apolipoprotein E-deficient mice. Am J Clin Nutr 71:1062–1076.

Aviram M, Rosenblat M, Gaitini D, Nitecki S, Hoffman A, Dornfeld L, Volkova N, et al. 2004. Pomegranate juice consumption for 3 years by patients with carotid artery stenosis reduces common carotid intima-media thickness, blood pressure and LDL oxidation. Clin Nutr 23: 423–433.

Basu A, Rhone M, Lyons TJ. 2010. Berries: emerging impact on cardiovascular health. Nutr Rev 68:168–177.

Baty JJ, Hwang H, Ding Z, Bernard JR, Wang B, Kwon B, Ivy JL. 2007. The effect of a carbohydrate and protein supplement on resistance exercise performance, hormonal response, and muscle damage. J Strength Cond Res 21:321–329.

Beaton LJ, Allan DA, Tarnopolsky MA, Tiidus PM, Phillips SM. 2002. Contraction-induced muscle damage is unaffected by vitamin E supplementation. Med Sci Sports Exerc 34:798–805.

Beelen M, Burke LM, Gibala MJ, Van Loon LJC. 2010. Nutritional strategies to promote postexercise recovery. Int J Sport Nutr Exerc Metab 20:515–532.

Bentinger M, Tekle M, Dallner G. 2010. Coenzyme Q – Biosynthesis and functions. Biochem Biophys Res Commun 396:74–79.

Betts JA, Williams C. 2010. Short-term recovery from prolonged exercise: exploring the potential for protein ingestion to accentuate the benefits of carbohydrate supplements. Sports Med 40:941–959.

Biewenga GP, Haenen GRMM, Bast A. 1997. The pharmacology of the antioxidant: lipoic acid. Gen Pharmacol 29:315–331.

Bilska A, Włodek L. 2005. Lipoic acid – the drug of the future? Pharmacol Rep 57:570–577.

Bird S, Tarpenning K, Marino F. 2006. Liquid carbohydrate/essential amino acid ingestion during a short-term bout of resistance exercise suppresses myofibrillar protein degradation. Metabolism 55: 570–577.

Bjelakovic G, Nikolova D, Gluud LL, Simonetti RG, Gluud C. 2007. Mortality in randomized trials of antioxidant supplements for primary and secondary prevention: systematic review and meta-analysis. JAMA 297:842–857.

Boirie Y, Dangin M, Gachon P, Vasson M, Maubois J, Beaufrere B. 1997. Slow and fast dietary proteins differently modulate postprandial protein accretion. Proc Natl Acad Sci USA 94:14930–14935.

Bolling BW, McKay DL, Blumberg JB. 2010. The phytochemical composition and antioxidant actions of tree nuts. Asia Pac J Clin Nutr 19:117–123.

Børsheim E, Cree MG, Tipton KD, Elliott TA, Aarsland A, Wolfe RR. 2004. Effect of carbohydrate intake on net muscle protein synthesis during recovery from resistance exercise. J Appl Physiol 96:674–678.

Bos C, Metges CC, Gaudichon C, Petzke KJ, Pueyo ME, Morens C, Everwand J, et al. 2003. Postprandial kinetics of dietary amino acids are the main determinant of their metabolism after soy or milk protein ingestion in humans. J Nutr 133:1308–1315.

Boveris A, Oshino N, Chance B. 1972. The cellular production of hydrogen peroxide. Biochem J 128:617–630.

Bowtell JL, Sumners DP, Dyer A, Fox P, Mileva KN. 2011. Montmorency cherry juice reduces muscle damage caused by intensive strength exercise. Med Sci Sports Exerc 43:1544–1551.

Breen L, Tipton KD, Jeukendrup AE. 2010. No effect of carbohydrate-protein on cycling performance and indices of recovery. Med Sci Sports Exerc 42:1140–1148.

Brickson S, Ji LL, Schell K, Olabisi R, St. Pierre Schneider B, Best TM. 2003. M1/70 attenuates blood-borne neutrophil oxidants, activation, and myofiber damage following stretch injury. J Appl Physiol 95: 969–976.

Burke LM, Castell LM, Stear SJ. 2009. BJSM reviews: A-Z of supplements: dietary supplements, sports nutrition foods and ergogenic aids for health and performance Part 1. Br J Sports Med 43:728–729.

Cabrera C, Artacho R, Giménez R. 2006. Beneficial effects of green tea – a review. J Am Coll Nutr 25:79–99.

Calder PC. 2006. *n*-3 Polyunsaturated fatty acids, inflammation, and inflammatory diseases. Am J Clin Nutr 83:1505S–1519S.

Calder PC. 2007. Immunomodulation by omega-3 fatty acids. Prostaglandins Leukot Essent Fatty Acids 77:327–335.

Calder PC. 2009. Polyunsaturated fatty acids and inflammatory processes: new twists in an old tale. Biochimie 91:791–795.

Calder PC, Yaqoob P, Harvey DJ, Watts A, Newsholme EA. 1994. Incorporation of fatty acids by concanavalin A-stimulated lymphocytes and the effect on fatty acid composition and membrane fluidity. Biochem J 300:509–518.

Cannon JG, St. Pierre BA. 1998. Cytokines in exertion-induced skeletal muscle injury. Mol Cell Biochem 179:159–167.

Carr A, Frei B. 1999. Does vitamin C act as a pro-oxidant under physiological conditions? FASEB J 13:1007–1024.

Casey A, Mann R, Banister K, Fox J, Morris PG, Macdonald IA, Greenhaff PL. 2000. Effect of carbohydrate ingestion on glycogen resynthesis in human liver and skeletal muscle, measured by 13C MRS. Am J Physiol Endocrinol Metab 278:E65–E75.

Chacko SM, Thambi PT, Kuttan R, Nishigaki I. 2010. Beneficial effects of green tea: a literature review. Chin Med 5:13.

Chen CYO, Blumberg JB. 2008. Phytochemical composition of nuts. Asia Pac J Clin Nutr 17:329–332.

Cheung K, Hume PA, Maxwell L. 2003. Delayed onset muscle soreness: treatment strategies and performance factors. Sports Med 33:145–164.

Childs A, Jacobs C, Kaminski T, Halliwell B, Leeuwenburgh C. 2001. Supplementation with vitamin C and N-acetyl-cysteine increases oxidative stress in humans after an acute muscle injury induced by eccentric exercise. Free Radic Biol Med 31:745–753.

Churchley EG, Coffey VG, Pedersen DJ, Shield A, Carey KA, Cameron-Smith D, Hawley JA. 2007. Influence of preexercise muscle glycogen content on transcriptional activity of metabolic and myogenic genes in well-trained humans. J Appl Physiol 102:1604–1611.

Clarkson PM, Hubal MJ. 2002. Exercise-induced muscle damage in humans. Am J Phys Med Rehabil 81:S52–S69.

Clarkson PM, Thompson HS. 2000. Antioxidants: what role do they play in physical activity and health? Am J Clin Nutr 72:637s–646s.

Cockburn E, Bell PG, Stevenson E. 2013. Effect of milk on team sport performance after exercise-induced muscle damage. Med Sci Sports Exerc 45:1585–1592.

Cockburn E, Hayes PR, French DN, Stevenson E, St Clair Gibson A. 2008. Acute milk-based protein-CHO supplementation attenuates exercise-induced muscle damage. Appl Physiol Nutr Metab 33: 775–783.

Cockburn E, Stevenson E, Hayes PR, Robson-Ansley P, Howatson G. 2010. Effect of milk-based carbohydrate-protein supplement timing on the attenuation of exercise induced muscle damage. Appl Physiol Nutr Metab 35:270–277.

Connolly Da J, McHugh MP, Padilla-Zakour OI. 2006. Efficacy of a tart cherry juice blend in preventing the symptoms of muscle damage. Br J Sports Med 40:679–683.

Coombes JS, Powers SK, Rowell B, Hamilton KL, Dodd SL, Shanely RA, Sen CK, Packer L. 2001. Effects of vitamin E and α-lipoic acid on skeletal muscle contractile properties. J Appl Physiol 90:1424–1430.

Costill DL, Pascoe DD, Fink WJ, Robergs RA, Barr SI, Pearson D. 1990. Impaired muscle glycogen resynthesis after eccentric exercise. J Appl Physiol 69:46–50.

Cotelle N. 2001. Role of flavonoids in oxidative stress. Curr Top Med Chem 1:569–590.

Creer A, Gallagher P, Slivka D, Jemiolo B, Fink W, Trappe S. 2005. Influence of muscle glycogen availability on ERK1/2 and Akt signaling after resistance exercise in human skeletal muscle. J Appl Physiol 99:950–956.

Crozier SJ, Kimball SR, Emmert SW, Anthony JC, Jefferson LS. 2005. Oral leucine administration stimulates protein synthesis in rat skeletal muscle. J Nutr 135:376–382.

Cuthbertson D, Smith K, Babraj J, Leese G, Waddell T, Atherton P, Wackerhage H, et al. 2005. Anabolic signaling deficits underlie amino acid resistance of wasting, aging muscle. FASEB J 19:422–424.

Dangin M, Guillet C, Garcia-Rodenas C, Gachon P, Bouteloup-Demange C, Reiffers-Magnani K, Fauquant J, et al. 2003. The rate of protein digestion affects protein gain differently during aging in humans. J Physiol 549:635–644.

Defuria J, Bennett G, Strissel KJ, Perfield Ii JW, Milbury PE, Greenberg AS, Obin MS. 2009. Dietary blueberry attenuates whole-body insulin resistance in high fat-fed mice by reducing adipocyte death and its inflammatory sequelae. J Nutr 139:1510–1516.

Di Meo S, Venditti P. 2001. Mitochondria in exercise-induced oxidative stress. Biol Signals Recept 10:125–140.

Díaz-Castro J, Guisado R, Kajarabille N, García C, Guisado IM, De Teresa C, Ochoa JJ. 2012. Coenzyme Q10 supplementation ameliorates inflammatory signaling and oxidative stress associated with strenuous exercise. Eur J Nutr 51:791–799.

Djordjevic B, Baralic I, Kotur-Stevuljevic J, Stefanovic A, Ivanisevic J, Radivojevic N, Andjelkovic M, Dikic N. 2012. Effect of astaxanthin supplementation on muscle damage and oxidative stress markers in elite young soccer players. J Sports Med Phys Fitness 52:382–392.

Doyle JA, Sherman WM, Strauss RL. 1993. Effects of eccentric and concentric exercise on muscle glycogen replenishment. J Appl Physiol 74:1848–1855.

Ebbeling CB, Clarkson PM. 1989. Exercise-induced muscle damage and adaptation. Sports Med 7:207–234.

Ehlenfeldt MK, Prior RL. 2001. Oxygen radical absorbance capacity (ORAC) and phenolic and anthocyanin concentrations in fruit and leaf tissues of highbush blueberry. J Agric Food Chem 49:2222–2227.

Enoka RM. 1996. Eccentric contractions require unique activation strategies by the nervous system. J Appl Physiol 81:2339–2346.

Evans WJ. 2000. Vitamin E, vitamin C, and exercise. Am J Clin Nutr 72: 647S–652S.

Evans WJ, Cannon JG. 1991. The metabolic effects of exercise-induced muscle damage. Exerc Sport Sci Rev 19:99–125.

Favero TG. 1999. Sarcoplasmic reticulum Ca2+ release and muscle fatigue. J Appl Physiol 87:471–483.

Ferretti G, Bacchetti T, Belleggia A, Neri D. 2010. Cherry antioxidants: from farm to table. Molecules 15:6993–7005.
Fielding RA, Manfredi TJ, Ding W, Fiatarone MA, Evans WJ, Cannon JG. 1993. Acute phase response in exercise III. Neutrophil and IL-1β accumulation in skeletal muscle. Am J Physiol Regul Integr Comp Physiol 265:R166–R172.
Finaud J, Lac G, Filaire E. 2006. Oxidative stress: relationship with exercise and training. Sports Med 36:327–358.
Fogarty MC, Devito G, Hughes CM, Burke G, Brown JC, McEneny J, Brown D, et al. 2013. Effects of α-lipoic acid on mtDNA damage after isolated muscle contractions. Med Sci Sports Exerc 45:1469–1477.
Galli C, Calder PC. 2009. Effects of fat and fatty acid intake on inflammatory and immune responses: a critical review. Ann Nutr Metab 55:123–139.
García-Lafuente A, Guillamón E, Villares A, Rostagno MA, Martínez JA. 2009. Flavonoids as anti-inflammatory agents: implications in cancer and cardiovascular disease. Inflamm Res 58:537–552.
Gerber M. 2003. Biofactors in the Mediterranean diet. Clin Chem Lab Med 41:999–1004.
Gomes EC, Silva AN, de Oliveira MR. 2012. Oxidants, antioxidants, and the beneficial roles of exercise-induced production of reactive species. Oxid Med Cell Longev 2012:756132.
González-Gallego J, García-Mediavilla MV, Sánchez-Campos S, Tuñó MJ. 2010. Fruit polyphenols, immunity and inflammation. Br J Nutr 104:S15–S27.
Gorąca A, Huk-Kolega H, Piechota A, Kleniewska P, Ciejka E, Skibska B. 2011. Lipoic acid – biological activity and therapeutic potential. Pharmacol Rep 63:849–858.
Green MS, Corona BT, Doyle JA, Ingalls CP. 2008. Carbohydrate-protein drinks do not enhance recovery from exercise-induced muscle injury. Int J Sport Nutr Exerc Metab 18:1–18.
Guigoz Y. 2011. Dietary proteins in humans: basic aspects and consumption in Switzerland. Int J Vitam Nutr Res 81:87–100.
Gülçin I. 2012. Antioxidant activity of food constituents: an overview. Arch Toxicol 86:345–391.
Halliwell B. 2000. The antioxidant paradox. Lancet 355:1179–1180.
Hampton MB, Kettle AJ, Winterbourn CC. 1998. Inside the neutrophil phagosome: oxidants, myeloperoxidase, and bacterial killing. Blood 92:3007–3017.
Hawley JA, Tipton KD, Millard-Stafford ML. 2006. Promoting training adaptations through nutritional interventions. J Sports Sci 24:709–721.
Heim KE, Tagliaferro AR, Bobilya DJ. 2002. Flavonoid antioxidants: chemistry, metabolism and structure-activity relationships. J Nutr Biochem 13:572–584.
Howatson G, Hoad M, Goodall S, Tallent J, Bell PG, French DN. 2012. Exercise-induced muscle damage is reduced in resistance-trained males by branched chain amino acids: a randomized, double-blind, placebo controlled study. J Int Soc Sports Nutr 9:20.
Howatson G, McHugh MP, Hill JA, Brouner J, Jewell AP, Van Someren KA, Shave RE, Howatson SA. 2010. Influence of tart cherry juice on indices of recovery following marathon running. Scand J Med Sci Sports 20:843–852.
Howatson G, Van Someren KA. 2008. The prevention and treatment of exercise-induced muscle damage. Sports Med 38:483–503.
Howell JN, Chleboun G, Conatser R. 1993. Muscle stiffness, strength loss, swelling and soreness following exercise-induced injury in humans. J Physiol 464:183–196.
Ingalls CP, Warren GL, Armstrong RB. 1998. Dissociation of force production from MHC and actin contents in muscles injured by eccentric contractions. J Muscle Res Cell Motil 19:215–224.
Insel PM, Turner RE, Ross D. 2007. Nutrition. Sudburt (MA): Jones and Bartlett Publishers.
Jackman SR, Witard OC, Jeukendrup AE, Tipton KD. 2010. Branched-chain amino acid ingestion can ameliorate soreness from eccentric exercise. Med Sci Sports Exerc 42:962–970.
Jeukendrup AE. 2010. Carbohydrate and exercise performance: the role of multiple transportable carbohydrates. Curr Opin Clin Nutr Metab Care 13:452–457.
Jiang R, Jacobs Jr DR, Mayer-Davis E, Szklo M, Herrington D, Jenny NS, Kronmal R, Barr RG. 2006. Nut and seed consumption and inflammatory markers in the Multi-Ethnic Study of Atherosclerosis. Am J Epidemiol 163:222–231.
Karp JR, Johnston JD, Tecklenburg S, Mickleborough TD, Fly AD, Stager JM. 2006. Chocolate milk as a post-exercise recovery aid. Int J Sport Nutr Exerc Metab 16:78–91.
Kelly MK, Wicker RJ, Barstow TJ, Harms CA. 2009. Effects of N-acetylcysteine on respiratory muscle fatigue during heavy exercise. Respir Physiol Neurobiol 165:67–72.
Kerksick CM, Kreider RB, Willoughby DS. 2010. Intramuscular adaptations to eccentric exercise and antioxidant supplementation. Amino Acids 39:219–232.
Kew S, Mesa MD, Tricon S, Bitckley R, Minihane AM, Yaqoob P. 2004. Effects of oils rich in eicosapentaenoic and docosahexaenoic acids on immune cell composition and function in healthy humans. Am J Clin Nutr 79:674–681.
Komulainen J, Kalliokoski R, Koskinen SOA, Drost MR, Kuipers H, Hesselink MKC. 2000. Controlled lengthening or shortening contraction-induced damage is followed by fiber hypertrophy in rat skeletal muscle. Int J Sports Med 21:107–112.
Kon M, Tanabe K, Akimoto T, Kimura F, Tanimura Y, Shimizu K, Okamoto T, Kono I. 2008. Reducing exercise-induced muscular injury in kendo athletes with supplementation of coenzyme Q10. Br J Nutr 100:903–909.
Koopman R, Beelen M, Stellingwerff T, Pennings B, Saris WHM, Kies AK, Kuipers H, Van Loon LJC. 2007. Coingestion of carbohydrate with protein does not further augment postexercise muscle protein synthesis. Am J Physiol Endocrinol Metab 293:E833–E842.
Kozlov AV, Gille L, Staniek K, Nohl H. 1999. Dihydrolipoic acid maintains ubiquinone in the antioxidant active form by two-electron reduction of ubiquinone and one-electron reduction of ubisemiquinone. Arch Biochem Biophys 363:148–154.
Leeuwenburgh C, Heinecke JW. 2001. Oxidative stress and antioxidants in exercise. Curr Med Chem 8:829–838.
Lemon PWR, Mullin JP. 1980. Effect of initial muscle glycogen levels on protein catabolism during exercise. J Appl Physiol 48:624–629.
Lin YS, Tsai YJ, Tsay JS, Lin JK. 2003. Factors affecting the levels of tea polyphenols and caffeine in tea leaves. J Agric Food Chem 51: 1864–1873.
Littarru GP, Tiano L. 2010. Clinical aspects of coenzyme Q10: an update. Nutrition 26:250–254.
Luden ND, Saunders MJ, Todd MK. 2007. Postexercise carbohydrate-protein-antioxidant ingestion decreases plasma creatine kinase and muscle soreness. Int J Sport Nutr Exerc Metab 17:109–123.
MacDougall JD, Ray S, Sale DG, McCartney N, Lee P, Garner S. 1999. Muscle substrate utilization and lactate production during weightlifting. Can J Appl Physiol 24:209–215.
Machefer G, Groussard C, Zouhal H, Vincent S, Youssef H, Faure H, Malardé L, Gratas-Delamarche A. 2007. Nutritional and plasmatic antioxidant vitamins status of ultra endurance athletes. J Am Coll Nutr 26:311–316.
Malm C, Lenkei R, Sjödin B. 1999. Effects of eccentric exercise on the immune system in men. J Appl Physiol 86:461–468.
Malm C, Svensson M, Sjöberg B, Ekblom B, Sjödin B. 1996. Supplementation with ubiquinone-10 causes cellular damage during intense exercise. Acta Physiol Scand 157:511–512.
Marzocchella L, Fantini M, Benvenuto M, Masuelli L, Tresoldi I, Modesti A, Bei R. 2011. Dietary flavonoids: molecular mechanisms of action as anti-inflammatory agents. Recent Pat Inflamm Allergy Drug Discov 5: 200–220.
Matsumoto K, Koba T, Hamada K, Sakurai M, Higuchi T, Miyata H. 2009. Branched-chain amino acid supplementation attenuates muscle soreness, muscle damage and inflammation during an intensive training program. J Sports Med Phys Fitness 49:424–431.
Maughan RJ, King DS, Lea T. 2004. Dietary supplements. J Sports Sci 22:95–113.
McCune LM, Kubota C, Stendell-Hollis NR, Thomson CA. 2011. Cherries and health: a review. Crit Rev Food Sci Nutr 51:1–12.
McGinley C, Shafat A, Donnelly AE. 2009. Does antioxidant vitamin supplementation protect against muscle damage? Sports Med 39: 1011–1032.
McKay DL, Blumberg JB. 2002. The role of tea in human health: an update. J Am Coll Nutr 21:1–13.
McLeay Y, Barnes MJ, Mundel T, Hurst SM, Hurst RD, Stannard SR. 2012. Effect of New Zealand blueberry consumption on recovery from eccentric exercise-induced muscle damage. J Int Soc Sports Nutr 9:19.
Medjakovic S, Jungbauer A. 2013. Pomegranate: a fruit that ameliorates metabolic syndrome. Food Funct 4:19–39.
Mickleborough TD. 2013. Omega-3 polyunsaturated fatty acids in physical performance optimization. Int J Sport Nutr Exerc Metab 23: 83–96.

Mondazzi L, Arcelli E. 2009. Glycemic index in sport nutrition. J Am Coll Nutr 28:455S–463S.

Moore DR, Robinson MJ, Fry JL, Tang JE, Glover EI, Wilkinson SB, Prior T, et al. 2009. Ingested protein dose response of muscle and albumin protein synthesis after resistance exercise in young men. Am J Clin Nutr 89:161–168.

Nakhostin-Roohi B, Babael P, Rahmani-Nia F, Bohlooli S. 2008. Effect of vitamin C supplementation on lipid peroxidation, muscle damage and inflammation after 30-min exercise at 75% VO_{2max}. J Sports Med Phys Fitness 48:217–224.

Newham DJ, McPhail G, Mills KR, Edwards RHT. 1983. Ultrastructural changes after concentric and eccentric contractions of human muscle. J Neurol Sci 61:109–122.

Nguyen HX, Tidball JG. 2003. Interactions between neutrophils and macrophages promote macrophage killing of rat muscle cells in vitro. J Physiol 547:125–132.

Nieman DC, Henson DA, Davis JM, Dumke CL, Gross SJ, Jenkins DP, Murphy EA, et al. 2007a. Quercetin ingestion does not alter cytokine changes in athletes competing in the Western States endurance run. J Interferon Cytokine Res 27:1003–1011.

Nieman DC, Henson DA, Davis JM, Murphy EA, Jenkins DP, Gross SJ, Carmichael MD, et al. 2007b. Quercetin's influence on exercise-induced changes in plasma cytokines and muscle and leukocyte cytokine mRNA. J Appl Physiol 103:1728–1735.

Nosaka K, Sacco P, Mawatari K. 2006. Effects of amino acid supplementation on muscle soreness and damage. Int J Sport Nutr Exerc Metab 16:620–635.

O'Fallon KS, Kaushik D, Michniak-Kohn B, Dunne CP, Zambraski EJ, Clarkson PM. 2012. Effects of quercetin supplementation on markers of muscle damage and inflammation after eccentric exercise. Int J Sport Nutr Exerc Metab 22:430–437.

O'Reilly KP, Warhol MJ, Fielding RA. 1987. Eccentric exercise-induced muscle damage impairs muscle glycogen repletion. J Appl Physiol 63: 252–256.

Östman B, Sjödin A, Michaëlsson K, Byberg L. 2012. Coenzyme Q10 supplementation and exercise-induced oxidative stress in humans. Nutrition 28:403–417.

Packer L. 1997. Oxidants, antioxidant nutrients and the athlete. J Sports Sci 15:353–363.

Packer L, Kraemer K, Rimbach G. 2001. Molecular aspects of lipoic acid in the prevention of diabetes complications. Nutrition 17: 888–895.

Palazzetti S, Rousseau AS, Richard MJ, Favier A, Margaritis I. 2004. Antioxidant supplementation preserves antioxidant response in physical training and low antioxidant intake. Br J Nutr 91:91–100.

Peake J, Nosaka K, Suzuki K. 2005. Characterization of inflammatory responses to eccentric exercise in humans. Exerc Immunol Rev 11: 64–85.

Pedersen BK, Hoffman-Goetz L. 2000. Exercise and the immune system:regulation, integration, and adaptation. Physiol Rev 80: 1055–1081.

Pendersen BK, Toft AD. 2000. Effects of exercise on lymphocytes and cytokines. Br J Sports Med 34:246–251.

Pergola C, Rossi A, Dugo P, Cuzzocrea S, Sautebin L. 2006. Inhibition of nitric oxide biosynthesis by anthocyanin fraction of blackberry extract. Nitric Oxide 15:30–39.

Peternelj TT, Coombes JS. 2011. Antioxidant supplementation during exercise training: beneficial or detrimental? Sports Med 41: 1043–1069.

Phillips SM. 2011. The science of muscle hypertrophy: making dietary protein count. Proc Nutr Soc 70:100–103.

Powers S, Nelson WB, Larson-Meyer E. 2011a. Antioxidant and vitamin D supplements for athletes: sense or nonsense? J Sports Sci 29: S47–S55.

Powers SK, Jackson MJ. 2008. Exercise-induced oxidative stress: cellular mechanisms and impact on muscle force production. Physiol Rev 88: 1243–1276.

Powers SK, Nelson WB, Hudson MB. 2011b. Exercise-induced oxidative stress in humans: cause and consequences. Free Radic Biol Med 51: 942–950.

Pravst I, Žmitek K, Žmitek J. 2010. Coenzyme Q10 contents in foods and fortification strategies. Crit Rev Food Sci Nutr 50:269–280.

Pritchett K, Bishop P, Pritchett R, Green M, Katica C. 2009. Acute effects of chocolate milk and a commercial recovery beverage on postexercise recovery indices and endurance cycling performance. Appl Physiol Nutr Metab 34:1017–1022.

Proske U, Morgan DL. 2001. Muscle damage from eccentric exercise: mechanism, mechanical signs, adaptation and clinical applications. J Physiol 537:333–345.

Proteggente AR, Pannala AS, Paganga G, Van Buren L, Wagner E, Wiseman S, Van De Put F, et al. 2002. The antioxidant activity of regularly consumed fruit and vegetables reflects their phenolic and vitamin C composition. Free Radic Res 36:217–233.

Rankinen T, Lyytikainen S, Vanninen E, Penttila I, Rauramaa R, Uusitupa M. 1998. Nutritional status of the Finnish elite ski jumpers. Med Sci Sports Exerc 30:1592–1597.

Riccioni G. 2009. Carotenoids and cardiovascular disease. Curr Atheroscler Rep 11:434–439.

Robergs RA, Pearson DR, Costill DL, Fink WJ, Pascoe DD, Benedict MA, Lambert CP, Zachweija JJ. 1991. Muscle glycogenolysis during differing intensities of weight-resistance exercise. J Appl Physiol 70: 1700–1706.

Robinson MJ, Burd NA, Breen L, Rerecich T, Yang Y, Hector AJ, Baker SK, Phillips SM. 2013. Dose-dependent responses of myofibrillar protein synthesis with beef ingestion are enhanced with resistance exercise in middle-aged men. Appl Physiol Nutr Metab 38:120–125.

Rodriguez NR, Di Marco NM, Langley S. 2009. Nutrition and athletic performance. Med Sci Sports Exerc 41:709–731.

Romano-Ely BC, Todd MK, Saunders MJ, St. Laurent T. 2006. Effect of an isocaloric carbohydrate-protein-antioxidant drink on cycling performance. Med Sci Sports Exerc 38:1608–1616.

Ros E, Mataix J. 2006. Fatty acid composition of nuts – implications for cardiovascular health. Br J Nutr 96:S29–S35.

Round JM, Jones DA, Cambridge G. 1987. Cellular infiltrates in human skeletal muscle: exercise induced damage as a model for inflammatory muscle disease? J Neurol Sci 82:1–11.

Roy BD. 2008. Milk: the new sports drink? A review. J Int Soc Sports Nutr 5:15.

Sacheck JM, Blumberg JB. 2001. Role of vitamin E and oxidative stress in exercise. Nutrition 17:809–814.

Samadi A, Gaeini AA, Kordi MR, Rahimi M, Rahnama N, Bambaeichi E. 2012. Effect of various ratios of carbohydrate-protein supplementation on resistance exercise-induced muscle damage. J Sports Med Phys Fitness 52:151–157.

Saunders MJ, Kane MD, Kent Todd M. 2004. Effects of a carbohydrate-protein beverage on cycling endurance and muscle damage. Med Sci Sports Exerc 36:1233–1238.

Saunders MJ, Luden ND, Herrick JE. 2007. Consumption of an oral carbohydrate-protein gel improves cycling endurance and prevents postexercise muscle damage. J Strength Cond Res 21:678–684.

Saunders MJ, Moore RW, Luden ND, Pratt CA, Kies AK. 2009. Carbohydrate and protein hydrolysate coingestion's improvement of late- exercise time-trial performance. Int J Sport Nutr Exerc Metab 19: 136–149.

Schoenfeld BJ. 2012. Does exercise-induced muscle damage play a role in skeletal muscle hypertrophy? J Strength Cond Res 26:1441–1453.

Seeram NP, Momin RA, Nair MG, Bourquin LD. 2001. Cyclooxygenase inhibitory and antioxidant cyanidin glycosides in cherries and berries. Phytomedicine 8:362–369.

Seifert JG, Kipp RW, Amann M, Gazal O. 2005. Muscle damage, fluid ingestion, and energy supplementation during recreational alpine skiing. Int J Sport Nutr Exerc Metab 15:528–536.

Semba RD, Lauretani F, Ferrucci L. 2007. Carotenoids as protection against sarcopenia in older adults. Arch Biochem Biophys 458: 141–145.

Shimomura Y, Yamamoto Y, Bajotto G, Sato J, Murakami T, Shimomura N, Kobayashi H, Mawatari K. 2006. Nutraceutical effects of branched-chain amino acids on skeletal muscle. J Nutr 136:529S–532S.

Silva LA, Pinho CA, Silveira PCL, Tuon T, De Souza CT, Dal-Pizzol F, Pinho RA. 2010. Vitamin E supplementation decreases muscular and oxidative damage but not inflammatory response induced by eccentric contraction. J Physiol Sci 60:51–57.

Skillen RA, Testa M, Applegate EA, Heiden EA, Fascetti AJ, Casazza GA. 2008. Effects of an amino acid-carbohydrate drink on exercise performance after consecutive-day exercise bouts. Int J Sport Nutr Exerc Metab 18:473–492.

Smith C, Kruger MJ, Smith RM, Myburgh KH. 2008. The inflammatory response to skeletal muscle injury: illuminating complexities. Sports Med 38:947–969.

St-Pierre J, Buckingham JA, Roebuck SJ, Brand MD. 2002. Topology of superoxide production from different sites in the mitochondrial electron transport chain. J Biol Chem 277:44784–44790.

Staples AW, Burd NA, West DWD, Currie KD, Atherton PJ, Moore DR, Rennie MJ, et al. 2011. Carbohydrate does not augment exercise-induced protein accretion versus protein alone. Med Sci Sports Exerc 43:1154–1161.

Suzuki K, Sato H, Kikuchi T, Abe T, Nakaji S, Sugawara K, Totsuka M, et al. 1996. Capacity of circulating neutrophils to produce reactive oxygen species after exhaustive exercise. J Appl Physiol 81: 1213–1222.

Symons T, Schutzler S, Cocke T, Chinkes D, Wolfe R, Paddon-Jones D. 2007. Aging does not impair the anabolic response to a protein-rich meal. Am J Clin Nutr 86:451–456.

Szajdek A, Borowska E. 2008. Bioactive compounds and health-promoting properties of berry fruits: a review. Plant Foods Hum Nutr 63:147–156.

Tall JM, Seeram NP, Zhao C, Nair MG, Meyer RA, Raja SN. 2004. Tart cherry anthocyanins suppress inflammation-induced pain behavior in rat. Behav Brain Res 153:181–188.

Tee JC, Bosch AN, Lambert MI. 2007. Metabolic consequences of exercise-induced muscle damage. Sports Med 37:827–836.

Teixeira VH, Valente HF, Casal SI, Marques AF, Moreira PA. 2009. Antioxidants do not prevent postexercise peroxidation and may delay muscle recovery. Med Sci Sports Exerc 41:1752–1760.

Theodorou AA, Nikolaidis MG, Paschalis V, Koutsias S, Panayiotou G, Fatouros IG, Koutedakis Y, Jamurtas AZ. 2011. No effect of antioxidant supplementation on muscle performance and blood redox status adaptations to eccentric training. Am J Clin Nutr 93: 1373–1383.

Tidball JG. 2005. Inflammatory processes in muscle injury and repair. Am J Physiol Regul Integr Comp Physiol 288:R345–R353.

Torres R, Ribeiro F, Alberto Duarte J, Cabri JMH. 2012. Evidence of the physiotherapeutic interventions used currently after exercise-induced muscle damage: systematic review and meta-analysis. Phys Ther Sport 13:101–114.

Trombold JR, Barnes JN, Critchley L, Coyle EF. 2010. Ellagitannin consumption improves strength recovery 2–3 d after eccentric exercise. Med Sci Sports Exerc 42:493–498.

Trombold JR, Reinfeld AS, Casler JR, Coyle EF. 2011. The effect of pomegranate juice supplementation on strength and soreness after eccentric exercise. J Strength Cond Res 25:1782–1788.

Tsao R. 2010. Chemistry and biochemistry of dietary polyphenols. Nutrients 2:1231–1246.

Urso ML, Clarkson PM. 2003. Oxidative stress, exercise, and antioxidant supplementation. Toxicology 189:41–54.

Valentine RJ, Saunders MJ, Todd MK, Laurent TGS. 2008. Influence of carbohydrate-protein beverage on cycling endurance and indices of muscle disruption. Int J Sport Nutr Exerc Metab 18:363–378.

Van Loon LJC, Saris WHM, Kruijshoop M, Wagenmakers AJM. 2000. Maximizing postexercise muscle glycogen synthesis: carbohydrate supplementation and the application of amino acid or protein hydrolysate mixtures. Am J Clin Nutr 72:106–111.

Visioli F, De La Lastra CA, Andres-Lacueva C, Aviram M, Calhau C, Cassano A, D'archivio M, et al. 2011. Polyphenols and human health: a prospectus. Crit Rev Food Sci Nutr 51:524–546.

Vollaard NBJ, Shearman JP, Cooper CE. 2005. Exercise-induced oxidative stress: myths, realities and physiological relevance. Sports Med 35:1045–1062.

Volpi E, Kobayashi H, Sheffield-Moore M, Mittendorfer B, Wolfe RR. 2003. Essential amino acids are primarily responsible for the amino acid stimulation of muscle protein anabolism in healthy elderly adults. Am J Clin Nutr 78:250–258.

Wallis GA, Hulston CJ, Mann CH, Roper HP, Tipton KD, Jeukendrup AE. 2008. Postexercise muscle glycogen synthesis with combined glucose and fructose ingestion. Med Sci Sports Exerc 40:1789–1794.

Wang H, Cao G, Prior RL. 1996. Total antioxidant capacity of fruits. J Agric Food Chem 44:701–705.

Warren GL, Ingalls CP, Lowe DA, Armstrong RB. 2001. Excitation-contraction uncoupling: major role in contraction-induced muscle injury. Exerc Sport Sci Rev 29:82–87.

White JP, Wilson JM, Austin KG, Greer BK, St. John N, Panton LB. 2008. Effect of carbohydrate-protein supplement timing on acute exercise-induced muscle damage. J Int Soc Sports Nutr 35:270–277.

Wilkinson SB, Tarnopolsky MA, Macdonald MJ, Macdonald JR, Armstrong D, Phillips SM. 2007. Consumption of fluid skim milk promotes greater muscle protein accretion after resistance exercise than does consumption of an isonitrogenous and isoenergetic soy-protein beverage. Am J Clin Nutr 85:1031–1040.

Wojcik JR, Walberg-Rankin J, Smith LL, Gwazdauskas FC. 2001. Comparison of carbohydrate and milk-based beverages on muscle damage and glycogen following exercise. Int J Sport Nutr 11:406–419.

Wojtaszewski JFP, Macdonald C, Nielsen JN, Hellsten Y, Grahame Hardie D, Kemp BE, Kiens B, Richter EA. 2003. Regulation of 5′-AMP-activated protein kinase activity and substrate utilization in exercising human skeletal muscle. Am J Physiol Endocrinol Metab 284:E813–E822.

Youdim KA, Mcdonald J, Kalt W, Joseph JA. 2002. Potential role of dietary flavonoids in reducing microvascular endothelium vulnerability to oxidative and inflammatory insults. J Nutr Biochem 13:282–288.

Young VR. 1991. Soy protein in relation to human protein and amino acid nutrition. J Am Diet Assoc 91:828–835.

Zembron-Lacny A, Ostapiuk J, Szyszka K. 2009a. Effects of sulphur-containing compounds on plasma redox status in muscle-damaging exercise. Chin J Physiol 52:289–294.

Zembron-Lacny A, Slowinska-Lisowska M, Szygula Z, Witkowski K, Stefaniak T, Dziubek W. 2009b. Assessment of the antioxidant effectiveness of α-lipoic acid in healthy men exposed to muscle-damaging exercise. J Physiol Pharmacol 60:139–143.