Available online at www.sciencedirect.com

SCIENCE DIRECT®

Nutrition Research 25 (2005) 917–924

NUTRITION RESEARCH

www.elsevier.com/locate/nutres

Oxidative stress in handball players: effect of supplementation with a red orange extract

Francesco P. Bonina[a], Carmelo Puglia[a], Francesco Cimino[b], Domenico Trombetta[b], Giovanni Tringali[c], Anna Maria Roccazzello[c], Elio Insirello[c], Paolo Rapisarda[d], Antonella Saija[b,*]

[a]*Dept. Scienze Farmaceutiche, University of Catania, Viale Andrea Doria 6, 95125 Catania, Italy*
[b]*Dept. Farmaco-Biologico, University of Messina, Contrada Annunziata, 98168 Messina, Italy*
[c]*Istituto Ricerca Medica ed Ambientale (IRMA), Via Paolo Vasta 158C, 95024 Acireale (CT) Italy*
[d]*Istituto Sperimentale per l'Agrumicoltura, Corso Savoia 190, 95024 Acireale (CT), Italy*

Received 15 September 2004; revised 25 August 2005; accepted 13 September 2005

Abstract

Intense physical exercise represents a condition that is often associated with increased production of reactive oxygen species and free radicals in various tissues; supplementation of antioxidants may be desirable to reduce oxidative stress and provide a larger protective margin against its possible consequences. The aim of the present study was to evaluate, in a group of professional handball players, the effects of short-term dietary supplementation with a standardized red orange extract (containing anthocyanins, flavanones, hydroxycinnamic acids, and ascorbic acid; Red Orange Complex [ROC]) on some noninvasive biomarkers of oxidative stress. Eighteen professional handball players and 17 healthy volunteers were enrolled in this study. The supplementation consisted of 50 mg ROC per capsule in micronized form; all subjects were recommended to take 1 capsule twice a day for 2 months. The end points of oxidative stress taken in consideration were the serum total antioxidant status, the serum level of thiol groups, lipid hydroperoxides and malondialdehyde, and the frequency of spontaneous sister chromatide exchanges in peripheral lymphocytes. The results obtained clearly reflect an overall lower level of oxidative stress in the athletes examined after short-term dietary supplementation with the ROC. Dietary supplementation with the ROC (which is endowed with strong antioxidant capacity) is able to decrease oxidative

* Corresponding author. Tel.: +39 90 6766530; fax: +39 90 3533142.
E-mail address: saija@pharma.unime.it (A. Saija).

0271-5317/$ – see front matter
doi:10.1016/j.nutres.2005.09.008

stress and thus might protect against its short- and long-term health consequences in athletes engaged in regular training programs.

Keywords: Red oranges; Cyanidin-3-*O*-glucoside; Antioxidants; Exercise; Human; Dietary supplementation

1. Introduction

Intense physical exercise represents a condition that is often associated with increased production of reactive oxygen species (ROS) and free radicals in various tissues [1,2]. Physical activity increases the generation of free radicals in several ways, including increased cellular oxidative phosphorylation, catecholamine release, prostanoid metabolism, metmyoglobin release from damaged muscle, and radical release from macrophages recruited to repair damaged tissue [3,4].

To prevent oxidative stress, the body contains a large number of enzymatic and nonenzymatic antioxidants that either prevent ROS formation or scavenge radical species. Exercise can produce an imbalance between ROS and antioxidants, which is referred to as oxidative stress. Oxidative stress can lead to damage or destruction of tissue and cell macromolecules, such as lipids, proteins, and nucleic acids. Therefore, oxidative stress has been associated with decreased physical performance, muscular fatigue, muscle damage, and overtraining. Although there is no conclusive evidence that this affects sporting performance in the short term, exercise-induced oxidative stress may have longer-term health consequences.

Because the endogenous amount of antioxidants may not be sufficient to prevent exercise-induced oxidative stress [5], supplementation of antioxidants may be desirable to reduce oxidative stress and provide a larger protective margin against its possible consequences [6,7]. In fact, antioxidant supplements are marketed for and used by athletes as a means to counteract the oxidative stress of exercise. However, the results of studies that investigate whether antioxidant supplementation reduces exercise-induced oxidative stress are not consistent, perhaps because of the differences in the types and timing of the supplement, in the kinds and intensity of the exercises, and in the outcome measures.

Today, much evidence shows that diet supplementation with plant biophenols may be a successful strategy to decrease the risk of pathologic conditions related to free radical overproduction and/or to prevent their complications. In fact, plant-derived biophenols, such as flavonoids and hydroxycinnamic acids, have been shown to possess several biologic properties, many of which may be related, partially at least, to their free radical–scavenging, metal-chelating, and enzyme-inhibiting ability [8,9]. Particularly, cyanidin and its glycosides are considered dietary compounds with a potential beneficial role for human health [10] and are excellent free radical scavengers and metal chelators [11,12].

The Red Orange Complex (ROC) is a standardized red orange extract, obtained from three red orange varieties (*Citrus sinensis* var Moro, Tarocco, and Sanguinello) and has recently been proposed as a new antioxidant food supplement. The main active principles of the ROC are phenolic compounds (anthocyanins, flavanones, and hydroxycinnamic acids) and ascorbic acid, the antioxidant activity of which are well recognized [9,13-15]; in the fresh fruit, these

antioxidant compounds act as a protective system against extreme climatic fluctuations that occur in Sicily's Etna area, where the pigmented orange cultivars grow almost exclusively. A previous study showed that the ROC possesses strong "in vitro" free-radical scavenging/antioxidant activity and "in vivo" photoprotective effectiveness against UV-B–induced skin erythema [16]. Furthermore, in vitro, the ROC was demonstrated as able to protect human skin–derived cells (NTTC 2544 keratinocytes and HFFF2 fibroblasts) against iron-induced lipid peroxidation [17]. Finally, dietary supplementation with the ROC increases serum thiol groups in healthy smoker volunteers [18] and in type 2 diabetic patients [19].

The aim of the present study was to evaluate, in a group of professional handball players, the effects of short-term dietary supplementation with the ROC on some noninvasive biomarkers of oxidative stress. The end points of oxidative stress taken in consideration were the serum total antioxidant status (TAS), the serum level of thiol (SH) groups (an indirect measurement of glutathione activity in serum), lipid hydroperoxides and malondialdehyde (MDA; a final product of lipid peroxidation), and the frequency of spontaneous sister chromatide exchanges (SCEs; a biomarker of early cytogenetic damage) in peripheral lymphocytes.

2. Methods and materials

2.1. Study design

A group of 18 handball players (males, age 18-26 years) engaged in the "*Ecocert Puntese Pallamano*" club (a team with high training loads and performing competition sessions in the A2 division, Catania, Italy) were enrolled in the present study. The trial was started 1 month after the beginning of the competition season (spring 2002); all blood samples were obtained from each player 3 days before an official meeting.

A sex- and age-matched control group of sedentary, healthy individuals (17 males, aged 19-30 years) recruited from IRMA (Istituto Ricerca Medica ed Ambientale, Acireale, CT, Italy) were used as controls and underwent the same experimental schedule.

The study was conducted in accordance with the Declaration of Helsinki; written informed consent was obtained from each subject participating in the study, which was approved by the local ethics committee. All subjects were submitted to a routine clinical checkup, including hematology and liver and kidney function tests; they were taking no medication (including vitamin and antioxidant supplements) and were required not to modify their dietary habits during the course of the study. Exclusion criteria were obesity, active smoking, occupational exposure to toxic agents, the use of antioxidant dietary supplementation, and vegetarian dietary habits.

The ROC was a gift from Bionap (Rome, Italy). It was obtained by a patented process from oranges of three pigmented *Citrus sinensis* varieties (Moro, Tarocco, and Sanguinello) and was composed of 3.1% anthocyanins (cyanidin-3-glucoside), 2.07% hydroxycinnamic acids (caffeic, cumaric, ferulic, and sinapic acids), 8.1% flavanone glycosides (narirutin and hesperedin), and 7% ascorbic acid.

The supplementation consisted of 50 mg ROC per capsule in micronized form. All subjects were recommended to take 1 capsule twice a day (breakfast and bedtime).

Compliance was checked by counting the remaining capsules. During the first visit, baseline measurements were made; thereafter, the treatment was started. The patients were reassessed after 1 and 2 months.

2.2. Analytical methods

At the beginning of the study and after 1 and 2 months, blood samples were taken from the antecubital vein of the fasting patients. Blood biochemistry parameters were measured by routine laboratory kits.

The serum TAS and the serum levels of SH groups, lipid hydroperoxides, and MDA were measured according to the methods described by Rice-Evans and Miller [20], Ellman [21], Cornelli et al [22], and Gerard-Monnier et al [23], respectively, by means of commercial kits purchased from Randox Laboratories Ltd (Crumlin, UK) for TAS, from Diacron (Grosseto, Italy) for total thiol groups (−SHp test) and lipid hydroperoxides (D-Roms test), and from Calbiochem-Novabiochem Corporation (La Jolla, Calif) for MDA. Briefly, the technique used to determine the TAS measures the relative ability of antioxidant substances to scavenge the 2,2′ -azinobis(3-ethylbenzothiazoline-6-sulfonate) radical cation ($ABTS^{\bullet+}$), generated in the aqueous phase from ABTS through the peroxidative action of metmyoglobin; the radical cation $ABTS^{\bullet+}$ is a blue-green chromogen with a characteristic absorption at 734 nm. The SH group determination system uses 5,5′ -dithiobis-2-nitrobenzoic acid, which reacts specifically with thiol groups to give a highly colored yellow anion measured at 405 nm. The lipid hydroperoxide determination system is based on the ability of transition metals to catalyze in the presence of peroxides with formation of radicals that are trapped by an alkylamine; the alkylamine reacts forming a colored radical detectable at 505 nm; the results are expressed as Carratelli units (U Carr). The MDA determination system uses a chromogenic reagent, which reacts with MDA at 45°C to give a stable chromophore with maximal absorbance at 586 nm.

To determine spontaneous SCE frequency, 0.8 mL of whole heparinized blood was cultured in 10 mL RPMI-1640 medium (Biochrom, Berlin, Germany) supplemented with 20% fetal calf serum, 2% phytohemagglutinin, 100 U/mL penicillin, and 100 μg/mL streptomycin (all from Biochrom). The cultures were incubated at 37°C for 70 hours in an atmosphere of 5% CO_2 in air. 5-Bromo-2-deoxyuridine (Fluka, Milan, Italy) was used to identify the first and subsequent metaphases and was added at a concentration of 10 μg/mL at 24 hours of culture. Colchicine (0.2 μg/mL) was added 2 hours before harvesting to arrest the cells at metaphase. After hypotonic treatment (0.75 mol/L KCl at 37°C for 15 minutes) and fixation in Carnoy (3:1 methanol-acetic acid), the cells were resuspended and dropped onto clean slides. The slides were stained with fluorescence dye Hoechst 33258 (Fluka) and then by the Giemsa staining solution (Sigma, Milan, Italy) [24]. All slides were blindly coded and scored by one investigator to minimize observer bias. The second division metaphase with more than 46 chromosomes and good differential staining was selected for the scoring of SCEs. About 20 second division metaphases were randomly selected and scored as SCE per cell.

2.3. Statistical analysis

Data are expressed as mean ± SD; they were analyzed using the 2-way analysis of variance. A level of probability of less than .05 was taken as indicating statistical significance.

3. Results and discussion

In the present study, we have evaluated the effects on some noninvasive biomarkers of oxidative damage of a 2-month dietary supplementation with the ROC in a group of athletes under regular training. The results are reported in Table 1.

The D-Roms method evaluates serum lipid peroxidation by determining lipid hydroperoxides, thus reflecting the oxidative alterations taking place in several pathologic conditions [25,26]. At the onset of our study, before beginning the dietary supplementation, serum lipid hydroperoxide levels measured in the players appeared significantly higher than in controls. However, in the group of players, ROC administration elicited a marked decrease in D-Rom values toward values suggestive of a normal oxidative stress status.

One of the most reliable indices of exercise-induced oxidant production is blood thiol oxidation [27-29]. Cellular thiols are critically important in maintaining the cellular antioxidant defense network; in addition, thiols play a key role in regulating redox-sensitive signal transduction process. Also, the TAS test is used as an indicator of exercise-related oxidative stress, although its results may be significantly affected by various endogenous components (particularly plasma urate and total protein levels) and technical details (plasma dilution, use of inhibition percentage at a fixed time without considering the length of inhibition time, etc) [30]. At the beginning of our study, serum TAS and SH group levels appeared significantly lower in players than in controls. After 2 months of ROC supplementation, both these parameters appeared unmodified in healthy subjects, but almost completely restored in players.

Aldehydes and especially MDA have been frequently used as markers of oxidative damage. In trained athletes, we found, at the beginning of the study, circulating MDA levels

Table 1
Blood measurements of oxidative stress/antioxidant capacity and of lymphocyte SCE frequency in professional handball players and healthy subjects enrolled in the trial

Parameters	Treatments					
	Controls			Players		
	Inclusion	1 mo	2 mo	Inclusion	1 mo	2 mo
Lipid hydroperoxides (U Carr)	275 ± 25	277 ± 22	288 ± 25	369 ± 31[a]	298 ± 42[b]	259 ± 38[b]
TAS (mmol/L Trolox)	1.05 ± 0.16	1.08 ± 0.14	1.18 ± 0.14	0.51 ± 0.24[a]	1.01 ± 0.33[b]	1.19 ± 0.32[b]
SH groups (μmol/L)	472 ± 52	475 ± 82	458 ± 73	376 ± 41[a]	555 ± 85[b]	633 ± 40[a,b]
MDA (μmol/L)	1.28 ± 0.68	1.23 ± 0.71	1.36 ± 0.33	1.98 ± 0.94	1.72 ± 0.82[b]	1.48 ± 0.42[b]
SCE frequency (mean SCE per cell)	7.07 ± 0.34	7.01 ± 0.40	6.92 ± 0.39	9.91 ± 0.46[a]	0.02 ± 0.55[a,b]	7.88 ± 0.56[b]

Values were calculated at inclusion and after 1 and 2 months of supplementation with the ROC. Data, expressed as mean ± SD, were analyzed using a 2-way analysis of variance and values in columns having different superscripts are significant.

[a] $P < .05$ vs the respective control.

[b] $P < .05$ vs the respective inclusion.

significantly higher than those of control subjects, also if not in a statistically significant way; these values returned toward control values after 2 months of ROC supplementation.

An increased frequency of SCEs is considered a sensitive indicator of exposure to agents or conditions capable of producing DNA damage. Few studies are reported in literature concerning the effects of exercise on oxidative DNA damage [31,32] and use urinary 8-hydroxy-deoxyguanosine excretion as a measure of DNA oxidation in response to free radicals. This is the first report concerning a possible early cytogenetic damage induced by regular physical exercise. In our investigation, a statistically significant increase in spontaneous SCE frequency was found in peripheral lymphocytes from athletes at the beginning of the trial, in comparison with normal subjects. However, SCE frequency appeared to return to normal values partially after 1 month and almost completely after 2 months of ROC supplementation. Consistently with these observations, an anthocyanin-rich extract is able to protect against oxidative DNA damage induced by vitamin E deficiency in the rat [33], and flavonoids protect diabetic human lymphocytes against oxidative damage to DNA [34]. Furthermore, cyanidin and cyanidin-3-glucoside proved to be able to protect against DNA cleavage in vitro [35]. The ROC treatment was well tolerated by all subjects enrolled in the present trial because no unpleasant side effect was reported.

The present findings reflect an overall lower level of oxidative stress in trained athletes after short-term dietary supplementation with the ROC. Although we cannot understand the exact mechanism subserving this beneficial effect, one could speculate that ROC ingredients protect endogenous antioxidants, such as vitamin C and E, from consumption by the oxidative process. In fact, maintenance of vitamin C and E levels would also protect thiol groups in proteins, such as the enzyme glutathione peroxidase, which are especially vulnerable to oxidative damage and inactivation by the formation of sulfur-seleno bridges [36]. Phenolic phytochemicals present in complex mixtures have been suggested to act synergistically as antioxidants in a mechanism in which the easily oxidized phenols are regenerated by less active phenols [37]. Specifically, in orange juice, phenolic antioxidants were found to protect vitamin C against oxidative decomposition [38].

In conclusion, although preliminary, our results clearly demonstrate that dietary supplementation with the ROC (which is endowed with strong antioxidant capacity) is able to decrease oxidative stress and thus might protect against its short- and long-term health consequences in athletes engaged in regular training programs. Interestingly, besides being inexpensive, treatment with the ROC should have the additional advantage of being free of side effects. In fact, natural anthocyanins are prescribed as medicines in many countries, and grape skin extracts and anthocyanins were approved by the US Food and Drug Administration as a food colorant. Furthermore, bioflavonoids seem to have a potential role in treating musculoskeletal conditions because they might be beneficial to connective tissue by limiting inflammation and associated tissue degradation, improving local circulation, and promoting a strong collagen matrix [39]. Finally, one has to point out that in humans, anthocyanins have proven to be absorbed, after ingestion, in their unchanged glycated forms [40]. Further studies are in progress to clarify the exact mode of action subserving the observed beneficial action of dietary ROC supplementation in athletes during habitual training.

Acknowledgment

This study was supported by the Italian Government (MiPAF, Prog Ricerche e Sperimentazione nel Settore dell'Agrumicoltura Italiana, Azione n.4).

References

[1] Konig D, Wagner KH, Elmadfa I, Berg A. Exercise and oxidative stress: significance of antioxidants with reference to inflammatory, muscular, and systemic stress. Exerc Immunol Rev 2001;7:108-33.
[2] Urso ML, Clarkson PM. Oxidative stress, exercise, and antioxidant supplementation. Toxicology 2003;189:41-54.
[3] Cooper CE, Vollaard NB, Choueiri T, Wilson MT. Exercise, free radicals and oxidative stress. Biochem Soc Trans 2002;30:280-5.
[4] Jackson MJ. Free radicals in skin and muscle: damaging agents or signals for adaptation? Proc Nutr Soc 1999;58:673-6.
[5] Chevion S, Moran DS, Heled Y, Shani Y, Regev G, Abbou B, et al. Plasma antioxidant status and cell injury after severe physical exercise. Proc Natl Acad Sci U S A 2003;100:5119-23.
[6] Ji LL. Antioxidants and oxidative stress in exercise. Proc Soc Exp Biol Med 1999;222:283-92.
[7] Schroder H, Navarro E, Tramullas A, Mora J, Galiano D. Nutrition antioxidant status and oxidative stress in professional basketball players: effects of a three compound antioxidative supplement. Int J Sports Med 2000;21:146-50.
[8] Cao G, Prior RL, Cutler RG, Yu BP. Effect of dietary restriction on serum antioxidant capacity in rats. Arch Gerontol Geriatr 1997;25:245-53.
[9] Rice-Evans CA, Miller NJ, Paganga G. Structure-antioxidant activity relationships of flavonoids and phenolic acids. Free Radic Biol Med 1996;20:933-56.
[10] Galvano F, La Fauci L, Lazzarino G, Fogliano V, Ritieni A, Ciappellano S, et al. Cyanidins: metabolism and biological properties. J Nutr Biochem 2004;15:2-11.
[11] Kähkönen MP, Heinonen M. Antioxidant activity of anthocyanins and their aglycons. J Agric Food Chem 2003;51:628-33.
[12] Noda Y, Kaneyuki T, Mori A, Packer L. Antioxidant activities of pomegranate fruit extract and its anthocyanidins: delphinidin, cyanidin, and pelargonidin. J Agric Food Chem 2002;50:166-71.
[13] Wang H, Cao G, Prior RL. Oxygen radical absorbing capacity of anthocyanins. J Agric Food Chem 1997;45:304-9.
[14] Chen JH, Ho CT. Antioxidant activities of caffeic acid and its related hydroxycinnamic acid compounds. J Agric Food Chem 1997;45:2374-8.
[15] Saija A, Tomaino A, Lo Cascio R, Trombetta D, Proteggente A, De Pasquale A, et al. Ferulic and caffeic acids as potential protective agents against photooxidative skin damage. J Sci Food Agric 1999;79:476-80.
[16] Bonina F, Saija A, Tomaino A, Lo Cascio R, Rapisarda P, Dederen JC. In vitro antioxidant activity and in vivo photoprotective effect of red orange extract. Int J Cosmet Sci 1998;20:331-42.
[17] Morini F, Dusatti F, Bonina FP, Saija A, Ferro M. Iron-induced lipid peroxidation in human skin–derived cell lines: protection by a red orange extract. Altern Lab Anim 2000;28:427-33.
[18] Cornelli U, Bonina F, Valsasina R, Cornelli M. Attività antiossidante del Red Orange Complex (ROC). Prog Nutr 2000;1:21-7.
[19] Bonina FP, Leotta C, Scalia G, Puglia C, Trombetta D, Tringali G, et al. Evaluation of oxidative stress in diabetic patients after supplementation with a standardised red orange extract. Diabetes Nutr Metab 2002;15:14-9.
[20] Rice-Evans C, Miller NJ. Total antioxidant status in plasma and body fluids. Methods Enzymol 1994;234:279-93.
[21] Ellman GL. Tissue sulphydryl groups. Arch Biochem Biophys 1959;82:70-7.
[22] Cornelli U, Terranova R, Luca S, Cornelli M, Alberti A. Bioavailability and antioxidant activity of some food supplements in men and women using the D-Roms test as a marker of oxidative stress. J Nutr 2001;131:3208-11.

[23] Gerard-Monnier D, Erdelmeier I, Regnard K, Moze-Henry N, Yadan JC, Chaudiere J. Reactions of 1-methyl-2-phenylindole with malondialdehyde and 4-hydroxyalkenals. Analytical applications to a colorimetric assay of lipid peroxidation. Chem Res Toxicol 1998;11:1176-83.
[24] Perry P, Wolff S. New Giemsa method for the differential staining of sister chromatids. Nature 1974;251:156-8.
[25] Gerardi G, Usberti M, Martini G, Albertini A, Sugherini L, Pompella A, et al. Plasma total antioxidant capacity in hemodialyzed patients and its relationships to other biomarkers of oxidative stress and lipid peroxidation. Clin Chem Lab Med 2002;40:104-10.
[26] Incandela L, Belcaro G, Cesarone MR, De Sanctis MT, Griffin M, Cacchio M, et al. Oxygen-free radical decrease in hypertensive patients treated with lercanidipine. Int Angiol 2001;20:136-40.
[27] Sen CK. Update on thiol status and supplements in physical exercise. Can J Appl Physiol 2001;26:S4-S12.
[28] Sen CK, Packer L. Thiol homeostasis and supplements in physical exercise. Am J Clin Nutr 2000;72: 653S-69S.
[29] Inayama T, Oka J, Kashiba M, Saito M, Higuchi M, Umegaki K, et al. Moderate physical exercise induces the oxidation of human blood protein thiols. Life Sci 2002;70:2039-46.
[30] Cao G, Prior RL. Measurement of oxygen radical absorbance capacity in biological samples. Methods Enzymol 1999;299:50-62.
[31] Almar M, Villa JG, Cuevas MJ, Rodriguez-Marroyo JA, Avila C, Gonzalez-Gallego J. Urinary levels of 8-hydroxydeoxyguanosine as a marker of oxidative damage in road cycling. Free Radic Res 2002;36:247-53.
[32] Sato Y, Nanri H, Ohta M, Kasai H, Ikeda M. Increase of human MTH1 and decrease of 8-hydroxydeoxyguanosine in leukocyte DNA by acute and chronic exercise in healthy male subjects. Biochem Biophys Res Commun 2003;305:333-8.
[33] Ramirez-Tortosa C, Andersen OM, Gardner PT, Morrice PC, Wood SG, Duthie SJ, et al. Anthocyanin-rich extract decreases indices of lipid peroxidation and DNA damage in vitamin E-depleted rats. Free Radic Biol Med 2001;31:1033-7.
[34] Lean ME, Noroozi M, Kelly I, Burns J, Talwar D, Sattar N, et al. Dietary flavonols protect diabetic human lymphocytes against oxidative damage to DNA. Diabetes 1999;48:176-81.
[35] Acquaviva R, Russo A, Galvano F, Galvano G, Barcellona ML, Li Volti G, et al. Cyanidin and cyanidin 3-*O*-beta-D-glucoside as DNA cleavage protectors and antioxidants. Cell Biol Toxicol 2003;19:243-52.
[36] Li R, Cowan DB, Mickle DAG, Weisel RD, Burton GW. Effect of vitamin E on human glutathione peroxidase (GSH-PX1) expression in cardiomyocytes. Free Radic Biol Med 1996;21:419-26.
[37] Kanner J, Frankel E, Granit R, German B, Kinsella JE. Naturales antioxidants in grapes and wines. J Agric Food Chem 1994;42:64-9.
[38] Miller NJ. Flavonoids and phenylpropanoids as contributors to the antioxidant activity of fruit juices. In: Rice-Evans C, Packer L, editors. Flavonoids in health and disease. New York: Marcel Dekker Inc, 1998. p. 387-404.
[39] Teixeira S. Bioflavonoids: proanthocyanidins and quercetin and their potential roles in treating musculoskeletal conditions. J Orthop Sports Phys Ther 2002;32:357-63.
[40] Cao G, Muccitelli HU, Sanchez-Moreno C, Prior RL. Anthocyanins are absorbed in glycated forms in elderly women: a pharmacokinetic study. Am J Clin Nutr 2001;73:920-6.