VOLUME 58 · SUPPL. I TO No. 3 · SEPTEMBER 2016

PANMINERVA MEDICA

DELPHINOL® STANDARDIZED MAQUI BERRY EXTRACT SIGNIFICANTLY LOWERS BLOOD GLUCOSE AND IMPROVES BLOOD LIPID PROFILE IN PREDIABETIC INDIVIDUALS IN THREE MONTHS CLINICAL TRIAL

Jorge ALVARADO, Frank SCHOENLAU, Andrés LESCHOT, Ana M. SALGADO, Pilar VIGIL PORTALES

EDIZIONI · MINERVA · MEDICA

PUBBLICAZIONE PERIODICA TRIMESTRALE - POSTE ITALIANE S.P.A. - SPED. IN A. P. D.L. 353/2003 (CONV. IN L. 27/02/2004 N° 46) ART. 1, COMMA 1, DCB/CN - ISSN 0031-0808 TAXE PERÇUE

Online version at http://www.minervamedica.it
Panminerva Medica 2016 September;58(Suppl. 1 to No. 3):1-6

ORIGINAL ARTICLE

Delphinol® standardized maqui berry extract significantly lowers blood glucose and improves blood lipid profile in prediabetic individuals in three-month clinical trial

Jorge ALVARADO, Frank SCHOENLAU, Andrés LESCHOT, Ana M. SALGADO, Pilar VIGIL PORTALES*

Reproductive Health Research Institute, Pontificia Universidad Católica de Chile, Santiago, Chile

*Corresponding author: Pilar Vigil Portales, Reproductive Health Research Institute, Pontificia Universidad Católica de Chile, Santiago, Chile.
E-mail: pvigil@bio.puc.cl

ABSTRACT

BACKGROUND: Previous research has suggested that supplementation with delphinidin-rich maqui berry extract Delphinol® significantly alters postprandial carbohydrate metabolism and acutely lowers both insulin and glucose at fasting conditions. Additionally, the maqui berry extract affects absorption of glucose, which was attributed by other groups to SGLT1-inhibition.
METHODS: Because this activity profile suggests promising potential for improving glucose metabolism in prediabetes, we investigated in a three months trial the effects of Delphinol® in 31 subjects, presenting just diagnose, moderate glucose intolerance, measuring HbA_{1c}, glucose tolerance and lipid profile in monthly intervals.
RESULTS: Average levels of glycosylated hemoglobin decreased from initial 5.65±0.09% (SE) to 5.50±0.08% (SE) (P=0.084) after one month, 5.39±0.08% (SE) (P=0.010) after two months and 5.35±0.08% (SE) (P=0.003) after three months of daily supplementation with 180 mg Delphinol® in the morning. Fasting insulin and glucose were non-significantly lowered. Oral Glucose Tolerance Test (OGTT) performed in monthly intervals did not result in significant alterations compared to baseline characteristics. Blood lipid measurements showed significant reduction of LDL after three months (P=0.001), VLDL already decrease after one month (P=0.019). VLDL values subsequently raise again showing no statistical difference with the starting condition. HDL increased significantly over baseline during the entire treatment period. Total cholesterol and triglycerides did not present with significant changes.
CONCLUSIONS: Our findings point to considerable health potentials benefits of Delphinol, particularly related to the improvement of glucose metabolism. Delphinol® was well tolerated and no adverse effects occurred.

(*Cite this article as*: Alvarado J, Schoenlau F, Leschot A, Salgado AM, Vigil Portales P. Delphinol® standardized maqui berry extract significantly lowers blood glucose and improves blood lipid profile in prediabetic individuals in three months clinical trial. Panminerva Med 2016;58(Suppl. 1 to No. 3):1-6)

Key words: Prediabetic state - Delphinidin - Glucose intolerance - Atherosclerosis.

The maintenance of glucose homeostasis is of vital importance to human physiology, thus being subject to strict hormonal control. A rapidly growing number of research projects point to postprandial hyperglycemia as a contributing factor for weight gain, fasting hyperglycemia and, left inappropriately addressed, leading to glucose intolerance or insulin resistance and type II diabetes.

Non-caloric food constituents, such as dietary fibers and secondary plant metabolites, prolong food digestion and absorption and contribute to moderate excess postprandial blood glucose peaks. Numerous plant polyphenols currently gain attention due to their ability to naturally moderate blood sugar levels in prediabetic, diabetic, as well as healthy individuals.[1] The underlying mechanisms are diverse, ranging from α-glucosidase inhibition,[2] α-amylase inhibition,[3] maltase inhibition [4] and sodium-glucose co-transporter (SGLT) inhibition.[5] Soy isoflavonoids genistein and daidzein have been ascribed to benefit pancreatic func-

tion in terms of augmented insulin secretion.[6] Benefits of polyphenols on glucose homeostasis identified in animal models are corroborated by epidemiologic investigations, especially the Nurses' Health Studies, which identified decreased risk for developing type II diabetes associated with higher consumption of anthocyanins and anthocyanin-rich fruit.[7]

Our group previously described that delphinidin anthocyanins extracted from maqui berries (*Aristotelia chilensis*) dose-dependently lowers fasting glucose and insulin in prediabetic individuals. The maqui berry extract (Delphinol®, trademark of MNL Chile) is standardized to bear no less than 25% delphinidin anthocyanins.[8] In order to elucidate whether Delphinol may exert meaningful contributions to healthier blood sugar levels, we chose to carry out a 3-month clinical trial for measuring HbA_{1c}, OGTT and lipids profile in prediabetic individuals. The quality judgment most commonly applied to measure good glycemic control, is the achievement of an HbA_{1c} level below 7%.[9] For our study we chose to demonstrate glucose metabolism improvement showing preventive effects of Delphinol in subjects with moderate hyperglycemia, with HbA_{1c} levels ranging from minimum 5.0 to maximum 7.6, previously undiagnosed with prediabetes.

Materials and methods

Subjects

We recruited generally healthy, previously undiagnosed subjects with prediabetes. We screened for suitable subjects searching for individuals with polycystic ovaries, acne, alopecia or hirsutism, symptoms known to frequently coincide with altered glucose and or insulin regulation, at the San Cristobal Medical Foundation (Vitacura, Santiago, Chile).

We aimed to investigate possible glucose metabolism improvements in medication-naïve volunteers with previously undiagnosed and untreated prediabetes, to demonstrate that timely intervention with a natural product, taken in conjunction with lifestyle improvements, may arrest progression to further advanced glucose intolerance.

Eligible participants comprised men and women, aged 18 to 50 years, presenting an abnormal glucose tolerance response, as judged from Oral Glucose Tolerance Test (OGTT), defined as presence of any of the following characteristics: basal glucose values >100 mg/dL, basal insulin >15 µIU/mL, postprandial glucose >140 mg/dL, any postprandial insulin >100 µIU/mL, 120 min postprandial glucose >120 mg/dL.

Exclusion criteria were defined as a fasting glucose of ≥126 mg/dL, requirement of hypoglycemic medication, current or past use of fibrates or statins during the past three months. All patients provided written informed consent. The experimental protocol was approved by the ethical committee of the Mutual de Seguridad in Santiago, Chile.

Subjects were recruited with the requirement to follow diversified diets, explicitly not following specific weight loss, prescribed, religious, or other specific food diets.

Study design

This study was carried out applying an open prospective design. All recruited subjects were advised to take one capsule containing 180 mg Delphinol in the morning with approximately 200 mL water before breakfast. In case tablet intake in the morning was forgotten, it was permissible to take it later during the day even if not in fasting conditions.

Clinical examination of subjects was performed at trial start and in monthly intervals until completion, measuring weight, height, waist circumference (at midpoint between the lowest rib and the iliac crest). Subjects were advised to avoid eating large food portions, especially carbohydrates, and refrain from strenuous exercise on days prior to their visit to the clinic. Study participants were instructed to turn up at the clinic in the early morning (8 AM) having fasted overnight, at least eight hours. At this occasion fasting blood was drawn for subsequent analysis of basal blood glucose and insulin, followed by an OGTT consisting of 75 g glucose in 296 mL liquid (Trutol, Thermoscientific, Waltham, MA, USA.), consumed within less than 5 min. Subjects remained at rest while blood was collected at baseline and at 30, 60, 90 and finally 120 min. During this period, only water intake was allowed. Glucose was analyzed by GOD-PAP colorimetry and insulin by chemoluminescence as described elsewhere. Glycemic responses characteristic to OGTT were assigned to four categories, with normal response as class I, low glucose tolerance as class II, altered insulin response (class III) and impaired

glucose tolerance coinciding with altered insulin response (class IV). The collected fasting blood samples were further analyzed for HbA_{1c} using HPLC, as well as lipid profiles comprising triglycerides, LDL, VLDL, HDL, and total cholesterol, according to routine practice by means of spectrophotometry.

At every visit, an interview on tolerability of the product took place, and body weight and waist circumference were recorded. Tolerability and safety were assessed by interview and from blood specimen taken at trial start and after completion, measuring uric acid, urea, bilirubin, alkaline phosphatase, total globulin, glutamic oxaloacetic transaminase (GOT), lactate dehydrogenase (LDH), calcium, phosphate, total protein, albumin and globulins.

We used a commercially available Delphinol® food supplement bearing 180 mg standardized Delphinol maqui berry extract, capsuled by Barnafi Krause Farmacéutica S.A., Santiago, Chile. Capsules contained Delphinol batch 13156, manufactured in 2013 by MNL Chile, bearing 31.5% delphinidin glycosides and 39.4% total anthocyanins (HPLC), according to product certificate of analysis.

Results

Subjects

Thirty-one otherwise healthy subjects, 20 women and 11 men, who met prediabetes recruitment criteria, controlled by diet and lifestyle alone, were enrolled in the city of Santiago, Chile. Anthropometric and cardiovascular health details are presented in Table I. The majority of enrolled subjects (N=24) of both genders presented were overweight or slightly obese, with a 35 ≥BMI ≥25 kg m^{-2}. Abdominal obesity, with waist circumference >103 cm and >88 cm for men and women, respectively, was apparent in 11 men and 18 participating women. Ten participants presented with elevated triglycerides (≥150 mg/dL). Seventeen participants had moderately elevated blood pressure (>120/80) during enrollment, though none did require prescription medication. During each of three visits after enrollment, subjects were interviewed on unwanted effects and were equipped with another package containing 30 Delphinol capsules (180 mg each). All subjects with the exception of one woman, who chose to discontinue the trial for private reasons, unrelated to treatment, completed the three months investigational period.

Primary outcome

Supplementation of subjects with 180 mg Delphinol once daily in the morning led to continuously lowered HbA_{1c} levels from the first month of treatment until trial completion after three months, as presented in Figure 1. Following the first month of treatment, HbA_{1c} levels dropped from an initial average of 5.65%±0.09 (SE), to 5.39%±0.08 (SE) (P=0.010) and 5.35%±0.08 (SE) (P=0.03), after 60 and 90 days of treatment, respectively.

Mean fasting glucose of participants remained unchanged following 3 months of daily Delphinol consumption. At baseline women and men had 89.5 mg/dL±9.3 (SE) and 93.8 mg/dL±6.4 (SE) respectively, and 89.8 mg/dL±7.6 (SE) and 100.6 mg/dL±4.3 (SE)

TABLE I.—*Anthropometric and cardiovascular health characteristics of study participants at trial start and after completion. No significant differences were detected between baseline and 3-month treatment in any case.*

	Female		Male	
	Baseline	3 months	Baseline	3 months
	Mean±SD (Min-Max)		Mean±SD (Min-Max)	
Age (years)	32.3±9.7 (20-51)		32.4±9.50 (20-49)	
Body weight (kg)	69.4±14.9 (47.0-98.6)	68.2±13.4 (51.4-90.5)	95.3±22.0 (77.0-154.0)	95.1±21.9 (75.0-149.2)
Height (m)	1.57±0.07 (1.46-1.71)		1.72±0.06 (1.61-1.81)	
BMI ($kg \cdot m^2$)	28.4±6.4 (19.1-42.5)	28.5±6.1 (21.0-40.72)	32.0±6.4 (26.3-48.1)	31.5±6.3 (24.9-46.6)
Waist circum-ference (cm)	94.0±13.7 (72-120)	94.5±14.2 (75.0-120.0)	104.6±13.0 (91.0-137.0)	103.3±14.0 (89-135)
Systolic blood Pressure (mmHg)	120.1±13.1 (95-148)	121.5±12.5 (107-153)	126.7±10.7 (110-140)	119.9±7.8 (106-130)
Diastolic blood Pressure (mmHg)	74.3±7.5 (60 -85)	76.0±8.0 (65-90)	80.0±7.4 (68-90)	74.8±7.9 (59-85)
Fasting glucose (mg/dL)	89.5±9.3 (76 -110)	89.8±7.55 (77.0-109)	93.8±6.4 (83.0-106.0)	101.5±4.3 (94.0-107.0)
Fasting insulin (U/L)	14.6±6.7 (4.9-26.5)	18.3±18.3 (3.5-83)	13.7±6.7 (4.9-28.8)	17.9±7.9 (9.1-30.1)

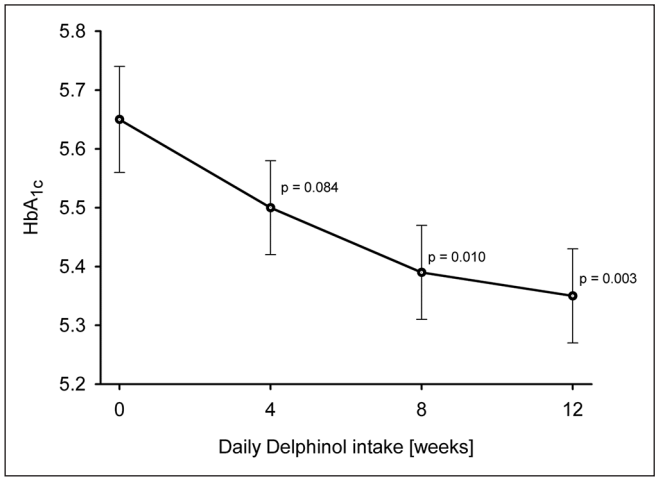

Figure 1.—HbA_{1c} values of 30 prediabetic subjects taking 180 mg Delphinol once a day in the morning over a period of three months.

respectively after three months of Delphinol intake. Oral glucose tolerance tests at trial start and after three months of Delphinol treatment did not show significant variations of postprandial glucose and insulin responses (data not shown).

Secondary outcomes

The blood lipid profile was found to improve considerably in response to three-month Delphinol supplementation, as presented in Table II. Mean total cholesterol of study participants decreased gradually from baseline 166.7 mg/dL±6.9 (SE) to 155.6±6.9 (SE) (P=0.004).

Mean VLDL cholesterol values dropped already after one month of Delphinol intake from 23.81 mg/dL±2.03 (SE) to 18.87 mg/dL±2.03 (SE), but slightly increase again on the second month of treatment till 21.74 mg/dL±2.03 (SE) and finally decrease once more on the third month to 21.13 mg/dL±2.03 (SE). These up and down on the VLDL values follow the pattern of an overdamped curve observed in biological control processes.

LDL mean values dropped after three months of Delphinol consumption from a mean of 109.00 mg/dL±6.18 (SE), to a final mean value of 95.39 mg/dL±6.20 (SE) (P<0.001). HDL cholesterol responded to Delphinol with significantly higher values from 2 months of treatment and onwards 34.13 mg/dL±1.52 (SE) to 39.07 mg/dL±1.52 (SE) (P<0.001). No effects were identified on triglycerides (Table II).

The mean relation HDL/LDL, significantly improved

TABLE II.—*Changes on blood lipid profile in response to supplementation with Delphinol for three months.*

Lipid species	Days	Serum Concentration mg/dL; (least square mean and SE)	Dunnet HSU comparisons [1] baseline *versus* treatment	Difference least square means	Adjusted P-value
Total cholesterol	0	166.74; 6.91			
	30	164.16; 6.91	0 *vs.* 30	2.58	0.514
	60	165.58; 6.91	0 *vs.* 60	1.16	0.640
	90	155.63; 6.93	0 *vs.* 90	11.11	0.004*
LDL cholesterol	0	109.00; 6.18			
	30	109.26; 6.18	0 *vs.* 30	-0.26	0.788
	60	103.84; 6.18	0 *vs.* 60	5.16	0.195
	90	95.39; 6.20	0 *vs.* 90	13.61	0.001*
VLDL cholesterol	0	23.81; 2.03			
	30	18.87; 2.03	0 *vs.* 30	-4.94	0.019*
	60	21.74; 2.03	0 *vs.* 60	-2.06	0.311
	90	21.13; 2.04	0 *vs.* 90	-2.68	0.163
HDL cholesterol	0	34.13; 1.52			
	30	36.10; 3.11	0 *vs.* 30	-1.97	0.077
	60	40.00; 3.11	0 *vs.* 60	-5.87	<0.001*
	90	39.25; 3.16	0 *vs.* 90	-4.94	<0.001*
Triglycerides	0	126.81; 15.10			
	30	128.06; 15.10	0 *vs.* 30	-1.26	0.797
	60	143.61; 15.10	0 *vs.* 60	-16.81	0.988
	90	121.77; 15.18	0 *vs.* 90	5.04	0.553

[1]One-tailed Dunnet HSU comparison.

TABLE III.—*Safety and tolerability assessment at baseline and following three months supplementation with Delphinol.*

Parameter	Trial Start	Trial Completion	P-value
Alkaline phosphatase	175.71±9.48	127.22±10.35	0.001
Glutamic-oxaloacetic Transaminase	27.29±4.63	21.99±5.03	
Lactate dehydrogenase	314.77±12.48	297.23±13.22	
Urea	25.13 ± 1.29	27.83±1.37	0.029
Albumin	3.94±0.04	4.11±0.05	0.001
Gamma globulins	2.82±0.05	2.53±0.05	<0.001
Total proteins	6.79±0.06	6.63 ± 0.06	0.005
Uric acid	4.88±0.37	5.51±0.39	
Bilirubin	0.57±0.06	0.56±0.06	
Calcium	12.25±1.88	9.58±2.05	
Phosphate	175.71±9.48	127.22±10.35	

for the participants, the starting value for this parameter was 0.31, slightly increase to 0.33 after the first month of treatment, then to 0.39 at the second month and finally reaching 0.41 at the third month of treatment.

Safety assessment and clinical chemistry

Supplementation with Delphinol was well tolerated. Subjects routinely interviewed during every visit to the clinic reported absence of unwanted effects and tolerability issues.

As presented in Table III, liver enzymes were not affected by treatment with Delphinol. All parameters remained at physiologic and healthy values and no significant alteration of any parameter was detected other than those signaled in Table III.

Discussion

The aim of our study was to examine if the regular consumption of a delphinidin-rich maqui berry extract, taken as a daily dietary supplement, may significantly improve glycemic control in individuals presenting elevated blood glucose, who have not previously been exposed to hypoglycemic medication.

With daily intake of Delphinol® HbA_{1c} levels decreased noticeably already after one month, with statistical significance apparent after two and three months of treatment. For people without diabetes, the normal range for the HbA_{1c} test is between 4% and 5.6%, HbA_{1c} levels between 5.7% and 6.4% indicate increased risk of diabetes. During this study our participants dropped from a mean HbA_{1c} of 5.65, indicating diabetic risk, to a mean of 5.35 which is considered a normal value. Unexpectedly, fasting glucose and insulin, tested at four week intervals, did not show significant reduction compared to baseline. OGTT, prospected bi-fortnightly, showed a trend indicative of improved glucose tolerance, although not reaching statistically relevant levels. In a previous study, we described that acute Delphinol intake dose-dependently alters glucose tolerance in OGTT, with delayed blood glucose absorption after glucose challenge (Alvarado *et al*. manuscript submitted to peer review). Delphinol bears the unique characteristic of not being limited to delaying complex carbohydrate metabolism, but also affecting glucose absorption by SGLT1-inhibition.[5] Another group identified improved glucose homeostasis using 240 mg of purified anthocyanins from blueberry and blackcurrant source (Medox, Norway) to type II diabetic patients over an investigative period of 24 weeks.[10] This study reports a significant decrease of fasting plasma glucose. However, treatment-related HbA_{1c} and plasma insulin reductions did not reach statistical significance, despite the much higher daily anthocyanin dosage applied in comparison to our protocol, which corresponds only to 63 mg of anthocyanins per day, using 180 mg of Delphinol.

Subjects in our study were not limited with regard to their dietary preferences. It is plausible that this circumstance may have contributed to pronounced inter-individual variations of investigated blood parameters, resulting in statistical insignificance of glucose tolerance improvements in OGTTs carried out every four weeks. This study was not aimed at improving obesity indexes and no significant variations in BMI were identifiable.

Further to the evaluation of subject's glycemia, we aimed at identifying effects on cardiovascular health parameters, which may manifest secondary to glucose metabolism improvements. Anthocyanins have previously been extensively researched for cardiovascular health benefits by other groups, as recently reviewed by Wallace *et al.*[11] A total of 55 clinical investigations were reviewed, which explored effects of anthocyanin consumption in subjects with hyperlipidemia and dyslipidemia. In our study we found improvements on the blood lipid profiles, with total cholesterol, LDL and VLDL cholesterol lowered and HDL cholesterol increased. Statistical significance was reached for LDL after three months treatment and for VLDL from the first month of treatment until trial end. Furthermore, HDL increased

significantly after 60 and 90 days of Delphinol consumption. Our results are in concordance with previous studies that used the afore mentioned mixed berry anthocyanin preparation Medox at a higher daily dosage of 320 mg purified anthocyanins to 120 dyslipidemic subjects, finding significantly improved LDL and HDL cholesterol values after twelve weeks.[12] This group ascribes this effect to both a decrease and inhibition of plasma cholesteryl-ester transfer protein in response to anthocyanins. Furthermore, berry anthocyanins were shown to improve dyslipidemia in a placebo-controlled study with 58 type II diabetic patients, some of which were medicated with oral glucose-lowering and lipid-lowering drugs.[10] This study described positive effects on insulin resistance based on significantly decreased HOMA-IR after 24 weeks of treatment with 180 mg anthocyanins twice a day. In confirmation of our findings, the group of Li *et al*. [10] described significant improvements of lipid profile. Furthermore, this research group describes significant reduction of diastolic and systolic blood pressure, from 82 mmHg±8 (SE) to 80 mmHg±10 (SE) and from 130 mmHg±13 (SE) to 126 mmHg±11 (SE) respectively. Participants in our study were normotensive and alterations were marginal and insignificant.

Previous studies on Delphinol with a higher daily dosage corresponding to approximately 160 mg anthocyanins, demonstrated significant reduction of blood lipid oxidation in a double-blind, placebo-controlled protocol.[13] Both plasma oxidized LDL and urinary F2-isoprostane were significantly lowered in a cohort of 42 moderately overweight cigarette smokers, following four-month supplementation with Delphinol. Despite the relatively high daily Delphinol dosage applied, no significant alterations to blood lipid profiles were reported.

Conclusions

In conclusion, maqui berry anthocyanins significantly improve blood glucose in individuals previously undiagnosed for early prediabetic stage, in absence of side effects.

In this study we found that with a much lower dose than that previously described in the treatment of pre diabetic patients, we obtained comparative results to earlier studies applying 3 to 6 times higher doses of anthocyanins.

Any other mechanisms of action to explain the maintenance of fasting glucose and insulin while there is a drop on the HbA1c levels and the improvement of the entire of the lipids profile need further investigation.

References

1. Xiao JB, Högger P. Dietary polyphenols and type 2 diabetes: current insights and future perspectives. Curr Med Chem 2015;22:23-38.
2. Yang X, Kong F. Evaluation of the in vitro α-glucosidase inhibitory activity of green tea polyphenols and different tea types. J Sci Food Agric 2016;96:777-82.
3. Beejmohun V, Peytavy-Izard M, Mignon C, Muscente-Paque D, Deplanque X, Ripoll C, *et al*. Acute effect of Ceylon cinnamon extract on postprandial glycemia: alpha-amylase inhibition, starch tolerance test in rats, and randomized crossover clinical trial in healthy volunteers. BMC Complement Altern Med. BioMed Central 2014;14:351.
4. Jo S-H, Cho C-Y, Lee J-Y, Ha K-S, Kwon Y-I, Apostolidis E. In vitro and in vivo reduction of post-prandial blood glucose levels by ethyl alcohol and water Zingiber mioga extracts through the inhibition of carbohydrate hydrolyzing enzymes. BMC Complement Altern Med. BioMed Central 2016;16:111.
5. Hidalgo J, Flores C, Hidalgo MA, Perez M, Yañez A, Quiñones L, *et al*. Delphinol® standardized maqui berry extract reduces postprandial blood glucose increase in individuals with impaired glucose regulation by novel mechanism of sodium glucose cotransporter inhibition. Panminerva Med 2014;56(2 Suppl 3):1-7.
6. Choi MS, Jung UJ, Yeo J, Kim MJ, Lee MK. Genistein and daidzein prevent diabetes onset by elevating insulin level and altering hepatic gluconeogenic and lipogenic enzyme activities in non-obese diabetic (NOD) mice. Diabetes Metab Res Rev 2008;24:74-81.
7. Wedick NM, Pan A, Cassidy A, Rimm EB, Sampson L, Rosner B, *et al*. Dietary flavonoid intakes and risk of type 2 diabetes in US men and women. Am J Clin Nutr 2012;95:925-33.
8. Watson RR, Schönlau F. Nutraceutical and antioxidant effects of a delphinidin-rich maqui berry extract Delphinol®: a review. Minerva Cardioangiol 2015;63(2 Suppl 1):1-12.
9. Vijan S, Sussman JB, Yudkin JS, Hayward RA. Effect of patients' risks and preferences on health gains with plasma glucose level lowering in type 2 diabetes mellitus. JAMA 2014;174:1227-34.
10. Li D, Zhang Y, Liu Y, Sun R, Xia M. Purified anthocyanin supplementation reduces dyslipidemia, enhances antioxidant capacity, and prevents insulin resistance in diabetic patients. J Nutr 2015;145:742-8.
11. Wallace TC, Slavin M, Frankenfeld CL. Systematic Review of Anthocyanins and Markers of Cardiovascular Disease. Nutrients 2016;8:32.
12. Qin Y, Xia M, Ma J, Hao Y, Liu J, Mou H, *et al*. Anthocyanin supplementation improves serum LDL- and HDL-cholesterol concentrations associated with the inhibition of cholesteryl ester transfer protein in dyslipidemic subjects. Am J Clin Nutr 2009;90:485-92.
13. Davinelli S, Bertoglio JC, Zarrelli A, Pina R, Scapagnini G. A Randomized Clinical Trial Evaluating the Efficacy of an Anthocyanin-Maqui Berry Extract (Delphinol®) on Oxidative Stress Biomarkers. J Am Coll Nutr 2015;34 Suppl 1:28-33.

Conflicts of interest.—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Manuscript accepted: September 8, 2016. - Manuscript received: July 4, 2016.