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FULL COMMUNICATION

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Dietary Supplementation with Polyphenol-Rich Chokeberry Juice Improves Skin Morphology in Cellulite

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ABSTRACT The aim of our study was to investigate possible beneficial effects of organic chokeberry juice (OCJ) consumption in the treatment of cellulite. Twenty-nine women aged 25–48 with a cellulite grade 2 according to the Nurnberger–Muller scale were included. Anthropometric and biochemical parameters were measured. Skin structure was analyzed by ultrasonography. All subjects consumed 100 mL of OCJ per day, during 90 days. Measurements of investigated parameters were performed at 0, 45, and 90 days of the study. A marked reduction in the subcutaneous tissue thickness was observed in all subjects, with the average reduction of 1.9 mm. The length of subcutaneous tissue fascicles (ScTFL) was reduced in 97% (28 out of 29) of subjects, with the average value of 1.18 mm. After 45 days of chokeberry juice consumption, reduction of edema was observed in 55.2% of the subjects with edema at the baseline, while at the endpoint of the study, edemas were not observed in any of the subjects involved in the study. OCJ could have beneficial effects on the cellulite condition, including the length of ScTFL, subcutaneous tissue, and dermis thickness as well as on edema reduction.

KEY WORDS: • ***anthropometric*** • ***biochemistry*** • ***cellulite*** • ***chokeberry*** • ***fascicles*** • ***subcutaneous tissue***

INTRODUCTION

Cellulite is a condition that occurs in over 85% of women and has also been diagnosed in men.[1] Although it is not recognized as a medical disorder, it is of special importance in esthetic medicine.[2,3] Cellulite is characterized by an irregular, dimpled appearance of the skin, mainly found on the thighs, buttocks, and abdomen.[4] Multifactorial etiology is assumed, including structural, genetic, and endocrine abnormalities. It was shown that weakened connective tissues, enlarged fat cells, and diminished microcirculation, play key roles in the pathophysiology of cellulite.[2,5–7]

Cellulite progression or reduction is evaluated using different techniques, including imprecise palpation and describing using various scales,[8] as well as instrumental methods such as termography,[9] macrophotography,[10] magnetic resonance, computed tomography, and ultrasonography.[11–15]

A variety of topical preparations, massage-based therapies, and surgical techniques, as well as herbal preparations for oral applications, functional foods, or changes in dietary habits have been used to improve cellulite conditions.[2,3,17,18] There is increasing demand for functional foods and in this category, functional beverages are the fastest growing segment.[19] A lot of them are made from berries, among them chokeberry products are very frequent.

Chokeberry (*Aronia melanocarpa*) is a rich source of proanthocyanidins, anthocyanins, flavonols, and phenolic acids and due to this diverse chemical profile it possesses numerous beneficial effects in humans and animals.[20–22] It is shown that chokeberry is among the plant species with the highest antioxidant activity.[20,23] A large number of intervention studies demonstrated the beneficial effects of chokeberry ingredients on various risk factors for cardiovascular diseases, the levels of total cholesterol, LDL, ox-LDL, triglycerides, glucose, HbA1c and systolic and diastolic blood pressure, body mass index, improving vasodilatation dependent on endothelial function as well as vasoactive and vasoprotective properties.[22,24–26] In addition, it was shown that anthocyanins play a role in the redistribution of microvascular blood[27] and together with other phenolics have beneficial effects on small blood vessel permeability.[28] According to our knowledge, there is no information in the literature about the effects of chokeberry juice on the condition of skin and subcutaneous tissue region affected by cellulite.

Taking into account all these facts, the aim of this study was to investigate the possible beneficial effects of organic chokeberry juice (OCJ) consumption in the treatment of cellulite in a female subject with cellulite type 2 according

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to the Nurnberger–Muller scale. Different parameters were monitored, including body mass index, percent of fat, the abdominal, thigh, knee, and hip circumference, blood tests, and also ultrasound examinations of the skin.

MATERIALS AND METHODS

Organic chokeberry juice

OCJ (*A. melanocarpa*) used in this study was imported and donated from Conimex Trade d.o.o. (Belgrade, Serbia). Producer of OCJ is Tlocznia Rembowscy (Popowko, Poland).

Total phenolics

The total concentration of phenols was estimated by the Folin–Ciocalteu method with slight modifications.[29] Two hundred microliters of properly diluted OCJ was added to 1 mL of 1:10 diluted Folin–Ciocalteu reagent. After 4 min, 800 μL of sodium carbonate (75 g/L) was added. After 2 h of incubation at room temperature, the absorbance at 765 nm was measured. Gallic acid (0–100 mg/L) was used for calibration of a standard curve. The results were expressed as milligrams of gallic acid equivalents per 100 g of juice (mg GAE/100 g FW). Triplicate measurements were taken and mean values were calculated.

Total anthocyanins

The total anthocyanin content was investigated according to the procedure described in European Pharmacopoeia 6.0,[30] with slight modifications. A 50-fold dilution of OCJ in a 0.1% v/v solution of hydrochloric acid in methanol was prepared. The absorbance of the solution was measured at 528 nm, using a 0.1% v/v solution of hydrochloric acid in methanol as the compensation liquid.

The percentage content of anthocyanins, expressed as cyanidin-3-glucoside chloride, was calculated from the expression: $A \times 5000/718 \times m$ (A = absorbance at 528 nm; 718 = specific absorbance of cyanidin-3-glucoside chloride at 528 nm; m = mass of the substance to be examined in grams).

1,1-Diphenyl-2-picrylhydrazyl radical scavenging activity

The free radical scavenging activity of OCJ on the stable 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical was carried out according to the procedure described previously,[31] with slight modifications. The antiradical capacity of OCJ was evaluated using a dilution series, to obtain a large spectrum of sample concentrations. The samples (100 μL) were mixed with 1400 μL of 80 μM methanolic solution of DPPH. Absorbance at 517 nm was measured after 20 min. The percentage of inhibition was calculated using the following equation:

$$\text{Inhibition} = [(A_0 - A_i)/A_0] \times 100,$$

where A_0 is absorbance of the control and A_i is absorbance of the samples. IC_{50} values were estimated using a nonlinear regression algorithm. All test analyses were run in triplicate. Trolox was used as a positive control.

Subjects

Twenty-nine women aged 25–48 (mean age 34.9) participated in the study. Cellulite grade 2 (orange peel appearance spontaneously visible and disappearing in layered position), according to the Nurnberger–Muller scale,[32] was the main inclusion criterion together with a regular monthly menstrual cycle. Exclusion criteria included age under 18 and over 50 years; body mass index over 30; significant changes in dietary habits, life style, or exercise program in the past 12 months; cardiovascular diseases; pregnancy or lactation; history of malignancy; any type of cellulite treatment applied within 12 months before the study; systemic lymphedema; menopause and premenopause.

Protocol

The study protocol was approved by the Ethics Committee of Faculty of Pharmacy, University of Belgrade, Serbia. The study was conducted in accordance with the revised Declaration of Helsinki. All participants provided written informed consent. The study was performed from February till May 2012. Subjects were instructed to consume 100 mL of OCJ per day, during 90 days, 30 min before the main meal and to retain their regular diet, exercise program, and life style. Analyzed parameters included parameters of epidermal, dermal, and subcutaneous structure measured by ultrasound (subcutaneous tissue thickness [ScTT], thickness of subcutaneous tissue and dermis, thickness of dermis and epidermis [DET], the length of subcutaneous tissue fascicles [ScTFL], the presence of edemas within the dermis), biochemical parameters (total cholesterol, triglycerides, HDL, LDL, glucose, urea, ALT, AST, iron and hemoglobin levels, leukocytes and erythrocytes counts, sedimentation), and anthropometric parameters (weight, body mass index, total body fat, arterial pressure, abdominal, thigh, knee, and hip circumference). Biochemical parameters were determined with a clinical chemistry analyzer (Cobas e411; Roche Diagnostics, Basel, Switzerland) and Roche Diagnostics kits according to the manufacturer's instructions, while full blood count was performed using a hematology analyzer (Coulter Ac.T Diff; Beckman Coulter, Miami, FL, USA).

Measurements of investigated parameters were performed at three time points, at 0, 45, and 90 days of the study for all parameters with the exception of biochemical parameters measured at the beginning and the end of the study.

The upper back and front part of the thigh were photographed at the beginning and the end of the study by a digital camera (Nikon D90, Nikor lens 18–105 mm) at standardized angles and positions.

At day 90, subjects were asked to fulfill a questionnaire on self perception of the treatment effects.

High-frequency ultrasound measurements

The high-frequency ultrasound examinations were carried out using SA 9900 Multi-beam 3D Ultrasound, system Kretz 5–12 MHz, and linear probe PB–99L5-12IR. The ultrasound

images obtained were saved on a personal computer, and then analyzed using experimental software. The examinations were performed on the posterior part of the thigh in triplicate, always at the same location.

Statistical analysis

Data are presented as mean and standard deviations for all 29 participants. All measurements were performed in triplicate. The paired Student's *t*-test and one-way ANOVA for repeated measures (with Bonferroni adjustment for multiple comparisons) were used to compare the data in two or three time points, respectively, where $P < .05$ was considered statistically significant. SPSS program, version 19 (SPSS, Inc., Chicago, IL, USA) was used for the analysis.

RESULTS

Chemical characteristics and radical scavenging activity of OCJ

Active ingredients were analyzed in our laboratories and characteristics of OCJ were as follows: soluble solids 10.94% (Mettler Toledao HB43-S); pH 3.35 (pH meter Testo 206); total phenolics 386 mg GAE/100 g of juice; total anthocyanins 25 mg/100 g of juice. The radical scavenging activity was investigated against synthetic DPPH radical and the obtained IC_{50} value for OCJ was 1.74 ± 0.04 mg/mL.

Effects of chokeberry juice consumption on epidermis, dermis, and subcutaneous tissue characteristics

The most significant changes that have been observed during this study were recorded by ultrasonography. In this study, statistically significant changes in all investigated characteristics of epidermis, dermis, and subcutaneous tissue, measured by ultrasound, were observed after the intervention and compared with the baseline values (Table 1). ScTT and the thickness of dermal and subcutaneous tissue (DScTT) were reduced in all subjects after 45 days of intervention, with further reduction until the end of the study. The average reductions of ScTT and DScTT at the end of the study were 1.9 and 2.1 mm (9.5% and 9.6%), respectively, compared with the baseline values. DET was reduced in 65% (19 out of 29) of subjects after 45 days of chokeberry juice consumption and in 90% (26 out of 29) of subjects, at the end of the study. An average reduction in DET for the whole group was 0.3 mm (10.2%), compared with the baseline values. The growth of the ScTFL into the dermis is a typical feature of cellulite[15,33] and in our study, the length of ScTFL was reduced in 97% (28 out of 29) of subjects after 45 days of the study, with further reduction at the end of the study observed in the same percentage of subjects. An average value of ScTFL reduction was observed at the end of the study.

T1 ▶

Table 1. Characteristics of Epidermis, Dermis, and Subcutaneous Tissue Measured by Ultrasound

Time point	*Dermis and subcutaneous tissue thickness (mm)*	*Subcutaneous tissue thickness (mm)*	*Dermis and epidermis thickness (mm)*	*Length of subcutaneous fascicles (mm)*
Day 0	22.23 ± 3.28^{a}	20.42 ± 3.26^{a}	2.69 ± 0.48^{a}	2.96 ± 0.72^{a}
Day 45	21.10 ± 3.23^{b}	19.44 ± 3.07^{b}	2.52 ± 0.51^{ab}	2.11 ± 0.40^{b}
Day 90	20.09 ± 3.33^{c}	18.52 ± 3.24^{c}	2.38 ± 0.39^{b}	1.61 ± 0.35^{c}

Values are mean ± SD ($n = 29$). All measurements were performed in triplicate. Data were analyzed by one-way repeated measures ANOVA, with Bonferroni confidence interval adjustment for multiple comparisons of main effects, whereas means followed by different letters differ significantly $P < .05$.

Table 2. Effect of Intervention on Subcutaneous Edema

Day of the study	*Subjects with edema (*n*, %)*
0	16/29 (55.2%)
45	6/29 (20.7%)
90	0

Chokeberry juice consumption also showed positive effects on edema reduction as shown in Table 2. At the beginning of the study, edema was observed in 60% (16 out of 29) of subjects. At the second time point (45 days after juice consumption), reduction of edema severity was observed in 37% (6 out of 16) of subjects, and the absence of edema in 63% (10 out of 16) of subjects in whom edema was diagnosed at the beginning of the study. At the end of the study, edema was not observed in any of the subjects included in the study.

◀ T2

Digital photographs of the upper back and front part of the thigh, taken at the beginning and at the end of the study, were evaluated for visual changes by 10 independent evaluators. Five of them noticed an improvement in cellulite appearance after the study was finished.

Biochemical and anthropometric measurements

Anthropometric and biochemical parameters of participants (29 women aged 25–48, with a height range from 156 to 181.5 cm and weight 49.3–93.8 kg) measured at the beginning and the end of the study are shown in Table 3. Although statistically significant difference of the results obtained before and after the study was not shown for any of analyzed parameters, beneficial changes were observed in certain number of participants. Regarding anthropometric parameters, at the end of the study, decrease in body weight was observed in 16 of 29 women, reduction in body fat (%) was noticed in the greatest number of subjects ($n = 20$), representing 69% of the study group, with the maximum value of 17%. Reduction in the abdominal circumference was observed in 62% (18 out of 29) of subjects. Thigh circumference reduction was not significant and was observed in only 12 subjects, which was inconsistent to the results of ultrasound measurements in the same region. Since only healthy subjects were included in the study, most of them were within the reference ranges for most of the biochemical parameters before entering the study and at the final point of control. Although not statistically significant for the whole study population, changes in biochemical parameters after the intervention were observed in more than 50% of the

◀ T3

Table 3. Anthropometric and Biochemical Characteristics of Subjects ($n=29$) Before and After the Study

	Before	*After*	P
BMI (%)	22.9±4.0	22.9±4.1	NS
Fat (%)	30.0±6.5	29.6±6.9	NS
Abdominal circumference (cm)	75.1±10.4	74.0±9.8	NS
Hip circumference (cm)	100.7±7.6	101.3±7.9	NS
Thigh circumference (cm)	58.5±4.8	58.6±4.9	NS
Knee circumference (cm)	42.1±4.7	42.1±4.2	NS
Glucose (mM)	4.5±0.4	4.4±0.5	NS
Triglycerides (mM)	0.9±0.4	0.8±0.4	NS
Total cholesterol (mM)	5.1±1.2	5.0±1.0	NS
HDL cholesterol (mM)	1.5±0.3	1.5±0.3	NS
LDL cholesterol (mM)	3.2±1.1	3.1±0.9	NS
Urea (mM)	3.9±0.8	4.1±1.2	NS
ALT (U/L)	17.8±9.4	17.0±8.0	NS
AST (U/L)	19.9±4.4	19.2±5.5	NS

Values are mean±standard deviation ($n=29$). Data were analyzed by a paired Student's *t*-test.

NS, statistically not significant if $P \geq .05$.

subjects. In addition, investigated parameters, which are indicators of liver and kidney function (urea, ALT, AST), remained in reference values thus indicating safety of chokeberry juice consumption.

Questionnaire analysis

Analysis of the answers from the questionnaire fulfilled by all subjects at the end of the study showed that 41.4% of subjects observed visual improvement in the condition of cellulite, 48.3% did not observed any change, while 10.3% of investigated subjects were ambivalent. The positive overall effect of chokeberry juice consumption, which was mainly referred on skin tightness, was reported by 69% of subjects. Side effects, related to the gastrointestinal system function (motility, constipation, diarrhea), were reported by 13.8% of subjects.

DISCUSSION

Considering that cellulite involves both the subcutaneous tissue and the dermis, different methods for the analysis of structure and characteristics of these tissues, including high-frequency ultrasonography, are applied in both the diagnosis and treatment of cellulite.[10,13,15] It was shown that some of the key roles in pathophysiology of cellulite play enlarged fat cells, weakened connective tissues, and diminished microcirculation.[6,7] It was shown that anthocyanins from bilberries could be effective in promoting and enhancing arteriolar rhythmic diameter changes that play a role in the redistribution of microvascular blood flow and interstitial fluid formation,[27] while phenolics from bilberries, cranberries, and grape seed extracts facilitate the repair of vessel damage responsible for small blood vessel permeability.[28] Positive effects of polyphenols that reach OCJ consummation in the treatment of cellulite could be connected with improvements in microcirculation as well as with protection and restoration of endothelial cells and consequently their function. It was shown previously that the flavonoid-rich extract from chokeberry might preserve the function of the endothelium and contributes to the prevention of atherosclerosis progression,[34] while the anthocyanin-rich chokeberry extract inhibited the releasing of PGE2 in normal human endothelial cells.[35] In addition, positive effects of chokeberry on fat metabolism could contribute to beneficial effects in cellulite conditions.[20,36]

Ultrasonography was also used in the study of Mlosek *et al.*[15] who investigated the effects of anticellulite cream which, among other components, contained cranberry extracts rich in polyphenols. Although two different approaches to the treatment were applied, similar results were obtained. They also noticed a decrease in all measured parameters, including thickness of subcutaneous tissue, length of ScTFL, and the number of women with dermal edemas. One of the mechanisms assumed was improvement in microcirculation.

Recent investigations on gene expression levels provided more insight in the pathophysiology of cellulite, and postulated new targets in the prevention and therapy of this cosmetic problem. Emanuele *et al.*[37,38] showed that adiponectin mRNA expression in the subcutaneous adipose tissue of the gluteal region was significantly lower in areas with cellulite compared with areas with normal skin and subcutaneous tissue architecture, without any change in plasma

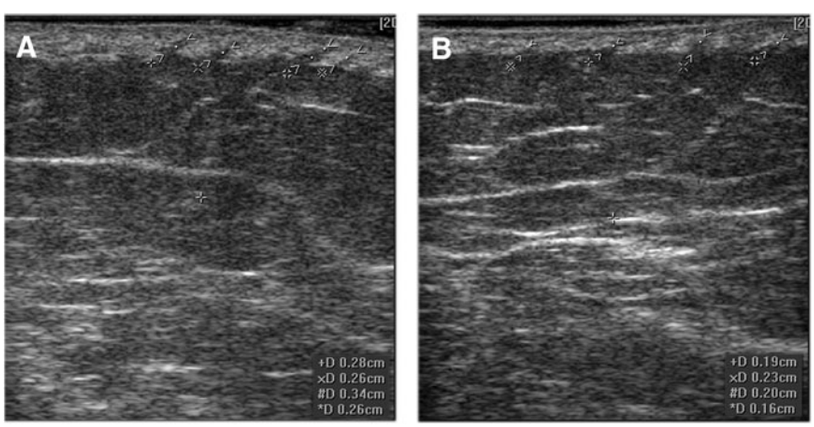

FIG. 1. Ultrasound images at the beginning **(A)** and end **(B)** of the study, indicating the reduction in the length fascicle. ◀AU7

adiponectin levels.[37] Based on the gene expression analysis, they also highlighted the independent role of angiotenzin-converting enzyme and hypoxia-inducible factor 1A in predisposing to cellulite.[38] At the same time, anthocyanins have shown a beneficial influence on gene expression of several adipocytokines, including adiponectine[39,40] in animal *in vivo* models. The inhibitory potential of anthocyanins and their metabolites on ACE activity *in vitro* was also reported.[41] These findings could hypothetically explain the observed beneficial effects of anthocyanin-rich chokeberry juice on morphological features of cellulite, measured by ultrasound.

On the other side, low sensitivity and reproducibility of circumference measurements could contribute to the obtained inconsistency, postulating the advantage of the direct analysis of skin and subcutaneous tissues thus indicating that cellulite disturbed architecture of these tissues could be the optimal target rather than fat tissue alone. Sasaki *et al.*[18] investigated the effectiveness of anticellulite gel combined with LED light and although they noticed positive changes using ultrasound imaging, significant changes in body weight, BMI, body fat indices, and thigh circumferences were not observed.

Results obtained in this study showed marked potential of anthocyanin-rich chokeberry juice to improve the morphology of skin and subcutaneous tissue in the regions affected by cellulite under *in vivo* conditions. These findings add new evidence in the dossier of beneficial effects of anthocyanins and postulate a new research strategy for both prevention and treatment of cellulite.

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AUTHOR DISCLOSURE STATEMENT

The authors disclose any commercial associations that might create a conflict of interest in connection with submitted manuscripts.

REFERENCES

1. Załeska-Żyłka I: Cellulit jako problem medyczny. *Probl Hig Epidemiol* 2008;89:487–491.
2. Khan MH, Victor F, Rao B, *et al.*: Treatment of cellulite: Part I. Pathophysiology. *J Am Acad Dermatol* 2010;62:361–370.
3. Rawlings AV: Cellulite and its treatment. *Int J Cosmet Sci* 2006;28:175–190.
4. Rossi AB, Vergnanini AL: Cellulite: a review. *J Eur Acad Dermatol Venereol* 2000;14:251–262.
5. de Godoy JM, de Godoy MF: Physiopathological hypothesis of cellulite. *Open Cardiovasc Med J* 2009;3:96–97.
6. Avram MM: Cellulite: a review of its physiology and treatment. *J Cosmet Laser Ther* 2004;6:181–185.
7. Draelos ZD: The disease of cellulite. *J Cosmet Dermatol* 2005; 4:221–222.
8. Nürnberger F, Müller G: So called cellulite: an invented disease. *J Dermatol Surg Oncol* 1978;4:221–229.
9. Vincent C, Szubert M, Dêbowska R, *et al.*: Zastosowanie termografii w diagnostyce cellulite. *Dermatol Estet* 2006;8:85–89.
10. Bielfeldt S, Buttgereit P, Brandt M, *et al.*: Non-invasive evaluation techniques to quantify the efficacy of cosmetic anti-cellulite products. *Skin Res Technol* 2008;14:336–346.
11. Ferrozzi F, Zuccoli G, Tognini G, *et al.*: An assessment of abdominal fatty tissue distribution in obese children. A comparison between echography and computed tomography. *Radiol Med* 1999;98:490–494.
12. Hexsel DM, Abreu M, Rodrigues TC, *et al.*: Side-by-side comparison of areas with and without cellulite depressions using magnetic resonance imaging. *Dermatol Surg* 2009;35:1471–1477.
13. Mlosek RK, Dębowska R, Lewandowski M, *et al.*: The use of high frequency ultrasonography in monitoring anti-cellulite therapy–own experience. *Pol J Cosmetol* 2008;11:283–294.
14. Querlux B, Cornillon C, Jolivet O: Anatomy and physiology of subcutaneous adipose tissue by *in vivo* magnetic resonance imaging and spectroscopy: relationships with sex and presence of cellulite. *Skin Res Technol* 2002;8:118–124.
15. Mlosek RK, Dębowska RM, Lewandowski M, *et al.*: Imaging of the skin and subcutaneous tissue using classical and high-frequency ultrasonographies in anti-cellulite therapy. *Skin Res Technol* 2011;17:461–468.
16. Leibaschoff G: A double-blind, prospective, clinical, surgical, histopathological and ultrasound study comparing the effectiveness and safety of liposuction performed using Laserlipolysis and Internal Ultrasound Lipoplasty method. *Eur J Aesth Med and Dermatol* 2012;2:78–93. ◀AU5
17. Lis-Balchin M: Parallel placebo-controlled clinical study of a mixture of herbs sold as a remedy for cellulite. *Phytother Res* 1999;13:627–629.
18. Sasaki GH, Oberg K, Tucker B, *et al.*: The effectiveness and safety of topical PhotoActif phosphatidylcholine-based anti-cellulite gel and LED (red and near-infrared) light on Grade II-III thigh cellulite: a randomized, double-blinded study. *J Cosmet Laser Ther* 2007;9:87–96.
19. Gruenwald J: Novel botanical ingredients for beverages. *Clin Dermatol* 2009;27:210–216.
20. Kulling SE, Rawel HM: Chokeberry (*Aronia melanocarpa*)–A review on the characteristic components and potential health effects. *Planta Med* 2008;74:1625–1634.
21. Kedzierska M, Olas B, Wachowicz B, *et al.*: An extract from berries of *Aronia melanocarpa* modulates the generation of superoxide anion radicals in blood platelets from breast cancer patients. *Planta Med* 2009;75:1405–1409.
22. Bell DR, Gochenaur K: Direct vasoactive and vasoprotective properties of anthocyanin-rich extracts. *J Appl Physiol* 2006;100:1164–1170.
23. Oszmiański J, Wojdyło A: *Aronia melanocarpa* phenolics and their antioxidant activity. *Eur Food Res Technol* 2005;221: 809–813.
24. Bell DR, Burt TD: Phenolic acids contained in anthocyanin enriched extracts from elderberry, bilberry and chokeberry possess endothelium dependent and independent vasorelaxation properties in porcine coronary arteries. *FASEB J* 2007;21:366.
25. Valcheva-Kuzmanova S, Kuzmanov K, Tancheva S, *et al.*: Hypoglycemic and hypolipidemic effects of *Aronia melanocarpa*

fruit juice in streptozotocin-induced diabetic rats. *Methods Find Exp Clin Pharmacol* 2007;29:101–105.
26. Skoczynska A, Jedrychowska I, Poreba R, *et al.*: The influence of chokeberry juice on arterial blood pressure. *Pharmacol Rep* 2007;59:66.
27. Colantuoni A, Bertuglia S, Magistretti M, *et al.*: Effects of *Vaccinium myrtillus* anthocyanosides on arterial vasomotion. *Arzneimittelforschung* 1991;41:905–909.
28. Christie S, Walker A, Lewith G: Flavonoids—a new direction for the treatment of fluid retention? *Phytother Res* 2001;15: 467–475.
29. Waterman P, Mole S: *Analysis of Phenolic Plant Metabolites*. Blackwell Scientific Publication, Oxford, 1994.
30. European Pharmacopoeia 6.0., Council of Europe, Strasbourg Cedex, France, 2008.
31. Silva B, Ferreres F, Malva J, *et al.*: Phytochemical and antioxidant characterization of *Hypericum perforatum* alcoholic extracts. *Food Chem* 2005;90:157–167.
32. Nootheti PK, Magpantay A, Yosowitz G, *et al.*: A single center, randomized, comparative, prospective clinical study to determine the efficacy of the VelaSmooth system versus the Triactive system for the treatment of cellulite. *Lasers Surg Med* 2006; 38:908–912.
33. Rosenbaum M, Prieto V, Hellmer J, *et al.*: An exploratory investigation of the morphology and biochemistry of cellulite. *Plast Reconstr Surg* 1998;101:1934–1939.
34. Zapolska-Downar D, Kosmider A, *et al.*: Flavonoids-rich extract from chokeberry fruits inhibits oxLDL-induced apoptosis of endothelial cells. *Atherosclerosis* 2006;7:223.
35. Han GL, Li CM, Mazza G, *et al.*: Effect of anthocyanin rich fruit extract on PGE2 produced by endothelial cells. *Wei Sheng Yan Jiu* 2005;34:581–584.
36. Valcheva-Kuzmanova S, Kuzmanov K, Tsanova-Savova S, *et al.*: Lipid-lowering effects of *Aronia melanocarpa* fruit juice in rats fed cholesterol-containing diets. *J Food Biochem* 2007;31:589–602.
37. Emanuele E, Minoretti P, Altabas K, *et al.*: Adiponectin expression in subcutaneous adipose tissue is reduced in women withcellulite. *Int J Dermatol* 2011;50:412–416.
38. Emanuele E, Bertona M, Geroldi D: A multilocus candidate approach identifies ACE and HIF1A as susceptibility genes for cellulite. *J Eur Acad Dermatol Venereol* 2010;24:930–935.
39. Qin B, Anderson RA: An extract of chokeberry attenuates weight gain and modulates insulin, adipogenic and inflammatory signalling pathways in epididymal adipose tissue of rats fed a fructose-rich diet. *Br J Nutr* 2012;108:581–587.
40. Tsuda T, Ueno Y, Yoshikawa T, *et al.*: Microarray profiling of gene expression in human adipocytes in response to anthocyanins. *Biochem Pharmacol* 2006;71:1184–1197.
41. Hidalgo M, Martin-Santamaria S, Recio I, *et al.*: Potential anti-inflammatory, anti-adhesive, anti/estrogenic, and angiotensin-converting enzyme inhibitory activities of anthocyanins and their gut metabolites. *Genes Nutr* 2012;7:295–306.

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