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IMPACT OF GRAPE SEED EXTRACT POWDER ON HEMOGLOBİN AND HEMATOCRİT LEVELS İN WOMEN AFTER VAGİNAL DELİVERY

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ABSTRACT

Introduction: one of the principle reasons for anemia in pregnant women is postpartum hemorrhage. Synthetic drugs with all their efficiency ,have distructive effects. Active bleeding control with chemical medications is popular and herbal medications are less used. a ccording to alternative medicine, herbal product usage is necessary . This study is done according to grape seed powder effect on hemoglobin and hematocrit levels postpartum.
Methods : This study was a Double blind clinical trial on 120 mothers were eligible for vaginal delivery. Randomly devided to 4 groups (each group includes 3o percent) according to cards. 3 groups are grape seed powder receivers (50 ,100,150 doses) and controller group (placebo capsule receiver which is filled by starch), each group take its dose with one glass of warm after placenta exodus .before and after delivery 24 hour ,blood sample was taken for Hemoglobin and Hematocrit levels measurements. After gathering information , data Spss softwareversion 15 .
Results:4 groups were equal in all case study variables. Upon main purpose of research , results showed that fall percentage of Hemoglobin and Hematocrit levels had significant difference between 4 groups,24 hours after delivery.
Conclusions: it is seen in present study that grape seed powder can reduce bleeding after delivery and it can prevent Hemoglobin and Hematocrit reduction caused by extra bleeding .as a result , grape seed powder can be used as a secondary medication for bleeding reduction in stage 3 and stage 4 of delivery ,we can teach the importance of its consumption in educational workshops . of course ,it needs more study in different doses, single dose and retentive.

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Introduction

Vitis vinifera (common grape vine) is a species of Vitis which has been used for the treatment of different patients about 6000 thousand years ago [1,2]. Pedanius Dioscorides (1st century AD) also used it to treat bleeding and bloody sputum. In traditional Iranian medicine, grape seed has a cold and dry nature and is regarded as excellent for its astringent because of the content and is also effective in treating uterine and menstrual bleeding [4,5]. Grape seed accounted for about 5.2 percent of the weight of grape and its functional and chemical ingredients are flavonoid with a phenolic structure (phenolic compounds include monomeric flavonols such as catechin, epicatechin, dimmer flavonols, trimmer flavonoid, procyanidin polymer, non-flavonoids (non-flavonoid compounds phenolic including resveratrol, fatty tartaric acids, phenol acrylic acid compounds) and materials such as gallic acid and epigallic acid, tannins, high levels of linoleic acid, high levels of omega-6 and less omega-3,

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vitamin E and C, peru anthocyanin and Karoon as well as magnesium, calcium, iron, phosphorus and potassium [6]. The protective and beneficial effects of grape extract against diseases such as cataracts [9], breast and colon cancers [10], increased plasma antioxidant power and strength and stabilization of collagen [8 &11], regeneration of blood vessels and restoring tissue blood flow [10,11], gastric ulcer and inhibition of oxidative stress [12], myocardial infarctions and ischemic [7,14], diabetes [15] and liver diseases [16] have been recognized. So far no single study was conducted to measure the impact of grape seed extraction and purification powder on postpartum hemorrhage and although various studies have documented the impacts of omega-6 linoleic acid [15], vitamin E [17], Vitamin C [16] and tannins [18] on the bleeding control, grape seed is a rich source of these products in pure and powder forms. Postpartum hemorrhage is one of the major causes of death and mortality, anemia in pregnant women [20]. Postpartum hemorrhage refers to the loss of blood volume of 500 ml or more after the completion of the third stage of vaginal delivery [21]. More bleeding occurs during the first 24 hours after childbirth, which has a major share of maternal mortality; as a consequence, prevention is an important objective of the prevention of maternal mortality after birth [20]. Calculation of changes in hemoglobin and hematocrit before and after delivery is considered one of the methods for measuring blood loss after delivery and these changes are acute and significant during the bleeding, and the initial hematocrit is at the highest level [15]. Safe, affective, affordable and acceptable methods appropriate for women and society should be used in order to reduce bleeding after delivery and decrease its complications, including anemia [22]. The use synthetic drugs in the labor management reduces the amount of blood loss but causes some side effects such as nausea, vomiting, hypertension and hypotension due to syntocinon *(*oxytocin*)* and it has resulted in finding safer alternatives for less dangerous drugs [21]. World Health Organization studies show that 80 percent of the world population especially women are related to medical aspects of plants; for this reason, the use of medicinal plants has received a lot of attention [23]. A lot of studies have documented the effectiveness of some medicinal plants including Xuesaitony and Xiaoyanzhixue, dill seed extract, Chan Lyba, cumin, dates in reducing postpartum bleeding and even are considered more effective than Oxytocin and synthetic drugs. These plants contain compounds such as Karun, tannins, amino acids and linoleic acid[20]. Since in traditional Iranian medicine, grape seed has been regarded as having astringent properties and considered effective in the control of bleeding, especially uterine bleeding as well as local midwives used it to decrease bleeding in women after childbirth; therefore, in order to find a natural, safe and effective product for bleeding after delivery and given the importance of postpartum hemorrhage and prevention of excessive bleeding and increased promotion of physiologic delivery in the current era without venipuncture and serum therapy during deliveries, I decided to conduct the present study in order to academically and scientifically determine the impact of grape seed powder on the hemoglobin and hematocrit levels after delivery due to the lack of scientific support, it is hoped that the results of the present study would be an important step in making decision regarding routine use of medication after delivery which in addition to maintaining the health of women after childbirth, can lead to cost savings as well.

Method

This is a controlled clinical trial with a single-blind intervention which was carried out on 120 women with vaginal delivery in 4 groups of 30 patients treated at doses of 50, 100 and 150 mg by black grape extract and a control group (receiving placebo capsules). The procedure is as follows:

Preparation of capsules: At this stage, after approval of the project and the necessary coordination with authorities, graduate Committee, research affairs of university, the ethics committee and the necessary coordination with head of laboratory of physiology at the University of Medical Sciences, researchers purchased red grape from the market and rural areas of Birjand.After *grape seeds* were *manually separated*,they were washed and dried under the sun for 72 hours.Then they *were manually milled* to a fine *powder* by researcher and it was shown to the professors of pharmacology and physiology at the university for confirming its quality status.Then, according to the Ethics Committee and Chang and Guidelinesstudy (2011) in using California grape seed powder, doses of grape seed powder in the formulation of the extract (8 grams extract is obtained per hundred grams of seed grape powder) were measuredand prepared and packaged in the form of capsules 50,150,100at the physiology laboratory of Birjand University by researcher and stored in the refrigerator.Placebo capsules were filled with starch powder by researcher and were placed in the refrigerator.

625 mg of grape seed powder = 50 mg capsules

1250 mg of grape seed powder = 100 mg capsules

1875 mg of grape seed powder = 150 mg capsules

Sampling: In this stage, after approval of the project and the necessary coordination with authorities, graduate Committee, research affairs of university, president and Department for safeguarding inValiasrhospital in Birjand,maternity and gynecological surgery ward as well as permanent presence of researcher in these wards and according to previous research (the study byMahdavian et al.,2002) and the sampling frame in women referred to Valiasr hospital in accordance with the inclusion criteria, the researcher firstly identified themand then explained the objectives and methodology of the study for mothers who were included in the study byobtaining a written consent.Before starting the study, four groups under study were recorded on 120 cards (30 cards for first Group, 30 cards for second group, 30 cards for third group, 30 cards in the control group).In total, 120 cards were stored in a box and after obtaining informed consent from the patients, they were asked to pick out a card from a box. Theywere assigned in one of three groups receiving grape seed powder (50,100 mg, 150 mg) and control group (receiving placebo capsule filled with starch powder) based on thepicked card.At the beginning and according to the

purpose of the study, blood samples from mothers (3 ml) were collected for testing HB, HCT and were taken to the laboratory of Imam Reza (AS) within half an hour by the researcher, and then laboratory results obtained wererecorded in form view and patient's record.Mothers were assigned in one of the studied groupsby their cards. They were prepared for vaginal delivery and took their determined capsule dose after birth and placenta delivery with half a glass of water from the researcher.It is noteworthy that patients do not need to get oxytocin in physiologic delivery; however, oxytocin was intravenously administered under the requirements of delivery sectionand in accordance with the delivery section regulations (20 IU oxytocin was poured into 1 liter of Ringer at 5 ml per minute, then the infusion rate was reduced to 1-2 ml for transferring mothers to gynecological surgeryward and oxytocin infusion was discontinued, and the mother was handed over to the women's department of surgery; this procedure usually took about 2 to 3 hours).All data such as oxytocin administration or lack of oxytocin were recorded by the researcher in the questionnaire.Immediately after the transfer of the mother from delivery room to the recovery room, a drape withspecial weight and plastic cover was placed under mother and *mother's perineal pad*;then any changedpad was weighed with digital scale every 2 hours to 24 hours after delivery by the researcher.Each gram of pad weight gain was considered equal to a blood sample and finally, the weight and number of the pads (amount of bleeding) were recorded in form view.Other necessary cares of the mother during the fourth stage of labor were also recorded in the form view(it should be noted that the number of patient's pads and drapes, bleeding or bleeding complications and the breastfeeding by mother in hospital and gynecological surgery were monitored for 24 hours and recorded by researchers in the checklist form).Medications for the treatment of third stage of labor including oxytocin produced by Iranian pharmaceutical industry, Rasht (ampoules 1 ml containing 10 IU oxytocin) and grape seed powder derived from the dried seeds of red grapes purchased from the market inBirjandwere prepared and packed into capsules 50, 150 100 by the researcher and were kept in the refrigerator and given to the researcher immediately after the placenta.

Third stage: After 24 hours, blood sample (3 ml) was taken for testing HB, Hct by the researcher and was sent to laboratory of Imam Reza Hospital within half an hour and the results were recorded by the researcher in the form view and patient records. In order to determine the reliability of hemoglobin and hematocrit tests, the first 10 samples were tested by two expert laboratories and the results were the same. All samples were then analyzed by a laboratory specialist by maxmix device manufactured by a company in Japan. Data were analyzed using SPSS statistical software version 16 and descriptive statistics including frequency, percentage, mean, standard deviation and chi-square tests, Fisher, and paired t-test. Normality of quantitative data was examined and all of them had the normal distribution.

Findings

Table 1: Comparison of age, height, age, pregnancy, in pregnant women in four groups

Groups Variable	Dose 50 mg N=30 X±SD	Dose 100 mg N=30 X±SD	Dose 150 mg N=30 X±SD	Control group X±SD	ANOVA test result
Age (years)	27 ± 6.4	25.7±5.4	24.8 ± 4.5	26.2± 4.5	3.16 =dF F=1 P= 0.39
Gestational age (weeks)	39.3 ± 1.2	39.2 ± 2.1	38.7 ± 1.9	39.1 ± 1	3.116 =dF F= 0.66 P=0.58
Maternal height (cm)	159.5 ± 2.5	158 ±2.9	159.5±3.1	158.9±2.2	df=3.116 F= 0.79 P= 0.05

According to the table above, no significant differences were observed in mean age, gestational age and maternal height in 4 groups and all 4 study groups were similar in terms of these variables.

Table 2: Comparison of the mean during labor and delivery stages and oxytocin administered in four groups of pregnant women

Groups Variable	Dose 50 mg N=30 X±SD	Dose 100 mg N=30 X±SD	Dose 150 mg N=30 X±SD	Control group X±SD	ANOVA test result
Duration of labor (hours)	11.2 ± 5.1	13 ± 5.1	8.8 ± 3.3	8.5 ± 2.9	7.5 =dF F3.116 P=0.001
First Stage of Labor (hours)	10.2 ±5.1	12.1 ± 5.1	8 ± 3.2	7.7 ± 2.8	7.3 =dF F= 3 P=0.001
Second stage of labor (minutes(	16.2 ± 7.1	17.3 ± 7.1	14.2 ± 2.9	15.8 ± 6.7	X^2= 2/04 dF=3 p=0/56
Third stage of labor (minutes(	8.8 ± 2.8	9.6 ± 3.6	9.8 ± 2.8	9.5 ± 4.1	X^2= 1/27 dF=3 p=0/74*
Oxytocin	26 ± 10	21.8 ± 8.7	28.9± 11.3	20 ±10	X^2=12/5 dF= 3 p=0/006 *

α= 05/0 is at significance level

According to the table above, no significant difference was observed in the mean duration of the second and third delivery in 4 study groups; but the average duration of delivery and the first stage of labor showed significant differences in 4 groups and Mann-Whitney test showed that the differences between the groups were not statistically significant as follows:

Control 100 mg P<0.001

100 mg and 150 mg P<0.001

Table 3: Comparison of hematocrit before and 24 hours after delivery in four study groups

Intervention Group	N= 30 X±SD Before intervention	24 hours after the intervention N= 30 X±SD	Wilcoxon test result
Group = 50 mg	2.5 ±35.1	2.5 ±34.4	Z= 4/36 , P<0/001*
Group= 100 mg	3.5 ±36.4	6.7± 34.3	Z= 2/83 P= 0/005
Group = 150 mg	2.7 ±36.3	2.4 ±37.3	Z= 3/89 P<0/001*
Control	2.8 ± 35.7	2.9±36.2	Z= 3/69 P=0/001*
- Kruskal-Wallis test result	X^2= 7/82 dF= 3 , p=0/05*	dF= 2،X^2= 11/3 0.001=P	

α= 05/0 is at significance level

Control 50 and 100 mg P<0.001

100 mg and 150 mg P= 0.004

Table 4: Comparison of hemoglobin before and 24 hours after delivery in four study groups

Intervention Group	N= 30 X±SD Before intervention	24 hours after the intervention N= 30 X±SD	Wilcoxon test result
Group = 50 mg	11.0 ±0.8	11.1 ±82%	Z= 4/79 , *P<0/001
Group= 100 mg	12.3 ±1	11.5± 1.3	Z= 4/2 , *P<0/001
Group = 150 mg	12 ±1.1	2.4 ±37.3	Z=3/16 ,* P= 0/002
Control	12 ±95%	11.7±1.3	Z=4/48 ,* P=0/001
- Kruskal-Wallis test result	X^2= 1/72 dF= 2 p=0/63	X^2=5/36 dF= 2 p=0/15	

According to the table above, the average hemoglobin showed a significant decrease 24 hours after treatment compared to before treatment in all groups.

Discussion

While bleeding, early diagnosis and taking the necessary measures to prevent complications are of great importance. Unfortunately, in many cases it is not easy to diagnose, because sometimes there is no obvious symptoms of decreased blood volume. Therefore a drop in hemoglobin value exceeds 10%, 24 hours after delivery was considered as postpartum hemorrhage [21] in order to assess the need for blood transfusions and iron therapy for pregnant women with knowledge of occult bleeding after childbirth [22]. The findings suggest that there is a significant statistical difference between the mean hematocrit and hemoglobin levels after delivery in the groups receiving grape seed powder and placebo showing that grape seed powder capsules can lead to decreased postpartum bleeding and avoid excessive reduction of hemoglobin and hematocrit. In this study, three doses of 50 mg, 100 mg and 150 mg of grape seed powder are used to find the proper doses with various effects; in addition, in this study, the mean decrease in hemoglobin and hematocrit levels in doses of 150 mg and placebo was less than other groups which is indicative of the effect of higher doses grape seed powder in reducing bleeding after vaginal delivery. Enrolled patients had no statistically significant difference in terms of the effective parameters such as age, gestational age, height, parity and parity that is in line with studies by Heydari Shirazi and Moafegh (33,31). So far, there have been a wide variety of treatments to control bleeding after childbirth; however, we did not find any studies that examine the impact of grape seed on hemoglobin and hematocrit levels and awareness of postpartum blood loss like our study. As a consequence, because of the presence of compounds such as tannins, fatty acids, and epicatechin, catechin in grape seed and confirming the impact of these ingredients on the volume of postpartum hemorrhage in studies conducted on palm, dill and cumin, it can be concluded that grape seed also has astringent properties. However, these studies have measured the impact of these plants within 3 hours after delivery which are inconsistent with our study which evaluated hemoglobin and hematocrit levels before and 24 hours after birth. However, few studies have investigated the impact of chemical drugs on reducing blood levels of hemoglobin and hematocrit before and after childbirth. In the study by Gon Gorodok et al (2011) in Turkey, which was conducted on 456 women, the average drop in hemoglobin and hematocrit levels after delivery in the intervention group was less than the control group, the difference was statistically significant [18]. In the study by Moafegh et al., (2011) which was carried out to evaluate the impact of tranexamic acid on reducing bleeding after cesarean section in Tehran on 100 women; there was no significant difference between the two groups in terms of hemoglobin levels 24 hours after delivery, but the average drop in hemoglobin 24 hours after delivery in the intervention group was 1.0 $\pm$ 0.4 in the control group and 1.8 $\pm$ 0.7 which this difference was statistically significant [21]. Mirghaforvand et al., (2011) conducted a study in Tabriz for evaluating the effect of tranexamic acid on hemoglobin and hematocrit levels after childbirth in women at low risk for postpartum hemorrhage on 120 pregnant women referring for vaginal delivery; administration of tranexamic acid had a significant effect in reducing the mean drop in hematocrit after delivery [22]. In these studies the effects of chemical drugs listed in reducing drop in hemoglobin and hematocrit levels confirm the results of this study for the plant. As you can see, the results of this study show that grape seed powder can have a significant impact in reducing bleeding and cause a drop in hemoglobin and hematocrit levels and reduce it to an acceptable size. During the study, no side effects were observed following consumption of grape powder within 24 hours after delivery; but it seems that more studies are required to be conducted in this field at the international level. The limitations of this study include the small sample size and investigating of women at low risk of bleeding, which limit the ability to generalize the results to the community. It is suggested to do further studies with larger sample size concerning its

effects on lowering levels of hemoglobin and hematocrit especially in the case of postpartum hemorrhage after delivery to prevent bleeding and anemia. The strengths of this study are the lack of sample loss, objective and subjective outcomes and lack of subjectivity of participants on the implications of the study and research blinding; so that the participants and the researchers did not have information about the type of treatment received, and assignment of each person in the group.

Conclusion

The average drop in hemoglobin and hematocrit levels in the group receiving grape seed powder was lower than the group receiving a placebo capsule; the decline at a dose of 150 mg was significantly lower than other groups and the placebo, which is indicative of the impact of the larger dose of grape seed powder on the decline of bleeding after vaginal delivery and reveals the high effect of a single dose of grape seed powder in postpartum hemorrhage. Thus, according to a new approach in using complementary treatments for complications caused by pregnancy and childbirth, it is suggested that grape seed can be used as an adjuvant in combination with other medications to prevent and reduce postpartum hemorrhage and thus reducing complications such as anemia and improving maternal health. Further assessment is also recommended regarding using of grape seed powder with preservatives in higher doses among pregnant women after childbirth.

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Refrence

1. aberrant crypts and breast tumors in a rat dual-organ tumor model. Nutr Cancer 2001; 39(2): 252-258.

2. Chuang Ch, Bumrungper A, Kennedy A, Overman A, Wes T, DawsonB, Michael K. Grape powder extract attenuates tumor necrosis factor α-mediated inflammation and insulin resistance in primary cultures of human adipocytes. Journal of Nutritional Biochemistry 22 (2011) 89–94.

3. Hashim E. Osman Christian G. Krueger, Jess D. Reed, John D. Folts. Grape Seed and Grape Skin Extracts Elicit a Greater Antiplatelet Effect When Used in Combination than When Used Individually in Dogs and Humans, *J. Nutr. December 2002 132: 12 3592-3598*.

4. Montaseri M, Izadi Z, Izadi M, Sohrabi M. The investigation of some components of grape seed oil quality and its effects on human health, functional food Conference, 2008, p207-213.
5. Yamakoshi J, Saito M, Kataoka S, Tokutake S. Procyanidin-rich extract from grape seeds prevents cataract formation in hereditary cataractous (ICR/f) rats. J Agric Food Chem 2002; 50(17): 4983- 4988.
6. Singletary KW, Meline B. Effect of grape seed proanthocyanidins on colon aberrant crypts and breast tumors in a rat dual-organ tumor model. Nutr Cancer 2001; 39(2): 252-258.

7. Hashim E. Osman Christian G. Krueger, Jess D. Reed, John D. Folts. Grape Seed and Grape Skin Extracts Elicit a Greater Antiplatelet Effect When Used in Combination than When Used Individually in Dogs and Humans, *J. Nutr. December 2002 132: 12 3592-3598*.

8. Aldini G, Carini M, Piccoli A, Rossoni G, Maffei Facino R. Procyanidins from grape seeds protect endothelial cells from peroxynitrite damage and enhance endothelium-dependent relaxation in human artery: new evidences for cardio-protection. Life Sci 2003; 73(22): 2883-2898.
9. Booth SL, Golly I, Sacheck JM, Roubenoff R, Dallal GE, Hamada K, et al. *Effect of vitamin* E supplementation on vitamin K status in adults with normal coagulation status.Am J Clin Nutr 2004; 80: 143-8.
10. Li k, Diao Y, Zhang H, Shouyu W, Zhen Zh, Bo Y, Shanshan H, Hong Y,Tannin extracts from immature fruits ofTerminalia chebula Fructus Retz. Promote cutaneous wound healing in rats, BMC Complementary and Alternative Medicine 2011, 11:86, Page 1-9.

11. -Mojahed Sh , Aflatunian A, Khadem N, Dehghani Firouzabadi R, Karimi Zarchi M , An Investigation into Effectiveness of Date(Rutab) on Postpartum Hemorrhage. Journal of Shahid Sadoughi University of Medical Sciences. Vol. 20, No. 2, May-Jun 2012 Pages: 159-166
12. Lalonde A, Daviss B, Acosta A, HerschderferK. Postpartum hemorrhage today: ICM/FIGO initiative 2004-2006 . International Journal of Gynecology&Obstetrics 2006;94:243-253.
13. Khadem N, Sharaphy A, Latifnejad R, Hammod N, Ibrahim Zadeh S. *Comparing the efficacy of and oxytocin in the management of postpartum hemorrhage.* Shiraz E- Med J 2007; 8(2) .[Persian].
14. Fazel N, Esmaeli H. *The effect of cumin oil on the hemorrhage after cesarian section*. Teb va Tazkiyeh 2008;9(68-69): 78-81.[Persian]
15. Mahdavian M, Golmakani N, Manssori Hossinzade H, Afzalaghaee M. *An Investigation of effectiveness of oral Dill extracts on postpartum hemorrhage.* Iran J Obstet Gynecol Infertil 2003; 4(7-8) .[Persian]
16. Tebib K, Rouanet JM, Besançon P. Effect of grape seed tannins on the activity of some rat intestinal enzyme activities, PubMed - indexed for MEDLINE, 1994-1995;48(1):51-60.
17. Movafegh A, Eslamian L, Dorabadi A. Effect of intravenous tranexamic acid administration on blood loss during and after cesarean delivery. Int J Gynaecol Obstet 2011 Dec;115(3):224-6.
18. Naseri M.Development of traditional medicin and WHO Guideline.Daneshvar Pezeshki J 2004;11(52):53-68.
19. Prendiville WJ, Elbourne D, McDonald S. Active versus expectant management in the third stage of labour. Cochrane Database Syst Rev 2000:CD000007
20. Dostar I, mohajeri D.Effect antioxidant grape seed extract in streptozotocin- induced diabetic rats. University of Medical Sciences Journal zahedan, Volume 12, Issue 1.2011, p9-14.
21. Myrzay Y, Myrzayy N, Myrzayy M, Dlavyz H. The effect of hydro-alcoholic extracts of grape seed and pair of acorn recognition caused by carbon tetrachloride in rat liver disert. South Medical Journal, Vol. 14, No. 4.2012, p230-239.
22. Agassi M, Athari S, Mousavi A. the effect of grape seed extract compounds on cardiovascular disease, Razi nineteenth year, 2009 (6), 576-586.
23. Zhang Y, Shi H, Wang W, Ke Z, Zhong Z, , Xiaoxi Li S, Wang S, Antithrombotic effect of grape seed proanthocyanidins extract in a rat model of deep vein thrombosis. JOURNAL OF VASCULAR SURGERY 2011;743-753.
24. Wannaporn S , Aramsri M, Sirintorn Yibchok A, Sirichai A. Preventive effect of grape seed extract against high-fructose diet-induced insulin resistance and oxidative stress in rats, journal homepage: www.elsevier.com/locate/foodchemtox, (2010) 1853–1857.