PHYTOTHERAPY RESEARCH
Phytother. Res. (2009)
Published online in Wiley InterScience
(www.interscience.wiley.com) **DOI**: 10.1002/ptr.2729

A Systematic Review on the Sambuci fructus Effect and Efficacy Profiles

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The berries of European elder are used in traditional German medicine for various complaints. Due to insufficient research data, elderberry fruit was not monographed by the German Commission E at the end of the last century. A comprehensive review of the literature was conducted to summarize the pharmacological and clinical effects of elderberry fruit. Several databases and other sources were searched to identify *in vitro* and animal studies, and clinical trials investigating elderberry fruit preparations. For the latter, the level of evidence was evaluated as described previously.

Elderberry fruit preparations may provide antioxidant, antiviral and antiproliferative effects *in vitro*. One animal experiment and one clinical trial were able to back the antioxidative impact in terms of a weak antilipidemic effect. Antibacterial and antiinflammatory effects seem possible, but need further support. In rats, an aqueous elderberry fruit extract produced central depression and analgesia and an ethanol fruit extract improved acetic acid-induced colitis. Several *in vitro* studies together with two exploratory studies in humans and one open study in chimpanzees indicate that the aqueous elderberry extract Sambucol^{R} may be useful for the treatment of viral influenza infections.

These promising effects of elderberry fruit preparations from experimental and clinical studies should be backed by more rigorous studies before these preparations are recommended in the prevention of diseases and in treatment schedules. Copyright © 2009 John Wiley & Sons, Ltd.

Keywords: elderberry; Sambuci fructus; Caprifoliaceae; effects; efficacy.

INTRODUCTION

The dried ripe or fresh berries of *Sambucus nigra* L. (European elder, Fam. Caprifoliaceae) are used in traditional German medicine for the treatment of constipation, to increase diuresis, as a diaphoretic in upper respiratory tract infections, for the alleviation of low back and/or neuropathic pain, headache and toothache. For treatment of these complaints, patients consume elderberry juice or they drink a cup of tea (aqueous extract) several times per day. The infusion is prepared from 10 g dried berries standing in cold water for several minutes, then slowly heated up, and briefly boiled. Before filtering, a drawing-time of 5 to 10 min is recommended (Anonymous, 1994). Despite widespread use, due to the lack of pharmacological and clinical evidence, the berries of European elder were not monographed by the German Commission E at the end of the last century (Blumenthal, 1998).

There is no doubt of the potential usefulness of Sambuci fructus. Co-active compounds identified in the berries include flavonoids (e.g. hyperoside, isoquercitrin and rutoside), up to 1% of anthocyanins, including chrysanthemin (= cyanidin-3-O-glucoside), cyanidin-3-O,5-O-diglucoside, cyanidin-3-O-sambubioside, cyanidin-3-O-sambubiosid-5-O-glucoside, sambucin (= cyanidin-3-O-rhamnoglucoside), sambucyanin (= cyanidin-3-O-xyloglucoside) and traces of essential oil. Fresh elderberries contain important vitamins (e.g. in 100 mg berries: B_2 (>60 mg), C and folic acid (~20 mg), biotin and nicotinic acid amide (~2 mg), and β-carotene, vitamin B_6 and pantothenic acid (<0.5 mg) (Anonymous, 1994). Consequently, health claims are made for a number of food supplements prepared from elderberry fruit (see www.sambucol.com/index.cfm?id=506; www.florahealth.com/flora/home/Canada/Products/8300.htm; www.herbalremedies.com/elderberry.html).

The aim of this study was to review the literature in order to update the data on the pharmacological effects and clinical efficacy of elderberry fruit (Sambuci fructus).

METHODS

Searches were conducted of several electronic databases: OVID(MEDLINE), PUBMED, Silverplatter and CENTRAL, using some or all of the search terms: elderberry, *Sambucus*, *Sambucus nigra*, Sambuci fructus. Hand searches were also conducted in order to capture literature not stored electronically (e.g. theses). Two authors extracted the data independently and discussed the findings. Disagreements were resolved by consensus.

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Received 31 August 2008
Accepted 5 May 2008

Data extracted from each study were: surname of first author, year of publication, country of origin; preparation investigated, applied intervention and observed effects. For the clinical trials, the methodological quality and the level of evidence were assessed as described in previous reviews (Chrubasik *et al.*, 2006, 2007).

RESULTS

A total of 811 references were checked and 22 references investigating elderberry fruit were identified for the review. An additional four references were found during hand searches (Sahpira-Nahor *et al.*, 1995; Morag *et al.*, 1997; Burge *et al.*, 1999; Balasingam *et al.*, 2006). The experimental and clinical studies are summarized in Table 1, and the quality of the clinical studies and their evidence of effectiveness in Table 2.

The *in vitro* data show that the fruits of elderberry are effective against oxidative stress, viruses (Table 3) and possibly *Helicobacter pylori* and cancer, but these results are not consistently confirmed in studies in animals or humans (Table 1). One animal experiment, in which rats were fed with a berry concentrate over 4 weeks demonstrated only little effect on cholesterol levels and fatty acid pattern in the liver (Bobek *et al.*, 2001). Likewise, a confirmatory clinical study, in which healthy volunteers consumed elderberry juice (anthocyanidin consumption 120 mg/day) showed little change in serum lipids and low density lipoprotein oxygenation (Frank *et al.*, 2002). In contrast, high doses of elderberry (anthocyanidin consumption 4 g per day) showed some reduction in postprandial serum lipids (Murkovic *et al.*, 2004). One animal experiment demonstrated that rats with acetic acid-induced colitis placed on an elderberry diet had significantly less macroscopic damage and 50% lower myeloperoxidase activity scores than did rats in the control diet group (Bobek *et al.*, 2001). Another experiment in rats demonstrated possible central depressant and central analgesic effects of aqueous elderberry extract (Jacovljevic *et al.*, 2000).

Two exploratory studies in patients with viral infections (mainly influenza) provided moderate evidence of effectiveness for the proprietary product Sambucol^{R} when taken over 3 to 5 days within 24 h after the onset of symptoms (Zakay-Rones *et al.*, 1995, 2004). These studies are backed by an exploratory study in chimpanzees (Burge *et al.*, 1999). One *in vitro* study investigated the immunomodulatory (pro- and antiinflammatory) effects of this product (Barak *et al.*, 2002). The evidence of effectiveness for Sambucol^{R} in the treatment of influenza is, thus, moderate.

The products investigated in the trials were well tolerated. Adverse events did not occur. Consumption of a proprietary juice concentrate (Sambu-Holunderkur^{R}, 200 mL per day based on 120 g fresh berries supplemented with flower juice and extract based on 3.9 g dried flowers, diluted 1:5, yielding 400 kcal/day divided into up to six portions) had no impact on urinary hydrogen concentrations or excretions (Walz and Chrubasik, 2008). It is worth noting, however, that consumption of unripe berries or self-prepared juice that has been insufficiently heated or contains leaf or stem may cause toxic effects (Anonymous, 1994).

DISCUSSION

The review shows promising effects for the fruits of European elder, and encourages further investigation of the usefulness of *Sambuci fructus* as a preventive and/or therapeutic measure. Further data on safety are urgently warranted. The guidelines of the International Conference of Harmonization recommend the design and conduct of such safety pharmacological studies (see www.fda.gov/cber/gdlns/ichs7a071201.htm).

In children, consumption of a few berries may cause emesis. Likewise, consumption of greater amounts of raw, insufficiently heated berries may produce nausea and emesis in adults (Anonymous, 1994; www.nlm.nih.gov/medlineplus/druginfo/herb_All.html#E), especially if the raw material accidentally contains unripe berries, leaf or stem. Consumption of toxic compounds is the mostly likely explanation for 8 of 11 people who had several glasses of juice made from the fruits of *Sambucus mexicana* picked the day before and reported nausea, vomiting, weakness, dizziness, numbness and stupor. One person who consumed five glasses of juice was hospitalized for stupor (www.cdc.gov/mmwr/preview/mmwrhtml/00000311.htm; Anonymous, 1984). Compounds involved in toxicity include lectins (Anonymous, 1994) and cyanogenic glycosides (e.g. sambunigrin) which are hydrolysed in the gastrointestinal tract to free cyanide.

Some people have reported rhinoconjunctivitis and asthmatic symptoms after inhalation or contact with elderberry blossoms and juice from elder flowers. Förster-Waldl and coworkers (2003) demonstrated that in about 1% of 3668 patients tested, a skin prick test and/or radioallergosorbent test against ribosome-inactivating protein was positive. The lectin type-2 ribosome-inactivating protein is the major elderberry fruit protein (Van Damme *et al.*, 1997; De Benito *et al.*, 1998; Gibres *et al.*, 1996). Allergy to elderberry fruit products is, thus, possible, although not reported in the literature. Elderberry seed also contain lectins which in part are distinct from bark lectins (Peumans *et al.*, 1991). Another lectin, *Sambucus nigra* agglutinin, was shown to induce the release of IL-4 from human basophils, precipitating the release of IL-13 and histamine (Haas *et al.*, 1999). Unfortunately, the toxic and allergenic lectins appear to be important in elderberry antiviral activities (Chen *et al.*, 2002; Vandenbussche *et al.*, 2004) and potential antiproliferative effects (Citores *et al.*, 2002). Greater understanding of the function of lectins is required in order to strike a balance between antiviral and allergenic properties of therapeutic goods derived from elderberries.

Anthocyanins are the most important group of water-soluble plant pigments visible to the human eye. Six of them (pelargonidin, peonidin, cyanidin, malvidin, petunidin and delphinidin) are common in higher plants (Kahkonen and Heinonen, 2003). The dark colour of the berries of European elder is mainly due to the presence of cyanidin-3-glucoside and cyanidin-3-sambubioside (Mateus *et al.*, 2004). Among 14 different anthocyanins, cyanidin-3-glucoside had the highest antioxidative activity, 3.5 times higher than that of a vitamin E analogue (Wang *et al.*, 1997). In order to produce any clinical effect, anthocyanidins need to be absorbed from the gastrointestinal tract and to reach the target cells. Youdim and co-workers (2000) demonstrated that the elderberry anthocyanins are taken up into the membranes and

DOI: 10.1002/ptr

Table 1. ***In vitro*** **studies, animal experiments and clinical trials with preparations from Samuci fructus**

Surname of first author	Year	Country of origin	Preparation investigated	Intervention	Effects observed
in vitro **studies**					
Zakay-Rones	1995	Israel	Sambucol*	Influenza virus hemagglutination and replication tests	Antiviral effect (details see Table 2)
Sahpira-Nahor	1995	Israel	Sambucol*	HIV infected peripheral lymphocytes	Antiviral effect
Morag	1997	Israel	Sambucol*	Herpes simplex virus-1-infected human diploid fibroblasts and buffalo green monkey cells	Antiviral effect
Abuja	1998	Austria	Spray-dried juice$	Copper- and peroxyl-radical-driven lipid peroxidation tests	Antioxidant and prooxidant effects
Pool-Zobel	1999	Germany	Anthocyanin fraction of juice	Ferric reducing ability assay, effect on H_2O_2-induced DNA strand breaks and on genotoxicity	Antioxidant effect, may protect cells against external oxidative stress, but affects only weakly intracellular oxidative stress
Espin	2000	Spain	Concentrate'	2,2-diphenyl-1-picrylhydrazyl radical scavenging activity	Antioxidative effect
Youdim	2000	USA	extract (solvent not stated)#	Uptake of anthocyanins by bovine aortic endothelial cells and reaction versus oxidative stressors (H_2O_2 etc)	incorporation of anthocyanins into cell membrane and cytosol (less) associated with a protection against oxidative stress
Barak	2002	Israel	Sambucol**	Cytokine release of human monocytes	Increase in the release of inflammatory and anti-inflammatory cytokines (IL-1β, TNF-α, IL-6, IL-
Roy	2002	USA	Extract (solvent methanol)#	Oxygen radical absorbing capacity	antioxidative effect
Lugasi	2003	Hungary	Juice	Hydrogen-donating ability in the presence of DPPH radical, reducing power, copper(II)-chelating activity, total antioxidant status	Antioxidative effect
Wu	2004	USA	Acetone, water, acetic acid extracts	Hydrophilic (H) and lipophilic (L) antioxidant capacities with respect to total phenolics (TP)	Total antioxidative capacity was produced mainly with H; H/TP was 7.5
Chatterjee	2004	USA	Extract (solvent not stated)	Growth of *Helicobacter pylori* strain 49 503	Antibacterial effect and increased susceptibility to clarithromycin
Ginsburg	2004	Israel	Sambucol**	Measure of chemoluminescence	Antioxidative effect
Nakajima	2004	Japan	Anthocyanin fraction of juice	2,2-diphenyl-1-picrylhydrazyl radical scavenging activity	Antioxidative effect weaker than that of Trolol
Lichtenthäler	2005	Germany	Juice	Total oxidant scavenging capacity	Antioxidative effect
Bell	2006	USA	Extract (solvent not stated)§	Isometric force recording studies using isolated porcine coronary arterial rings	No dose-dependent muscle relaxation, thus no potential vasodilatative effect
Balasingam	2006	Israel	Sambucol**	Virus, cytotoxicity assay, reduction of viral titre assay	No cytotoxic effect, reduction of avian influenza virus
Thole	2006	USA	Extract (solvent acetone 70%) and fractions	COX-1 and COX-2 assays, quinone reductase activity in mouse Hepa1c1c7 cells	Compounds inhibited COX-2 and induced quinone reductase indicating anti-cancer properties
Cheng	2007	USA	Extract (solvent not stated)	Heterocyclic amine formation in processed beef, preincubation	Reduction in genotoxic compounds

Table 1. (*Continued*)

Surname of first author	Year	Country of origin	Preparation investigated	Intervention	Effects observed
Animal experiments					
Burge	1999	Israel	Sambucol*	Flu-prophylactic and -therapeutic treatment in chimpanzees over 6 months (season 1), symptomatic treatment (season 2)	Reduction of days with flu-like symptoms by 2/3 (season 1); duration of symptoms less than 24 h (season 2)
Jacovljevic	2000	Yugoslavia	Aqueous extract$$	Pentobarbitone sleep induction time and sleeping time, reaction time to radiant heat directed on the tail of rats	Central depressant and analgesic effects
Bobek	2001	Slovakia	Ethanolic extract$$$	Dietary supplementation with 4% extract over 4 weeks in rats with acetic acid-induced colitis	Anti-inflammatory and antioxidative effects, macroscopic improvement of colon histology
Frank	2002	Sweden	Concentrate#	Dietary supplementation over 4 weeks in rats	Little effect on cholesterol levels and fatty acid pattern in the liver, but may spare vitamin E
Clinical trials					
Murkovic	2004	Austria	Juice (120 mg anthocyanins/day)	Open arm (n = 6) for power calculation and safety assessment	Reduction in serum cholesterol after 2 weeks, increase in resistance to oxidation after 3 weeks, no adverse events
			Juice (4000 mg anthocyanins)	n = 6, meal tolerance tests without and with a single oral dose	In the verum group serum triglyceride increase tended to be lower, no adverse events
			Juice (120 mg anthocyanins/day)	randomized double-blind study vs placebo on fasting and postprandial serum lipids and LDL lipid oxidation	After 2 wks, total cholesterol was not significantly different, resistance to copper-induced oxidation of LDL did not change within 3 weeks, no adverse events
Zakay-Rones	1995	Israel	Sambucol**	Open arm (n = 35) for safety assessment	No adverse events
			Sambucol**	Randomized double-blind study vs placebo in patients suffering from influenza/viral upper respiratory tract infection	Significant improvement in clinical symptoms and higher antibody titers in the verum group; no adverse events
Zakay-Rones	2004	Israel	Sambucol**	Randomized double-blind study vs placebo in patients suffering from influenza A and B virus infections	Beneficial effect: 4 days earlier symptom relief, less intake of rescue medication; no adverse events

** Sambucol[R] (Razei Bar Ltd, Jerusalem), a syrup containing elderberry juice, raspberry extract, glucose, citric acid and honey; flavonoid spectophotometric UV absorption at 516 nm: 0.6 ? (unit not stated).
* without glucose and honey.
$ Total anthocyanins 90 mg/g.
& total anthocyanidins 18 g/100 g; total phenolics 25 mg/100 g.
# 1.6–3 mg anthocyanidins/kg/day.
§ extracts from lyophilized powder that had the sugars removed.
$$ 10 g dried berries suspended and boiled in 100 mL water.
$$$ Colouring Concentrate From Black Elder Pomace[R], solvent 70% ethanol, drug extract ration 5-6:1; contains 5 anthocyanins.

Table 2. A eligibility criteria specified, B randomization appropriate, C treatment allocation concealed, E similarity at baseline, F outcome measures and control interventions explicitly described, G co-interventions comparable, H outcome measures relevant, I adverse events and J drop-outs fully described, K sample size based on a priori power calculation, L intention-to-treat analysis, N point estimates and measures of variability presented for the primary outcome measure, O appropriate timing giving a Total Score (TS) of 13. The level of evidence of effectiveness was defined as strong – pooling of data or at least 2 confirmatory studies demonstrating a clinical relevant effect, moderate – consistent findings among one confirmatory study with a clinical relevant effect and/or multiple exploratory studies of high internal validity, insufficient-multiple exploratory studies of low internal validity or one single study of high internal validity indicating effectiveness

	J Alt Compl Med 1995; **1**: 361–369	*J Int Med Res* 2004; **32**: 132–140	*Eur J Clin Nutr* 2004; **58**: 244–249
	$n = 37$	$n = 60$	$n = 34$
	Sambucol[R]	Sambucol[R]	Study Medication
	4 tablespoons over 3 day	4 × 15 mL over 5 day	3 × spray-dried juice/day
	randomized double-blind	randomized double-blind	randomized double-blind
	over 6 days		
	verum: influenza A $n = 0$,	over 2 ($n = 20$) or 3 weeks	over 2 ($n = 20$) or 3 weeks
	B $n = 13$, other virus $n = 2$	verified influenza virus	
	placebo: influenza A+B $n = 2$,	infections, within 48 h of	
A	B $n = 10$	symptom onset	healthy volunteers
B	yes	yes	yes
C	yes	yes	yes
E	don't know	yes	yes
F	yes	yes	yes
G	don't know	yes	yes
H	yes	yes	yes
I	don't know	yes	yes
J	probably no drop-out	yes	yes
K	no	no	no
L	probably yes	yes	yes
N	no	no	no
O	yes	yes	yes
TS	at most 8	11	11

Table 3. Anti-influenza virus activity of aqueous elderberry extract in cell cultures (numbers of tissue culture infective doses 50% that were completely inhibited by SambucolR dilutions) modified after Zakay-Rones *et al.*, 1995

	No of tissue culture infective dose 50%	
	1:8	1:16*
Human Influenza		
Type A/Shangdong 9/93 (H3N2)	40	40
Type A/Beijing 32/92 (H3/N2)	40	
Type A/Texas 36/91 (H1N1)	4	
Type A/Singapore 6/86 (H1N1)	2	
Type B/Panama 45/90	2	
Type B/Yamagata 16/88	20	10
Type B/Ann Arbor 1/86	7	
Animal Influenza		3.5
Type A/Sw/Ger 2/81	8	4
Type A/Tur/Ger 3/91	2	1
Type A/Sw/Ger 8533/91	8	2

* partial inhibition.

cytosol of vascular endothelial cells, which subsequently effectively protected them against oxidative insult (e.g. hydrogen peroxide, dihydrochloreide or $FeSO_4$/ascorbic acid) *in vitro*. After absorption from the gastrointestinal tract in mammals, anthocyanins were shown to be incorporated into plasma and liver keeping structurally intact glycoside forms (Miyazawa *et al.*, 1999). Likewise, human pharmacological studies revealed very low gastrointestinal absorption after intake of a juice concentrate (150 mL, anthocyanin content 3.6 g) or a berry extract (anthocyanin content 147 mg to 1852 mg) with less than 1% found in urine (Bitsch *et al.*, 2004; Frank *et al.*, 2005, 2007). Within 4 h after the intake of a berry extract (anthocyanin content 720–1600 mg) anthocyanidin metabolites were detected in plasma and urine, along with small amounts of unchanged cyanidin-3,5-diglucoside (Cao and Prior, 1999; Milbury *et al.*, 2002; Mülleder *et al.*, 2002; Wu *et al.*, 2002). Despite low absorption in humans, there is evidence from anthocyanidin research that even low quantities of anthocyanidins may modify the markers of oxidative stress (Farombi *et al.*, 2004).

For a proprietary product OptiBerry[R] that contains extract of Sambuci fructus as well as extracts of other berries (wild blueberry, wild bilberry, cranberry, strawberry) and raspberry seed extract, a number of promising biomedical effects were demonstrated: (i) inhibition of inducible vascular endothelial growth factor expression by human HaCaT keratinocytes, (ii) inhibition of basal transcription of monocyte chemotactic protein-1 and of NFκB activity, (iii) inhibition of hemangioma formation in mice and reduction of average mass of tumor growth, (iv) inhibition of *Helicobacter pylori* growth, (v) inhibition of *H. pylori*-induced IL-8 release in human gastric cancer cells MKN45 and (vi) reduction of atherosclerotic index in hamsters (Bagchi *et al.*, 2004). For this proprietary product, acute toxicity data are available (not, however, data on chronic toxicity) confirming that the product is reasonably safe for short-term use (Bagchi *et al.*, 2006). More rigorous data are

DOI: 10.1002/ptr

required to determine the long-term safety of preparations or food supplements derived from elderberry fruits. Confirmatory studies in which clinically relevant effect sizes are achieved are also required to confirm the posited antiviral, antioxidative, antiproliferative and antiinflammatory effects.

Specific berry anthocyanins improved capillary perfusion, improved brain function, reduced elevated plasma glucose levels, improved night vision and vascular retinopathy in diabetic or/and hypertensive patients and halted the progression of lens opacity in patients with mild cortical cataract without being associated with adverse events (Zafra-Stone *et al.*, 2007). Possible neuroprotective (Kang *et al.*, 2006) and antiaging (Galli *et al.*, 2002) effects were supported in a recent population-based prospective study indicating that fruit and vegetable juices may delay the onset of Alzheimer's disease (Dai *et al.*, 2006). It remains to be established whether any additional effects are associated with the popular elderberry diet (www.florahealth.com/flora/home/Canada/Products/8300.htm) over the weight loss occurring with any 400 kcal diet (Chrubasik *et al.*, 2008).

The average consumption of fruit phenols per person in the USA has been estimated to be 255 mg/day of catechin equivalents (Vinson *et al.*, 2003). Dietary reference intake values do not exist for anthocyanidins. A guideline on the optimal dose range for polyphenols is warranted which should be based on clinical studies demonstrating the health-promoting effects. Until guidelines are available, consumers are advised to be aware of their intake of phenolics in food supplements (e.g. from elderberry fruit), and to avoid excessive consumption.

Stating the amount of health-promoting compounds in a product is inadequate. The method of analysis also needs to be declared because less specific methods cannot distinguish between coactive compounds and their metabolites. We recently investigated the anthocyanin content in the dietary supplement Sambu Holunderkur^{R}. The anthocyanin contents obtained with the method described in the French Pharmacopoeia (Anonymous, 2000) was 762 mg/L, with the pH-differential spectrophotometric technique (Giusti and Wrolstad, 2000) 85 mg/L and with HPLC analysis with mass spectrometric identification of the cyanidin derivatives (Chandra *et al.*, 2001; Kammerer *et al.*, 2004) 4 mg/L. Only the latter method reveals the true anthocyanin content, which was negligible in the proprietary food supplement. In a mother concentrate (Wild GmbH, Eppelheim, Germany) used to prepare dietary supplements, 15 400 mg/kg of anthocyanidins was identified with the hyphenated technique (Chrubasik *et al.*, 2008). Health-promoting compounds may be destroyed during the preparation of a food supplement. Mixing of elder fruits with oxygen during processing, a low content of oxygen in the juice before tapping (Kaack and Austed, 1998), heating (Sadilova *et al.*, 2007), or storage at high temperatures (Heigl and Franz, 2003), result in degradation of the phenolic compounds and in a decline in the antioxidative capacity. Kaack and Austed (1998) have shown that ascorbic acid may protect anthocyanidins but not quercetin from oxidative degradation. Choosing starting material with a high content of ascorbic acid may be advantageous.

Enriching food supplements with phenolic compounds, in order to enhance health benefits, has been suggested (Vattem *et al.*, 2005) although it is unclear whether such supplementation is clinically useful. Comparisons of preparations enriched with synthetic compounds with concentrates of phenolics in their natural context are required. Another possibility to increase the content of health-promoting compounds is via selection of the *Sambucus* genotype. Important quality characteristics such as juice yield, turbidity, titratable acidity, soluble solids and content of phenolic acids and flavonoids are largely determined by the raw material (genotype), although other variables (ripening stage, process of juice production) do have some influence on juice yield and physicochemical characteristics (Kaack *et al.*, 2008). Factor analyses revealed correlations between the quality characteristics which may help manufacturers to identify the optimum *Sambucus nigra* genotype. Optimum time of harvest, towards complete maturity (the anthocyanin content increased continuously until the last harvest days), was shown to be associated with a maximum in antioxidative capacity (Stefanovits-Banyai *et al.*, 2004).

CONCLUSION

Elderberry fruit contains a number of health-promoting compounds. Although *in vitro* data on the antioxidative, antiviral and possible antiinflammatory, antibacterial and antiproliferative, effects are very promising, current clinical evidence of effectiveness is only poor to moderate. Further studies are needed to demonstrate clinical effects beyond any doubt.

Elderberry fruit preparations need to be fully characterized: besides drug extract ratios and solvents employed in the case of extracts, the anthocyanidin content should be declared using HPLC with mass spectrometric identification of the cyanidin derivatives. Other analyses are less reliable and may be misleading. By choosing high quality starting material, and avoiding preparatory processes that destroy the co-active compounds, food supplements with high anthocyanidin contents can be produced. Because some elderberry compounds may be toxic, rigorous safety data are urgently needed. Dietary reference intake values exist for vitamins and minerals. A similar guideline on the optimal dose range for polyphenols is warranted to prevent toxicity.

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DOI: 10.1002/ptr