Journal of Human Hypertension (2013) **27,** 126–130

www.nature.com/jhh

ORIGINAL ARTICLE

Kiwifruit decreases blood pressure and whole-blood platelet aggregation in male smokers

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Lifestyle modifications to reduce risk factors for cardiovascular diseases such as blood pressure (BP) and smoking have been emphasized. Fruits and vegetables may modify such risk factors. The major aim of this randomized, controlled trial was to investigate the effects of (1) kiwifruits and (2) an antioxidant-rich diet compared with (3) a control group on BP and platelet aggregation (that is, whole-blood platelet aggregation) after 8 weeks in male smokers (age 44–74 years, $n = 102$). The kiwifruit group received 3 kiwifruits per day, whereas the antioxidant-rich diet group received a comprehensive combination of antioxidant-rich foods. In the kiwifruit group, reductions of 10 mm Hg in systolic BP and 9 mm Hg in diastolic BP were observed ($P = 0.019$ and $P = 0.016$ (change from baseline in the kiwifruit group compared with change from baseline in the control group)). In the antioxidant-rich diet group, a reduction of 10 mm Hg in systolic BP was observed among hypertensives ($P = 0.045$). Additionally, a 15% reduction in platelet aggregation and an 11% reduction in angiotensin-converting enzyme activity was observed in the kiwifruit group ($P = 0.009$ and $P = 0.034$). No effects on these parameters were observed in the antioxidant-rich diet group. This study suggest that intake of kiwifruit may have beneficial effects on BP and platelet aggregation in male smokers.

Journal of Human Hypertension (2013) **27,** 126–130; doi:10.1038/jhh.2011.116; published online 19 January 2012

Keywords: dietary antioxidants; kiwifruit; platelet aggregation; ACE activity; cardiovascular diseases

INTRODUCTION

It is well accepted that dietary regimes such as the Dietary Approach to Stop Hypertension (DASH) diet exert beneficial effects on blood pressure (BP).[1] This is a comprehensive diet, with focus on increased intake of fruits and vegetables, as well as reduced intake of salt and dietary fat. Additionally, some initial studies suggest that addition of specific foods, such as tomatoes,[2] grapes,[3] berries[4] and dark chocolate,[5] to a regular diet may mediate similar effects.

No previous studies have investigated the effects of kiwifruit on BP. However, two recent clinical trials have observed that kiwifruit may have beneficial effects on other cardiovascular disease (CVD)-related parameters such as lipid profile and platelet aggregation,[6,7] suggesting a potential preventive role of kiwifruits.

Hypertension has been related to oxidative stress,[8] but antioxidant-rich foods and supplements have shown variable effects on BP in intervention trials.[9] It is therefore not clear whether oxidative stress reduction through consumption of dietary antioxidants may have a potential role in the prevention, or treatment, of hypertension.

We have recently measured the total antioxidant content of more than 3100 foods used worldwide.[10] This food table allows us to determine the habitual intake of total antioxidants and to design an antioxidant-rich diet that doubles the intake of dietary antioxidants. In a previous study[11] we have demonstrated that this diet significantly increases the concentrations of several plasma antioxidants. In this study, we also have investigated whether such a diet affects BP and platelet aggregation.

The major aim of this randomized, controlled trial was to investigate the effects of (1) kiwifruits and (2) an antioxidant-rich diet, compared with (3) a control group, on BP, platelet aggregation and angiotensin-converting enzyme (ACE) activity after 8 weeks in male smokers (age 44–74 years, $n = 102$). Male, middle-aged and elderly smokers were selected as these individuals have relatively high oxidative stress, and smoking is an established risk factor for hypertension.[12,13]

MATERIALS AND METHODS

Subjects

Participants were recruited through advertisement in local newspapers. Inclusion criteria were male, aged 45–75 years, smoking >5 cigarettes per day, stable weight range (<4-kg change last 12 weeks) and body mass index ($< 35\ kg\ m^{-2}$). The exclusion criteria were any history of CVD or other significant clinical disorders, following a vegetarian or near-vegetarian diet, or allergy to foods included in the intervention diets. We excluded subjects with a history of serious or unstable medical or psychiatric disorder; current use of lipid-lowering treatment, aspirin or non-steroidal anti-inflammatory drugs; nutritional supplements or herbs for weight loss; or participants in drug trials during the previous 30 days. Of the 102 study subjects, 8 reported ongoing use of BP-lowering agents (angiotensin-II receptor antagonists, ACE inhibitors, calcium antagonist and β-blockers). Use of drugs was stable through the run-in and intervention periods.

Study design and intervention

The study followed a randomized, parallel design with an 8-week intervention period, and a 4-week run-in period preceded the intervention period. During the run-in and intervention periods, participants were instructed to avoid use of vitamin or antioxidant supplementation, as well

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Received 18 October 2011; revised 12 December 2011; accepted 19 December 2011; published online 19 January 2012

as pain or cold remedies containing aspirin. Moreover, participants were asked to limit their consumption of berries, nuts, pomegranates, tomatoes, kiwifruit, tea and coffee (<3 cups per day). After the run-in period, subjects were randomly assigned to one of three groups, kiwifruit, antioxidant-rich diet or control group.

The kiwifruit group received 3 kiwifruits per day (*Actinidia deliciosa*; Odd Langdalen Frukt & Grønnsaker Engros AS, Oslo, Norway). This provided an addition of approximately 195 g fruit per day, providing 467 kJ day^{-1}. Subjects in both intervention groups were provided with intervention items at weekly follow-ups. For the antioxidant-rich diet group, the administered food items, as well as the amounts of dietary antioxidants provided, are specified in Table 1. To participants in the antioxidant-rich diet group, individual counseling was given by a trained nutritionist to help implement the provided foods in their habitual diet. The control group was advised to follow their habitual diet, and attended bi-weekly follow-ups. The study was approved by the regional ethics for medical research committee (REK Sør) and all participants gave written, informed consent. The study is registered as 'Oslo antioxidant study' (NCT00520819) at www.clinicaltrials.gov.

Dietary intake

Dietary intake was recorded using a 7-day food record with a picture book. Previous validation of this food record has demonstrated that reported energy and nutrient intakes are valid on a group level.[14] The food records were completed the last week of the run-in period and the last week of the intervention period. Average daily intakes were computed using the food database AE-07 and the KBS software system (version 4.9, 2008) developed at the Department of Nutrition. The food database is based on the 2006 edition of the Norwegian food composition table. The antioxidant values are based on our comprehensive antioxidant food database.[10] Data on dietary intakes were available for 32 participants in each group.

BP measurements

BP was measured by a trained nurse using a digital BP monitor (OMRON-Hem-705 CP, Kyoto, Japan) and appropriate cuff sizes after 5-min rest. BP was calculated as the mean of three measurements. BP was classified according to the '2007 Guidelines for the Management of Arterial Hypertension' of the European Society for Hypertension.[15] Accordingly, subjects were classified as 'optimal' if systolic BP was <120 mm Hg or diastolic BP was <80 mm Hg; 'normal/high normal' if systolic BP was 120–139 mm Hg and/or diastolic BP was 80–89 mm Hg; and 'hypertensive' if systolic BP was ⩾140 mm Hg and/or diastolic BP was ⩾90 mm Hg.

Laboratory analysis

Overnight, fasting blood samples were collected before and after the intervention period, between 0800 and 1000 hours. Plasma and serum were immediately prepared and stored at −70 °C until the time of analysis unless immediately analyzed.

The methods for assessment of serum lipids, enzyme activities, and inflammatory and hemostatic parameters related to CVD are provided in the Supplementary information.

Platelet aggregation and ACE activity

Adenosine diphosphate (ADP)-induced whole-blood platelet aggregation was assessed in citrated whole blood using a platelet aggregometer (Chrono-Log, Haverton, PA, USA) at a constant stirring speed of 1000 r.p.m. at 37 °C as described elsewhere.[7] Based on previous experiments, and the high number of samples assessed each day, ADP at 5 mM was the only agonist used.[7] Platelet aggregation was assessed within 2 h after blood sampling, and samples were kept at room temperature until the time of analysis. ACE activity was assessed in serum by its ability to cleave the synthetic substrate (FAPGG). The assays linear range is between 0 and 175 U l^{-1}. ACE activity was determined in thawed serum according to the

Table 1. Food items provided by the antioxidant-rich diet

Food item	*Provided weekly*	*Total antioxidants (mmol per week)*	*Energy (kJ per week)*
Twinings Green Java Tea	7 tea bags	20.86	45
Juice of rose hips, orange, apple and carrot (Mana Yellow)[a]	1.66 l	42.64	1397
Juice of cranberries, raspberries and grapes (Mana Red)[a]	1.66 l	10.95	1397
Juice of black chokeberry, bilberries, grapes and cherries (Mana Blue)[a]	1.66 l	33.18	1397
Bilberry juice (*Vaccinium myrtillus*)[b]	0.66 l	54.73	1069
Bilberry jam (*V. myrtillus*)[c]	345 g	10.50	555
Bilberries (*V. myrtillus*)[d]	200 g	16.24	312
Blackberries (*Rubus fruticosus*)[d]	200 g	9.20	288
Strawberries (*Fragaria x ananassa*)[d]	200 g	4.26	321
Raspberries (*Rubus idaeus*)[d]	200 g	5.87	169
Pomegranate (*Punica granatum*)[d]	200 g	3.43	608
Dark blue grapes (*Vitis sp.*)[d]	200 g	2.23	284
Brussel sprouts (*Brassica oleracea var. gemmifera*)[d]	200 g	2.01	288
Broccoli (*Brassica oleracea var. italica*)[d]	200 g	1.93	189
Red cabbage (*Oleracea var. capitata rubra*), outdoor cultivar[e]	200 g	3.82	189
Kale (*Brassica oleracea var. sabellica*)[e]	200 g	4.71	345
Blue potatoes (*Solanum tuberosum*, 'Blue congo')[d]	150 g	1.20	419
Tomatoes (*Solanum lycopersicum*)[d]	700 g	2.24	822
Dark chocolate, 70% cocoa[f]	100 g	11.22	1850
Pecan nuts (*Carya illinoinensis*)[g,h]	100 g	8.30	2787
Sunflower seeds (*Helianthus annuus*)[g,h]	100 g	6.31	2269
Walnuts (*Juglans californica*)[i,e]	200 g	44.48	5557
Extra Virgin Olive Oil (*Olea europaea*)[j]	0.063 l	0.19	2302
Rosemary (*Rosmarinus officinalis*)[k]	3 g	1.55	0
Thyme (*Thymus vulgaris*)[k]	3 g	1.69	0
Oregano (*Origanum vulgare gracile*)[k]	3 g	1.90	0
In total/week		305.60	24 857

Food items were provided by [a]Tine BA (Oslo, Norway), or purchased from the following: [b]Corona Safteri (Ranheim, Norway), [c]Heistad (Bergen, Norway), [d]Odd Langdalen Engros (Oslo, Norway), [e]The Norwegian University of Life Sciences (Ås, Norway), [f]Kraft Foods (Northfield, IL, USA), [g]Den lille nøttefrabrikken (Fredrikstad, Norway), [h]Provided as ingredients in bread (Åpent bakeri, Oslo, Norway). [i]Diamond Foods Inc. (Stockton, CA, USA), [j]Ybarra (Toano, Spain), [k]Black Boy (Bergen, Norway). Amounts of total antioxidants were assessed by FRAP assay.[10]

manufacturers instructions (ACE kinetic, kit number 01-KK-ACK; Bühlmann Laboratories AG, Schönenbuch, Switzerland). These assays have an inter-assay coeffecients of variation <7%.

Statistical analysis

Kruskal–Wallis one-way analysis of variance was used to compare baseline values or changes during the intervention period between groups. Changes (that is, intervention effects) were calculated by subtracting the baseline value from the post-intervention value. Where significant results were obtained, Student's *t*-test or Mann–Whitney non-parametric test was used to compare differences. Data from two excluded participants were not included in the analysis. All statistics were performed using SPSS version 18.0. *P*-value <0.050 was considered statistically significant.

RESULTS

A total of 137 subjects responded to the initial advertisement, and 118 were found eligible and screened. Of these, 102 were included in the study. Two subjects were excluded: one subject in the kiwifruit group owing to a non-fatal cardiovascular event and one in the antioxidant-rich diet group owing to lack of compliance. A total of 100 participants completed the study ($n=34$ in the control group, $n=33$ in each intervention group; Supplementary Figure SF1).

Baseline characteristics were similar between groups (Table 2), and no change in body mass index, body weight or cigarette smoking was observed during the intervention period. Compliance to both intervention diets was good.[11] Dietary intakes at baseline and changes during the intervention period are listed in Table 3. Dietary intake was similar between groups at baseline.

Baseline levels, as well as the effects of the dietary interventions on BP, are given in Table 4, for the overall study population, and among subjects with optimal, normal/high-normal BP, and hypertensives. In the kiwifruit group, reductions of 10 mm Hg in systolic BP and 9 mm Hg in diastolic BP ($P=0.007$ and $P=0.010$; change from baseline in the kiwifruit group compared with change from baseline in the control group) were observed in the overall study population. The largest effects were observed among subjects with normal/high-normal BP and hypertensives. Interestingly, a reduction of 10 mm Hg in systolic BP was also observed among hypertensives in the antioxidant-rich diet group ($P=0.045$).

Furthermore, we observed that the number of subjects with normal/high-normal BP, or hypertensives, in the kiwifruit group was significantly reduced, from 65% at baseline to 33% following the intervention ($P<0.050$; data not shown). Only minor changes were observed in the antioxidant rich-diet group.

Effects of the dietary interventions on platelet aggregation and ACE activity are presented in Table 5. In the kiwifruit group, a 15% reduction in platelet aggregation ($P<0.004$) and an 11% reduction in ACE activity ($P=0.013$) were observed. No similar effects were observed in the antioxidant-rich diet group.

No effects were observed on plasma lipids, other enzyme activities, and inflammatory and hemostatic parameters related to CVD (Supplementary Table ST1).

DISCUSSION

We demonstrate that intake of 3 kiwifruits per day promotes pronounced anti-hypertensive and anti-thrombotic effects in male smokers. Additionally, a substantial reduction in systolic BP among hypertensives following consumption of the antioxidant-rich diet was observed.

In the kiwifruit group, the observed overall reductions in systolic and diastolic BP were about 8–10 mm Hg. Among hypertensive subjects, even larger effects were observed. A reduction in systolic BP of about 10 mm Hg was also observed among hypertensive subjects following consumption of the antioxidant-rich diet. A recent meta-analysis suggested a 25–40% reduction in risk of cardiovascular events following a similar reduction in BP by therapeutic anti-hypertensive treatment.[16]

Table 2. Baseline descriptives

Variable	*Control* (n = *34*)	*Antioxidant-rich diet* (n = *33*)	*Kiwifruit* (n = *33*)	P*
	Baseline (range)	*Baseline (range)*	*Baseline (range)*	
Age (years)	56 (44-71)	57 (45-74)	57 (45-73)	0.770
BMI (kg m^{-2})	24.8 (21.6-30.4)	25.7 (19.4-32.0)	24.7 (18.8-32.2)	0.997
Body weight (kg)	83.7 (66.2-99.8)	79.3 (50.7-110)	76.8 (55.0-98.2)	0.270
Cigarettes per day	15 (6-35)	15 (5-40)	15 (5-25)	0.987
BP-lowering agents (*n*)	3	2	3	1.000

*P-value is from comparing baseline values between groups.

Table 3. Daily intake of macro- and micronutrients, baseline and change during intervention[a,b]

Variable	*Control* (n = *32*)		*Antioxidant-rich diet* (n = *32*)		*Kiwifruit* (n = *32*)		P
	Baseline (range)	*Change*	*Baseline (range)*	*Change*	*Baseline (range)*	*Change*	
Total energy (kJ)	9767 (4945-16 780)	−519 ± 2213	10 382 (5334-16 857)	1957* ± 2350	10 001 (5225-19 638)	−18.5* ± 1961	<0.001
Protein (E%)	16.3 (12.1-22.6)	−0.40 ± 2.0	16.1 (11.2-21.1)	−2.8* ± 2.7	16.6 (12.9-23.5)	−1.0* ± 2.53	0.001
Total fat (E%)	34.4 (23.7-48.9)	−0.02 ± 4.7	34.8 (25.5-53.9)	0.9 ± 5.7	35.3 (25.8-45.5)	−0.35 ± 4.50	0.671
Carbohydrates (E%)	42.2 (24.1-56.8)	−0.9 ± 7.4	41.2 (28.6-50.9)	4.5* ± 4.8	40.6 (31.2-57)	1.96* ± 4.32	0.001
Fiber (g)	22.5 (18.9-26.0)	−2.8 ± 6.6	20.2 (18.0-22.5)	17.3* ± 10.3	22.9 (20.3-25.6)	3.7* ± 4.00	<0.001
Cholesterol (mg)	376 (187-677)	−20 ± 165	376 (204-603)	−29 ± 164	378 (156-878)	−6 ± 137	0.226
Calcium (mg)	815 (217-1822)	−47 ± 261	834 (254-1597)	85 ± 386	792 (485-1810)	−17 ± 267	0.226
Magnesium (mg)	402 (214-961)	−22 ± 99	403 (237-608)	124* ± 119	390 (207-700)	40.8* ± 68.2	<0.001
Potassium (mg)	4020 (2020-6107)	−208 ± 884	4077 (2179-5920)	1187* ± 1324	4008 (1837-5348)	236* ± 704	0.002

*Significantly different as compared with control ($P<0.050$). [a]Based on 7-day food record. [b]All variables are normally distributed.

Table 4. Baseline values (range) and change in BP during the intervention; in the overall study population; and among subjects with optimal BP, normal/high-normal BP and hypertensives[a]

Variable	*Control* (n = *34*)		*Antioxidant-rich diet* (n = *33*)		*Kiwifruit* (n = *33*)		P
	Baseline (range)	*Change*	*Baseline (range)*	*Change*	*Baseline (range)*	*Change*	
Overall study population	34		33		33		
Systolic BP (mm Hg)	123 (108–187)	2 ± 11.1	127 (98–160)	−2 ± 10.7	126 (89–175)	−10* ± 11	0.019
Diastolic BP (mm Hg)	83 (70–102)	−2 ± 8.8	83 (67–113)	−4 ± 7.4	86 (64–110)	−9* ± 11	0.016
Subjects with optimal BP	11		11		12		
Systolic BP (mm Hg)	112 (108–117)	9 (2, 16)	109 (98–118)	3 (−4, 9)	111 (89–119)	−1* (−6, 4)	0.011
Diastolic BP (mm Hg)	75 (70–79)	4 (−3, 11)	76 (67–78)	−1* (−4, 3)	74 (64–79)	−3* (−7, 0)	0.006
Subjects with normal/ high-normal BP	12		13		12		
Systolic BP (mm Hg)	127 (120–135)	−3 (−9, 3)	129 (120–139)	−2 (−9, 4)	127 (120–132)	−13* (−19, −7)	0.046
Diastolic BP (mm Hg)	82 (80–89)	−2 (−8, 3)	82 (80–88)	−5 (−11, −1)	84 (80–89)	−8* (−14, −4)	0.049
Hypertensives	11		9		9		
Systolic BP (mm Hg)	153 (140–187)	−1 (−7, 5)	149 (140–160)	−10* (−17, −2)	153 (140–175)	−15* (−30, −2)	0.041
Diastolic BP (mm Hg)	98 (91–102)	−4 (−11, 3)	94 (92–113)	−6 (−11, 2)	99 (90–110)	−13* (−20, −5)	0.043

Abbreviation: BP, blood pressure, *Significantly different from change in the control group ($P < 0.050$, Mann–Whiney test). [a]BP is non-normally distributed in the overall study population and within sub-groups.

Table 5. Baseline values (range), and change in whole-blood platelet aggregation and ACE activity[a]

Variable	*Control* (n = *34*)		*Antioxidant-rich diet* (n = *33*)		*Kiwifruit* (n = *33*)		P
	Baseline	*Change*	*Baseline*	*Change*	*Baseline*	*Change*	
Aggregation (AU)	13.0 (10.0–18.5)	−0.5 (−1.3, 0.1)	13.0 (10.0–16.3)	−1.1 (−1.8, −0.3)	13.6 (10.0–18.3)	−2.1* (−3.1, −1.4)	0.009
ACE activity ($U\,l^{-1}$)	27.42 (6.89–59.23)	3.09 (−0.95, 6.05)	27.31 (15.05–62.73)	−1.4 (−3.20, 4.15)	28.45 (11.84–53.20)	−3.22* (−5.80, −1.15)	0.034

Abbreviation: ACE, angiotensin-converting enzyme. *Significantly different compared with control ($P < 0.050$, Mann–Whitney test). [a]Variables are non-normally distributed; baseline is median (range); change is median (95% CI).

Additionally, a reduction in ACE activity was observed in the kiwifruit group, indicating that the kiwifruit constituents inhibit its activity. ACE acts as a major regulator of BP through the renin–angiotensin system by its ability to produce the vasoconstrictor angiotensin-II. Thus, ACE activity is a major therapeutic target in treatment of hypertension. Previously, it has been observed that kiwifruit, as well as other antioxidant-rich plant foods, inhibit ACE activity in *in vitro* assays, possibly by forming a complex with one or several of the active sites of the enzyme.[17–20] A recent meta-analysis has indicated that the estimated effects of BP lowering by ACE inhibitors among hypertensives is −8 mm Hg in systolic BP and −5 mm Hg in diastolic BP.[21] This study demonstrates that addition of 3 kiwifruits per day to a regular diet may mediate similar effects.

It is not possible to determine which constituents in kiwifruits mediate ACE-inhibitory effects. Kiwifruit is rich in vitamin C and polyphenols,[22,23] constituents that are abundant in the antioxidant-rich diet. Thus, it is intriguing that no similar effects on ACE activity are observed in subjects following consumption of the antioxidant-rich diet. Possibly, specific polyphenols not present or abundant in other antioxidant-rich foods may be responsible for the effect.

Furthermore, a substantial reduction in ADP-induced platelet aggregation was observed in the kiwifruit group. This observation in male, middle-aged and elderly smokers is similar to the effect observed in healthy young subjects, as demonstrated in a previous study.[7] Platelet activation and aggregation are fundamental in a number of processes involved in the pathogenesis of CVD.[24] These data suggest that kiwifruit intake may mediate antithrombotic effects and thus decrease the risk of cardiovascular events. It has been demonstrated previously that kiwifruit consumption inhibits platelet aggregation.[7] *In vitro*, ADP-induced platelet aggregation was inhibited several fold as compared with other agonists such as arachidonic acid and collagen. However, when tested in blood samples following kiwifruit consumption, it was not possible to distinguish between the inhibitory effects using these different agonists.[7] Furthermore, owing to the high number of samples that were assessed each day, we were obliged to select between different agonists for the aggregation assay. Thus, ADP was the only agonist used in this study.

Interestingly, it has been demonstrated that ACE inhibitors not only reduce BP, but also may mediate reduction in platelet reactivity in hypertensives.[25] As a number of biochemical parameters unrelated to BP were analyzed, we acknowledge the possibility that the observed effect on platelet aggregation may be a chance finding. Further validity of the observation must be confirmed in future studies.

The food items provided by the antioxidant-rich diet provided 3550 $kJ\,day^{-1}$.[11] Intentionally, the participants should have replaced 1/3 of their habitual diet during the intervention. However, the participants reduced their energy intake from other food sources by only 1120 $kJ\,day^{-1}$, causing an increase in energy intake of 19% in this group. However, no increase in body weight was observed (−0.2 ± 3.2 kg in the antioxidant-rich diet group versus 0.1 ± 1.7 kg in the control group), although such an increase in energy intake for 8 weeks theoretically should promote a weight gain of about 3 kg. As the present study was not designed to accurately assess energy intake or expenditure, this apparent lack of effect on body weight needs to be addressed in future studies. Other major changes in dietary intakes include increases in intakes of carbohydrates, fiber, magnesium and potassium in the antioxidant-rich diet group, and increases in intakes of magnesium and potassium in the kiwifruit group. However, no

association between changes in dietary intakes and changes in BP, platelet aggregation or ACE activity were observed.

In conclusion, we demonstrate that administration of three kiwifruits per day to male, middle-aged and elderly smokers mediates anti-hypertensive effects after 8 weeks, possibly through inhibition of ACE activity. The effects were substantial, and have not been observed previously in dietary intervention studies. Furthermore, kiwifruit did demonstrate anti-thrombotic effects, and the antioxidant-rich diet reduced BP among hypertensive individuals. Thus, kiwifruits, and possibly also antioxidant-rich foods, may have a potential role in the prevention of CVDs. Such a dietary approach may be particularly useful in postponing pharmacological treatment in individuals with high-normal BP or hypertension. The effects observed in this randomized, controlled trial deserve further investigation, and further studies are needed to elucidate any potential dose–response relationship, the constituents mediating these effects, as well as the mechanisms involved.

What is known about this topic

- Certain dietary factors affect BP.
- Certain antioxidant-rich foods have demonstrated beneficial effects on BP.
- Kiwifruit has been demonstrated previously to affect blood lipids and platelet aggregation.

What this study adds

- No previous study has investigated the effect of kiwifruit on BP.
- Addition of 3 kiwifruits per day to a regular diet mediates anti-hypertensive and anti-thrombotic effects in male smokers. The observed anti-hypertensive effect may be mediated by inhibition of ACE activity.
- A comprehensive antioxidant-rich diet reduces BP in hypertensive male smokers.

CONFLICT OF INTEREST

RB and CAD have an interest in Bioindex AS (established by Birkeland Innovation, the Technology transfer office at the University of Oslo) and Vitas AS (established by the Oslo Innovation Center). Otherwise, the authors declare no potential conflict of interest.

ACKNOWLEDGEMENTS

Anne Randi Enget and Aud Jørgensen provided help in the laboratory; RB formulated the present hypothesis; MS and ST were responsible for inclusion of participants and their follow-up; CAD was responsible for handling of data on dietary intake; AK, IS and PL were responsible for statistical analysis; and AK was responsible for drafting the manuscript, which was revised and approved by all authors.

Sources of funding: This work was supported by The Throne Holst Foundation, The Norwegian Research Council and The Norwegian Cancer Society.

REFERENCES

1 Van HL, McCoin M, Kris-Etherton PM, Burke F, Carson JA, Champagne CM *et al.* The evidence for dietary prevention and treatment of cardiovascular disease. *J Am Diet Assoc* 2008; **108**(2): 287 - 331.
2 Willcox JK, Catignani GL, Lazarus S. Tomatoes and cardiovascular health. *Crit Rev Food Sci Nutr* 2003; **43**(1): 1 - 18.
3 Dohadwala MM, Vita JA. Grapes and cardiovascular disease. *J Nutr* 2009; **139**(9): 1788S - 1793S.
4 Erlund I, Koli R, Alfthan G, Marniemi J, Puukka P, Mustonen P *et al.* Favorable effects of berry consumption on platelet function, blood pressure, and HDL cholesterol. *Am J Clin Nutr* 2008; **87**(2): 323 - 331.
5 Ried K, Sullivan T, Fakler P, Frank OR, Stocks NP. Does chocolate reduce blood pressure? A meta-analysis. *BMC Med* 2010; **8**(1): 39.
6 Chang WH, Liu JF. Effects of kiwifruit consumption on serum lipid profiles and antioxidative status in hyperlipidemic subjects. *Int J Food Sci Nutr* 2009; **19**: 1 - 8.
7 Duttaroy AK, Jorgensen A. Effects of kiwi fruit consumption on platelet aggregation and plasma lipids in healthy human volunteers. *Platelets* 2004; **15**(5): 287 - 292.
8 Tandon R, Sinha MK, Garg H, Khanna R, Khanna HD. Oxidative stress in patients with essential hypertension. *Natl Med J India* 2005; **18**(6): 297 - 299.
9 Bjelakovic G, Nikolova D, Gluud LL, Simonetti RG, Gluud C. Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases. *Cochrane Database Syst Rev* 2008; (2). CD007176.
10 Carlsen MH, Halvorsen BL, Holte K, Bøhn SK, Dragland S, Sampson L *et al.* The total antioxidant content of more than 3100 foods, beverages, spices, herbs and supplements used worldwide. *Nutr J* 2010; **9**: 3.
11 Karlsen A, Svendsen M, Seljeflot I, Sommernes MA, Sexton J, Brevik A *et al.* Compliance, tolerability and safety of two antioxidant-rich diets: a randomised controlled trial in male smokers. *Br J Nutr* 2011; **106**(4): 557 - 571.
12 Chavez J, Cano C, Souki A, Bermúdez V, Medina M, Ciszek A *et al.* Effect of cigarette smoking on the oxidant/antioxidant balance in healthy subjects. *Am J Ther* 2007; **14**(2): 189 - 193.
13 Virdis A, Giannarelli C, Neves MF, Taddei S, Ghiadoni L. Cigarette smoking and hypertension. *Curr Pharm Des* 2010; **16**(23): 2518 - 2525.
14 Lillegaard IT, Andersen LF. Validation of a pre-coded food diary with energy expenditure, comparison of under-reporters v. acceptable reporters. *Br J Nutr* 2005; **94**(6): 998 - 1003.
15 Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G *et al.* 2007 Guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Eur Heart J* 2007; **28**(12): 1462 - 1536.
16 Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. *BMJ* 2009; **338**: b1665.
17 Chen CH, Lin JY, Lin CN, Hsu SY. Inhibition of angiotensin-I-converting enzyme by tetrahydroxyxanthones isolated from *Tripterospermum lanceolatum*. *J Nat Prod* 1992; **55**(5): 691 - 695.
18 Jung KA, Song TC, Han D, Kim IH, Kim YE, Lee CH. Cardiovascular protective properties of kiwifruit extracts *in vitro*. *Biol Pharm Bull* 2005; **28**(9): 1782 - 1785.
19 Lacaille D, Franck U, Wagner H. Search for potential angiotensin converting enzyme (ACE)-inhibitors from plants. *Phytomedicine* 2001; **8**(1): 47 - 52.
20 Persson IA, Persson K, Andersson RG. Effect of *Vaccinium myrtillus* and its polyphenols on angiotensin-converting enzyme activity in human endothelial cells. *J Agric Food Chem* 2009; **57**(11): 4626 - 4629.
21 Heran BS, Wong MM, Heran IK, Wright JM. Blood pressure lowering efficacy of angiotensin converting enzyme (ACE) inhibitors for primary hypertension. *Cochrane Database Syst Rev* 2008; (4): CD003823.
22 Park YS, Jung ST, Kang SG, Drzewiecki J, Namiesnik J, Haruenkit R *et al. In vitro* studies of polyphenols, antioxidants and other dietary indices in kiwifruit (*Actinidia deliciosa*). *Int J Food Sci Nutr* 2006; **57**(1 - 2): 107 - 122.
23 Szeto YT, Tomlinson B, Benzie IF. Total antioxidant and ascorbic acid content of fresh fruits and vegetables: implications for dietary planning and food preservation. *Br J Nutr* 2002; **87**(1): 55 - 59.
24 Angiolillo DJ, Guzman LA, Bass TA. Current antiplatelet therapies: benefits and limitations. *Am Heart J* 2008; **156**(2 Suppl): S3 - S9.
25 Skowasch D, Viktor A, Schneider-Schmitt M, Luderitz B, Nickenig G, Bauriedel G. Differential antiplatelet effects of angiotensin converting enzyme inhibitors: comparison of *ex vivo* platelet aggregation in cardiovascular patients with ramipril, captopril and enalapril. *Clin Res Cardiol* 2006; **95**(4): 212 - 216.

Supplementary Information accompanies the paper on the Journal of Human Hypertension website (http://www.nature.com/jhh)