

Can both fruits and juices influence cardiovascular risk?



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As 2021 is the Food and Agriculture Organization's (FAO) Year of Fruit and Vegetables,¹ it's timely to remind ourselves of the important role that these foods play in health promotion. Fruit and vegetables are rich in vitamins, minerals, fibre and bioactive compounds, such as polyphenols, and have been associated, in observational studies, with reduced risk of cardiovascular disease (CVD), type 2 diabetes and certain cancers.

But what about fruit juices – do they have similar effects? While 100% fruit juices (FJ) contain similar levels of nutrients and bioactives to whole fruits, and bioavailability can be better in some cases, FJ are lower in fibre and provide natural sugars – classified as free sugars according to the Scientific Advisory Committee on Nutrition (SACN).²

This article will review the evidence from meta-analyses and randomised controlled trials (RCTs) to consider whether FJ have a role to play in risk reduction, focusing on CVD.

Benefits of fruit & vegetables

The benefits of consuming fruit and vegetable have been extensively studied, with a low intake of fruit and vegetables associated with poorer health outcomes. The Global Burden of Disease study reported that low fruit intake is responsible for an estimated 2 million additional early deaths per year.³

One recent meta-analysis of 10 RCTs found a dose-dependent relationship between fruit and vegetable intake and markers of CVD risk.⁴ Increasing consumption to three or more servings daily significantly reduced blood triglycerides (-0.10 mmol/L) and diastolic blood pressure (BP; -1.99 mmHg), as well as reducing low-density lipoprotein cholesterol (LDL-c) and total cholesterol. A systematic review of meta-analyses found a non-linear dose response for the first 100 g/day of fruit intake equating to a risk reduction of 0.86 for stroke and 0.86 for coronary heart disease.⁵ This study found little protective effect at intakes beyond 200-300 g/day; however other meta-analyses of prospective studies have found a continued reduction in risk up to intakes of 800 g/day.^{6,7}

These studies support the general consensus on fruit and vegetable recommendations e.g. the World Health Organization currently advises a daily intake of at least 400 g (5 servings). However, average intakes across Europe are far lower than this⁸

and official EU data suggest that just two thirds of Europeans have at least one serving of fruit per day.⁹ In the UK, a third of adults but only 12% of older children achieve 5-a-day. Mean daily intakes of fruit and vegetables are 206 g in adults and 119 g in 11-18-year-olds – well below the recommended 400 g.¹⁰

The mechanisms related to improvements in cardiovascular health seen with fruit and vegetable intake are believed to relate to their rich vitamin and mineral (particularly potassium), bioactive polyphenol and soluble fibre content. In addition, benefits can potentially be gained from substitution of fruit and vegetables for other components of the diet, particularly if they displace high added sugar and high fat foods which are rich in calories.

Definition & composition

Beverages defined as FJ are strictly regulated in the EU (and now the UK post-BREXIT) by the Fruit Juice Directive, which states that FJ should only be extracted from the fresh, ripe fruit (by a number of approved methods) and shall have the '*characteristic colour, flavour and taste typical of the juice of the fruit from which it comes*'.¹¹ Because of this, no sugar can be added or removed from the extracted juice and the sugar content must reflect the composition of the whole fruit.

Hence, the nutritional composition of FJ is similar to that of whole fruit (see example in **Table 1**). One difference, which is often cited as a negative of FJ, is the lower fibre content since most of this is typically removed during the extraction process. However, this difference is only marginal and, as an example, substituting a whole orange for a 150 ml glass of orange juice would remove only 1.2 g fibre from the diet, whereas substituting an apple for cloudy apple juice would remove only 0.5 g fibre resulting in negligible changes to overall fibre intake.^{1,2}

Evidence from systematic reviews & meta-analyses

Looking at the evidence related to FJ and CVD risk, several systematic reviews and meta-analyses provide evidence, especially in relation to BP. One meta-analysis of 19 RCTs comprising 618 participants reported that FJ consumption reduced diastolic BP by 2.07 mmHg, on average, compared with a placebo.¹⁴ The authors estimated that such a reduction could lower the incidence of hypertension by 17% and coronary heart disease by 6%, suggesting a clinically significant effect. A second, more recent, meta-analysis of RCTs found that drinking FJ regularly significantly lowered BP by 3.14 mmHg for systolic and 1.68 mmHg for diastolic BP.¹⁵ A third meta-analysis of 8 RCTs, looking specifically at pomegranate juice, reported an average reduction in systolic BP of 4.96 mmHg and diastolic BP of 2.01 mmHg compared with placebo.¹⁶

These lowering effects on BP could explain why many observational studies report reductions in stroke risk when FJ is regularly included in the diet. A recent major systematic review and meta-analysis of more than 80 cohort studies followed up 4,031,896 individuals for an average of 11 years.¹⁷ The authors found that FJ consumption was statistically associated with a 33% reduced risk of stroke mortality, greater than the risk reduction seen for whole fruit (13%) and vegetables (6%). The previously mentioned study by D'Elia¹⁵ also found that regular FJ consumption was associated with a significantly lower risk of stroke (up to 22% dependent on intake) and a significant reduction in cardiovascular events.

Other favourable effects have been found; a meta-analysis of 10 RCTs evaluating 100% orange juice (OJ) consumption found a significant beneficial effect of drinking up to 500 ml/day on glucose, insulin, total cholesterol, LDL-c, total cholesterol and

inflammation.¹⁸ A meta-analysis of 16 RCTs, comprising 572 participants, reported that pomegranate juice significantly reduced markers of inflammation compared with placebo.¹⁹ The effects on inflammation are likely to be important as chronic inflammation is a marker of enhanced CVD risk. A previously described meta-analysis¹⁵ found no significant effects on blood lipids or inflammation when FJ was consumed.

With regards to obesity risk and weight management, several recent meta-analyses have examined data from RCTs. The meta-analysis of D'Elia¹⁵ found no statistical associations between FJ intake and body mass index (BMI) or weight gain, while that of Alhabeeb¹⁸ found that FJ consumption had no significant effect on body weight, BMI, waist circumference, fat mass or lean mass. A further meta-analysis, comprising 236 participants, found no significant change in body weight after daily intake of 250-500 ml OJ for 4-12 weeks.²⁰ Importantly, from the 17 RCTs available for this review, none of them individually reported any significant changes to body weight following daily intake of OJ – often in amounts exceeding the UK recommendation of 150 ml.

Turning to metabolic health, there has been speculation that FJ presents a similar risk to type 2 diabetes (T2D) development and poor glycaemic control as sugar-sweetened beverages, as both contain around 10% sugars. However, a meta-

analysis of four large prospective cohort studies concluded that FJ intake was not statistically correlated with the risk of developing T2D.²¹ A more recent meta-analysis, described above, drew the same conclusion based on data from prospective observational studies.¹⁵ Similar findings are seen in meta-analyses of RCTs looking at glycaemic control; one combining 18 RCTs which reported no effects of regular FJ consumption on fasting blood glucose, insulin resistance, insulin or glycated haemoglobin.²² Two other meta-analyses^{23, 24} have confirmed these findings indicating that consuming FJ does not appear to present any risk to glycaemic control.

Evidence from randomised controlled trials

Looking specifically at RCTs on citrus juice, a 4-week crossover RCT found that daily OJ intake significantly lowered diastolic BP and improved microvascular function.²⁵ The authors demonstrated that the effects were related to hesperidin, a citrus flavanone. A 12-week RCT examining the effects of hesperidin by providing it in an enriched OJ compared with a natural OJ found that both drinks significantly reduced levels of homocysteine (a metabolite associated with CVD risk).²⁶ They also found dose-dependent reductions in systolic BP and pulse pressure relative to the concentration of hesperidin in the drinks, indicating a dose response.

Table 1: Nutrition composition of 100% orange juice vs. whole orange

Per 100g	100% orange juice	Whole orange
Energy (kcal)	41	36
Total sugars (g)	9	8.2
Fibre (g)	Tr	1.2
Potassium (mg)	176	122
Vitamin C (mg)	45	52
Phosphorus (mg)	15.3	16
Calcium (mg)	11	24
Magnesium (mg)	9.5	8
Iron (mg)	0.2	0.1
Zinc (mg)	0.1	Tr
Thiamin (mg)	0.08	0.2
Riboflavin (mg)	0.02	0.03
Niacin (mg)	0.3	0.5
Vitamin B6 (mg)	0.07	0.05
Folate (µg)	21.5	33
Vitamin A (µg)	4.1	9
Vitamin E (µg)	0.8	0.4
Hesperidin (polyphenol) (mg)	52	222-240
Total carotenoids (mg)	0.7	0.33

Nutrients highlighted meet the UK/EU criteria for a 'source in' or 'rich in claim'

A further 2-week crossover RCT reported improved blood vessel function in healthy adults following daily red OJ consumption with meals.²⁷ Flow-mediated dilation (FMD) improved by 2%, which is a clinically significant change. Improvements in FMD of 2.9% on average were seen following daily red OJ consumption in a 7-day crossover RCT in adults at enhanced CVD risk.²⁸ Importantly, there were no changes in body weight during these three intervention trials despite a daily OJ intake of 400-500 ml. An acute crossover RCT found that mashed oranges, regular OJ and flavonoid-rich OJ similarly improved FMD when healthy, middle-aged men consumed two high fat test meals, designed to stress the cardiovascular system.²⁹

Further work on vascular health is planned with the announcement in 2020 that the Fruit Juice Science Centre is funding a major RCT, called HESPER-HEALTH. During the 2.5-year double-blind, placebo-controlled crossover study, participants at risk of CVD will consume 330 ml OJ daily and undergo a series of short- and long-term evaluations of vascular function, BP, gene interactions, polyphenol absorption and gut microbiota. The work will take place at the University of Clermont-Ferrand and INRAE in France, and the University of Geisenheim in Germany.

Research on mechanisms

The similar cardioprotective effects seen with consumption of both whole fruit and FJ could be related to their similar composition. Both provide a source of

potassium, folate, vitamin C (and other antioxidants), nitric oxide, carotenoids and polyphenol compounds. It has been proposed that the consistent positive vascular effects seen for FJ could be due to potassium – which has a claim in the EU for supporting normal BP – as well as vitamin C, nitrates, folate and polyphenols.³⁰ Inflammation and oxidative stress are known to be implicated in CVD so the antioxidant and anti-inflammatory effects of plant bioactives and vitamin C are also proposed as potential mechanisms of action.

Consistent evidence from blood biomarker studies confirms that the micronutrients and plant bioactives found in FJ are taken up by the body, meaning they are bioavailable. A long-term study examined the bioavailability of nutrients and plant bioactives in OJ.³¹ For three weeks, 13 healthy adults drank 236 ml juice three times daily. Compared with baseline levels, blood sampling revealed that vitamin C and folate levels increased by around 50%, while polyphenol levels rose by eight times and carotenoids increased by 22%. Although whole oranges contain double the hesperidin of OJ, people absorb a similar amount from both foods, indicating their nutritional equivalence.³² The poorer uptake of hesperidin from whole fruit is most likely due to its greater pectin content which inhibits polyphenol absorption.

In terms of effects on glycaemic control it is often queried why FJ (a source of free sugars) doesn't appear to have a negative impact. Two explanations have been proposed. Firstly, FJs are classified

as low glycaemic index (GI) meaning they have a smaller impact on blood glucose levels post-prandially than a reference food. For example, 100% apple juice has a GI of 41 and whole apple has a GI of 36,³³ while OJ has a GI of 50 and whole orange has a GI of 43. This compares favourably with an average sugar sweetened beverage, which has a GI of 63-68. A second reason is linked to the rich polyphenol content of FJ. Studies have found that hesperidin in citrus juice,³⁴ or punicalagin and punicalin in pomegranate juice,³⁵ slow glucose absorption from the gut resulting in a flatter post-consumption blood glucose peak.

Conclusion

The evidence from high quality studies, particularly systematic reviews and meta-analyses, reveals that regular moderate consumption of FJ does not represent a risk for metabolic health, body weight control or risk of T2D. Instead, drinking FJ appears to deliver a benefit for cardiovascular health by favourably modulating vascular function, with the potential for long-term reductions in blood pressure and stroke risk. FJ is a recognised source of vitamin C, folate and potassium – nutrients which have authorised health claims in the UK and EU. In several countries, a daily glass of FJ is viewed as complementary to fruit and vegetable consumption. Taken together, the evidence suggests that FJ could be part of the FAO's 2021 drive to boost intakes of fruit and vegetables.

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