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Effects of Tea Consumption on Measures of Cardiovascular Disease: A Systematic Review of Meta-Analysis Studies and Randomised Controlled Trials

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Abstract

Background: The results of meta-analysis studies and randomised controlled trials (RCTs) published in the last 10 years were collated and the effect of tea consumption on measures of cardiovascular disease (CVD) was considered.

Methods: PubMed was systematically searched for relevant meta-analysis papers and RCTs. Inclusion and exclusion of studies, data extraction, and quality assessment were conducted according to the PRISMA statement. The Jadad criteria was applied to decipher the quality of RCTs.

Results: Findings from 19 meta-analysis and 23 randomised controlled trials (n=1,422 participants) were evaluated. Clear evidence was found for blood pressure where 4 to 5 cups of black or green tea daily related to risk reduction. Moderate evidence was of a positive effect of green tea and its associated catechins on total and low-density lipoprotein (LDL) reduction. Growing evidence indicates that tea drinking could protect vascular health and reduce inflammation. A wider range of tea forms (chamomile tea, goishi tea, hibiscus tea, sour tea, rooibos tea) are increasingly being studied and also appear to have potentially favourable effects on markers of CVD.

Conclusion: Tea drinking appears to play a significant role in blood pressure reduction, particularly amongst those with prehypertension or hypertension. Green tea has beneficial effects on total and LDL cholesterol reduction. Tea drinking in general appears to aid vascular function and the reduction of inflammation. Ongoing long-term trials are needed especially in relation to other tea forms alongside black and green tea.

Keywords: Cardiovascular disease; Blood pressure; Hypertension; Inflammation; Green tea

Introduction

Originating in China, tea (*Camellia sinensis, Theaceae*) and the planting of tea spread in popularity and today more than 160 countries in the world are accustomed to tea drinking [1,2]. This makes the drinking of tea one of the most widely consumed beverages globally [2]. Tea has long been regarded for its health promoting properties - helping to maintain cardiovascular and metabolic health since ancient times [3]. Epidemiological data has also discovered that black and green tea may reduce coronary heart disease and stroke risk by between 10 and 20 per cent, respectively [4].

Black (aerated), green (non-aerated) and oolong (partially aerated) tea are three of the most popular tea forms consumed today – all produced from the leaves of the plant *Camellia sinensis* [5]. These have been found to possess antioxidative, anti-inflammatory, antihypertensive and cholesterol-lowering properties [5]. In particular, non-caffeine components - namely the flavonoids are thought to contribute to cardiovascular (CV) health [6]. Common bioactive compounds found in green teas include flavan-3-ols (catechins) (also called flavanols), proanthocyanidins (tannins) and flavonols. Black tea is a good provider of theaflavins and thearubigins whilst herbal teas can contain a diverse range of polyphenols [7].

CVD is a well-known global healthcare burden. It is thought that CVD risk may be lowered by adjusting modifiable risk factors such as the diet, and this includes habitual intakes of tea [8]. To define, CVD encompasses a range of disorders of the heart and blood vessels (Table 1). More people die annually from CVDs than from any other cause making this the number one cause of death globally. In 2015 17.7 million people died from CVDs which was equivalent to around a third (31%) of all global deaths [9]. In the UK it has been projected that programmes which could reduce CV events by just 1 per cent would contribute to health service savings worth at least £30 million ($48 million) compared to if no intervention was put into place [10].

A large body of observational evidence has made links between tea consumption and reduced risk of heart disease [11] alongside other factors such as reduced stroke risk, particularly ischaemic stroke [12]. Unfortunately, observational evidence can be confounded by lifestyle and dietary factors [13]. A number of new randomised controlled trials (RCTs) have been published within this field in recent years. RCTs are regarded as the gold-standard when determining whether cause-and-effect relationships exist between interventions and predefined outcomes [14].

Considering this, the present review article aims to collate evidence from both meta-analysis articles and RCTs to determine whether tea consumption has any effect on risk factors and pathways linked to the development of CVD.

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Methods

Eligibility criteria/study selection

A PubMed search was undertaken to identify relevant meta-analysis papers and RCTs using the selection filter. Filters were applied to identify English-language human trial published in the last 10 years to include most recent evidence.

Search terms applied were: tea [TIAB] AND 'cardiovascular function', blood pressure, 'cholesterol', 'lipid profile', 'inflammation' and 'c-reactive protein; CRP'. The same search terms were applied when first identifying meta-analysis papers (meta-analysis papers of RCTs and prospective cohorts) and then separate RCTs. The last search to identify included studies was undertaken on February 28th, 2018.

Quality/risk of bias assessment

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement was followed [15]. There were no exclusions based on age, ethnicity or health status of the baseline study population. The quality of RCTs was evaluated using the Jadad scale (Table 2) [16]. Quality scores were ranked between 1 and 5 with higher scores being indicative of higher quality.

For RCTs specifically these were included if the following criteria were met:

(1) the trial was randomised and involved human subjects;

(2) the trial was a controlled intervention providing tea in beverage form and a control beverage;

(3) the trial specified the form and amount of tea ingested – all types of tea were included – black, green and herbals using the generic search term 'tea';

(4) the trial studied the specified measures of cardiovascular disease (vascular function, blood pressure, cholesterol, lipid profile, inflammation, CRP)

(5) the trial did not use tea extracts, powders, supplements, gargles or combined multi-component interventions (Figure 1).

Data extraction/collection

Key findings were collated from meta-analysis papers and summarised in table form so these could be compared and contrasted. This included data on the type and amount of tea ingestion where specified. The methodology developed by the Joanna Briggs Institute was read with interest and largely applied when developing the review methodology [17,18].

For RCTs, all eligible trials were reviewed and relevant data were extracted, including: name of the first author, publication year, study design, geographic location, demographic and health characteristics of the study population (e.g. age, sex, presence of obesity or a chronic disease, body mass index), sample size, intervention duration, tea type, amount ingested, a description of the control product, and outcomes measured. Relevant data extracted from the studies included volume of tea ingested per day (cups or ml), information on randomisation method, double-blinding and withdrawal rates. This information was used to develop quality scores for each study based on Jadad criteria.

Results

The PubMed search identified 315 papers and after an adjustment for replica papers 292 articles were further examined for assessment. Of these, a further 161 papers were discarded after reviewing the abstracts as they did not meet the inclusion criteria. This left 131 full-text articles to be reviewed.

Of these an additional 44 were excluded as these used irrelevant interventions including tea gargles, powders or extracts. Twenty-five were discarded as these focused on tea components such as epigallocatechin gallate rather than tea as a drink per se. A further seven studied health outcomes that were not aligned with the specified criteria, eight applied multi-component interventions e.g. tea consumption along with exercise or supplements and four were not RCTs.

Subsequently a total of 19 meta-analysis papers (including those collating evidence from prospective cohorts and trials) and 23 RCTs were identified (Figure 1). Of these 16 meta-analysis papers focused on tea consumption in relation to blood pressure, cholesterol or lipid profile and 14 trials also investigated tea consumption in relation to these specific parameters. Remaining meta-analysis papers and RCTs looked at tea consumption in relation to vascular function of markers of inflammation, including CRP.

Blood pressure

There is a large body of evidence looking at inter-relationships between tea and blood pressure. This is reflected by the number of meta-analysis papers published (Table 3). Eight meta-analysis papers were identified [8,19-25]. Of these, regular consumption of black and green tea was associated with reductions in blood pressure which could be important for CV health at population level [8,20]. Effects were most prominent in adults with blood pressure in pre-hypertensive and hypertensive ranges (19) and long-term black and green tea drinkers consuming this for more than 12 weeks [21]. One meta-analysis linked (*Hibiscus sabdariffa L.*) consumption to reduced blood pressure [25,26].

As shown in Table 4 seven separate RCTs looked at the effects of tea drinking on blood pressure [27-33]. In these trials participants were typically asked to consume 2 to 3 cups of tea daily. In one 8-day trial black tea consumption (2 cups daily) significantly reduced systolic and

Disorder	What this is	Outcomes studied in the present review
Cerebrovascular disease	Disease of the blood vessels supplying the brain.	The present review focused solely on tea consumption in relation to: o Cardiovascular function/health o Blood pressure o Cholesterol levels o Lipid profile o Inflammation o c-reactive protein levels.
Congenital heart disease	Malformations of heart structure - exists at birth.	
Coronary heart disease	Disease of the blood vessels supplying the heart muscle.	
Deep vein thrombosis and pulmonary embolism	Blood clots in the leg veins, which can dislodge and move to the heart and lungs.	
Peripheral arterial disease	Disease of blood vessels supplying the arms and legs.	
Rheumatic heart disease	Damage to the heart muscle and heart valves from rheumatic fever, caused by streptococcal bacteria.	

Source: WHO (2017) [9].

Table 1: Disorders categorised as cardiovascular diseases.

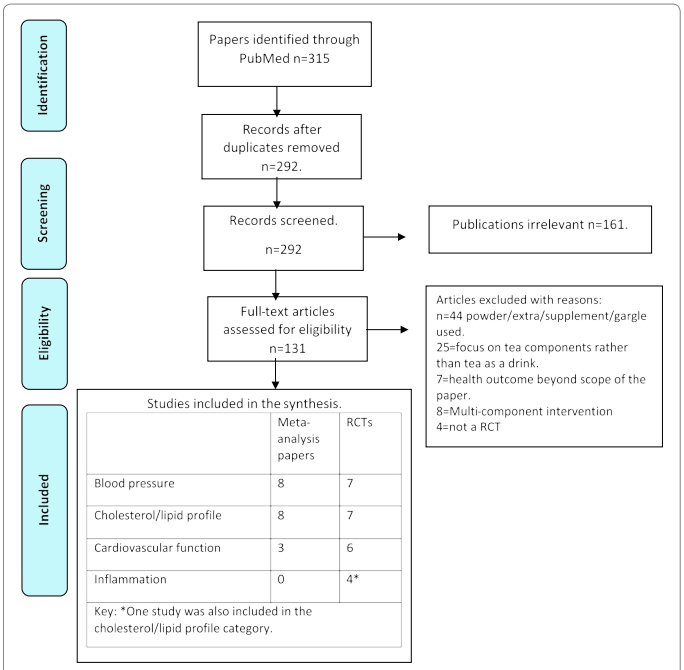

Figure 1: Study selection process.

diastolic blood pressure and prevented rises in blood pressure after the ingestion of a fat loaded meal [28]. Australian research showed that drinking 3 cups black tea daily over 6 months (supplying ≈ 429 mg polyphenols) reduced systolic and diastolic blood pressure by 2-3 mmHg [31]. Another trial by the same research team showed that similar amounts of tea led to sustained blood pressure lowering effects over 6-months which included a 10 per cent variation in blood pressure at night time [29].

Three RCTs have studied the effects of sour tea [27,30,33]. This was found to improve systolic blood pressure in healthy adult men [27] and reduce overall blood pressure in mildly hypertensive type 2 diabetic adults [30,33]. One trial found that 3 cups (240 ml) of brewed hibiscus tea daily significantly lowered blood pressure amongst pre- and mildly hypertensive adults [32]. Six out of the 7 trials (Table 4) had a Jadad score above 3 indicating that quality was above average.

Cholesterol and lipids

Eight meta-analysis articles studied the effects of tea consumption on cholesterol and lipid levels [8,22,23,34-38]. A large body of these suggest that green tea and its associated catechins could contribute to reductions in total and low-density lipoprotein (LDL) cholesterol [22,23,36-38]. Another investigation where black and green tea were analysed together showed favourable effects on LDL cholesterol [8] though the inclusion of green tea could have driven this. Meta-analytical

Publication	Randomisation	Method of randomisation described & appropriate	Blinding mentioned	Method of blinding described and appropriate	Withdrawal and dropout of subjects provided	Total score
Blood pressure						
Kafeshani et al. [27]	1	1	1	1	1	**5**
Grassi et al. [28]	1	1	0	0	1	**3**
Hodgson et al. [29]	1	1	1	0	1	**4**
Hodgson et al. [31]	1	0	1	0	0	**2**
Mozaffari-Khosravi et al. [30]	1	1	0	1	1	**4**
McKay et al. [32]	1	1	1	1	1	**5**
Mozaffari-Khosravi et al. [33]	1	1	0	0	1	**3**
Cholesterol & lipid profile						
Ishida et al. [39]	1	0	1	0	1	**3**
Ashigai et al. [40]	1	1	1	1	1	**5**
Rafraf et al. [41]	1	1	1	0	1	**4**
Troup et al. [42]	1	1	0	0	1	**3**
Bohn et al. [6]	1	1	1	1	1	**5**
Koutelidakis et al. [43]	1	1	1	0	1	**4**
Bahorun et al. [44]	1	1	0	0	1	**3**
Vascular function						
Grassi et al. [48]	1	0	1	0	1	**3**
Schreuder et al. [49]	1	0	1	0	1	**3**
Basu et al. [50]	1	1	1	1	1	**5**
Sone et al. [51]	1	1	1	1	1	**5**
Persson et al. [52]	1	0	0	0	0	**1**
Grassi et al. [53]	1	0	1	1	1	**4**
Inflammation						
Maghsoumi-Norouzabad et al.	1	0	0	0	1	**2**
Mahmoud et al. [55]	1	0	0	0	0	**1**
Koutelidakis et al. [43] *	1	1	1	0	1	4
Bahorun et al. [56]	1	0	0	0	1	**2**

Note: Total quality assessment score for which scores range between 1 and 5: with 1 being the lowest quality and 5 being the highest quality. *Included twice as markers of lipid metabolism and inflammation were recorded.

Table 2: Quality assessment used to assess RCTs identified in the systematic review.

Health outcome	Strength and amount of evidence from human studies	References
Blood pressure	Consumption of green or black tea can reduce BP in individuals within pre-hypertensive and hypertensive ranges.	Yarmolinsky et al. [19]
	Drinking 4-5 cups tea daily can significantly reduce systolic and diastolic BP.	Greyling et al. [20]
	Long-term tea ingestion of tea for more than 12 weeks can significantly reduce systolic and diastolic BP.	Liu et al. [21]
	Green tea intake and its catechins can significantly reduce systolic BP. Effects may be greater in those with systolic BP ≥ 130 mm Hg.	Khalesi S et al. [22]; Onakpoya I et al. [23]; Peng et al. [24]
	Green and black tea types analysed together (Cochrane review) show favourable effects on BP.	Hartley et al. [8]
	Sour tea (*Hibiscus sabdariffa L.*) can significantly reduce systolic and diastolic BP.	Serban et al. [25]
Cholesterol and lipids	Black tea can significantly reduce LDL cholesterol concentration. Subgroup analysis shows lowering effects tend to be more effective in subjects with higher cardiovascular risk.	Zhao et al. [34]
	Black tea might not have beneficial effects on concentrations of total cholesterol, HDL and LDL.	Wang et al. [35]
	Green tea intake and catechins results in significant reductions in total cholesterol, and LDL cholesterol.	Yuan et al. [36]; Khalesi S et al. [6]; Onakpoya I et al. [7]; Kim et al. [37]; Zheng et al. [38]
	Green and black tea types when analysed together (Cochrane review) show favourable effects on LDL cholesterol.	Hartley et al. [9]
Cardiovascular function	Drinking ≥4 cups or 1-3 cups of green tea per day can reduce risk of myocardial infarction and stroke compared to those drinking <1 cup/day. Those drinking ≥10 cups/day of green tea daily had lower LDL compared to those drinking <3 cups/day.	Pang et al. [45]
	Green tea consumption was significantly inversely associated with CVD and all-cause mortality.	Tang et al. [46]
	Tea enhances endothelial-dependent vasodilation. This may provide a mechanistic explanation for the reduced risk of cardiovascular events and stroke observed amongst tea drinkers.	Ras et al. [47]

Abbrevations: BP: Blood Pressure, CVD: Cardiovascular Disease, HDL: High-Density Lipoprotein, LDL: Low Density Lipoprotein.

Table 3: Tea and cardiovascular disease: meta-analysis papers.

Study (Location)	Population (age, sex, health)	Study Design	Intervention (duration, type of tea and amount ingested)	Outcomes measured	Findings
Blood pressure					
Kafeshani et al. [27] Iran	n=54 healthy adult men	6-month randomized, DB, placebo-controlled trial.	Received 450 mg (about 2 cups/d) green tea or sour tea and one placebo group.	BP	Sour tea supplementation led to decreased systolic BP in healthy men compared with the placebo.
Grassi et al. [28] Italy	n=19 healthy adults 18-75 years.	8-day randomized, DB, controlled, cross-over design trial. Measurements in a fasted state and after a fat load.	2 cups/d of black tea (129 mg flavonoids) or placebo.	Systolic, diastolic BP, refraction and stiffness index.	Black tea decreased systolic and diastolic BP and prevented BP increase after a fat load ($p<0.0001$). Regular consumption of black tea may be relevant for CV protection.
Hodgson et al. [29] Australia	n=111 men and women with systolic BP between 115 and 150 mm Hg at screening.	6-month randomized, controlled, DB parallel-designed trial.	3 cups/d of either powdered black tea solids (tea) or a flavonoid-free caffeine-matched beverage (control).	24-h ambulatory BP.	Across the 3 time points, tea, compared with the control, resulted in lower rates of systolic ($p=0.0045$) and diastolic ($p=0.016$) BP variation by ~10% during night-time.
Mozaffari-Khosravi et al. [30] Iran	n=100 mildly hypertensive patients with diabetes.	4-week randomized clinical trial.	Drank sour tea and green tea infusion, respectively, three times a day 2 hr after each meal.	Systolic, diastolic BP.	Mildly hypertensive type 2 diabetic individuals who drink three glasses of green or sour tea daily for 4 weeks show significant decreased systolic and diastolic BP.
Hodgson et al. [31] Australia	n=95 men and women 35 to 75 years, regular tea drinkers, BMI 19 to 35, daytime ambulatory SBP between 115 and 150 mm Hg at screening.	6-month randomized placebo-controlled DB 6-month parallel designed trial.	3 cups/d regular black tea.	Ambulatory BP.	Regular consumption of 3 cups/d of black tea over 6 months, supplying approximately 429 mg/d of polyphenols, resulted in lower systolic and diastolic BP of between 2 and 3 mm Hg.
McKay et al. [32] USA	n=65 pre- and mildly hypertensive adults, age 30-70 y, not taking blood pressure (BP)-lowering medications,	6-week randomized, DB placebo-controlled clinical trial.	3 cups/d (240-mL) of brewed hibiscus tea or placebo beverage	Systolic, diastolic BP.	Daily consumption of hibiscus tea lowers BP in pre- and mildly hypertensive adults and may prove an effective component of the dietary changes recommended for people with these conditions.
Mozaffari-Khosravi et al. [33] Iran	n=60 diabetic patients with mild hypertension, without taking antihypertensive or antihyperlipidaemic medicines.	1-month randomized trial.	Drank 2 cups/d of black tea or sour tea infusions (240 ml).	Systolic, diastolic BP.	Consuming sour tea infusions had positive effects on BP in type II diabetic patients with mild hypertension.
Cholesterol and lipid profile/distribution					

Ishida et al. [39] Japan	n=77 adults with LDL cholesterol (CHO) ≧120 mg/mL.	12-week randomized, DB placebo-controlled clinical study.	Goishi tea group daily consumption (122 mg of polyphenols) and the placebo group (12.2 mg of polyphenols).	Blood lipid profiles.	Goishi tea polyphenols tended to increase HDL and suppress the elevation of triglycerides particularly amongst those with a BMI <25 kg/m^2.
Ashigai et al. [40] Japan	n=24 healthy males and females, aged 20 to 64 years old, were enrolled.	Two 10-day periods. Randomized, Placebo-Controlled, DB crossover Study.	Drank either a beverage containing 55 mg BTP or a control beverage without BTP 3 times a day for 10 d.	Faecal lipid excretion.	Total lipid excretion increased from 5.51 ± 1.73 to 6.87 ± 1.91 g/3 d after BTP intake in comparison with intake of the control beverage. These results indicated that BTP increased lipid excretion.
Rafraf et al. [41] Iran	n=64 adults with T2DM 30 and 60 years.	8-week SB randomized controlled clinical trial.	Consumed 3 cups chamomile tea (3 g/150 mL hot water) immediately after meals or control water.	Fasting blood glycaemic and lipid profiles.	Chamomile tea significantly decreased total cholesterol (p=0.001), triglyceride (p<0.001), and low-density lipoprotein cholesterol (p=0.05) compared with control group.
Troup et al. [42] USA	n=57 borderline hypercholesterolemic individuals.	Diet controlled randomized trial. Two 4-week treatment periods.	5 cups per day of black tea alongside a controlled low-flavonoid diet plus or tea-like placebo.	Total cholesterol, HDL, LDL, triglycerides, LDL/HDL ratio.	No results were statistically or clinically significant.
Bohn et al. [6] Norway	n=111 regular tea drinking men and women (35-75 years)	6-month randomized controlled DB parallel-designed trial.	3 cups per day of powdered black tea solids (tea) or a flavonoid-free flavour- and caffeine-matched placebo (control).	Weight, waist- and hip-circumference, endothelial function, plasma biomarkers.	Short-term regular ingestion of black tea over 3 months can improve body fat distribution, compared to a caffeine-matched control beverage.
Koutelidakis et al. [43] Greece	n=43 patients with coronary artery disease	5-hours post ingestion. Randomized controlled, parallel design.	Consumed breakfast and 330 ml of green tea (4.5 g /330 ml, providing approximately 400 mg catechins) or water.	Total cholesterol, LDL, HDL, triglycerides, glucose, CRP, uric acid and pancreatic lipase levels.	Serum triglycerides levels significantly increased 3 h after breakfast with water (p=0.031), but not after breakfast with tea.
Bahorun et al. [44] Mauritius	n=77 normal population	12-week randomized controlled clinical trial	3 x 200 ml cups of black tea infusate/day for 12 weeks or a hot water control beverage.	HDL/LDL cholesterol, triglycerides, antioxidants.	Induced, a significant decrease in triglyceride levels (35.8%; p<0.01), a significant decrease in LDL/HDL plasma cholesterol ratio (16.6%; p<0.05) and a non-significant increase in HDL plasma cholesterol levels (20.3%).
Cardiovascular function					
Grassi et al. [48] Italy	n=19 never-treated hypertensive patients.	8-day randomized, DB controlled, cross-over study.	Black tea (150 mg polyphenols) or a placebo twice a day for eight days.	CACs, FMD	Black tea ingestion increased functionally active CACs and FMD. Fat challenge decreased FMD, while tea consumption counteracted FMD impairment (p<0.0001).
Schreuder et al. [49] Netherlands	n=20 healthy subjects	7-day randomized, crossover study.	3 cups per day of black tea or abstinence from tea.	Brachial artery endothelial FMD.	Tea consumption resulted in an immediate increase in FMD% whilst no such change occurred after ingestion of hot water.
Basu et al. [50] USA	n=41 adults age 42.5 years, body mass index 36.1 kg/m (2)]	8-week randomized controlled trial.	Randomly assigned to receive green tea (4 cups/d), green tea extract (2 capsules and 4 cups water/d), or no treatment (4 cups water/d)	Markers of MetS and cardiovascular health.	Green tea significantly reduced plasma serum amyloid alpha, an independent cardiovascular disease risk factor, in obese subjects with metabolic syndrome.
Sone et al. [51] Japan	n=51 healthy subjects	9-week randomized trial.	Green tea was either high catechin (400 mg/day) or low catechin (100 mg/day).	Changes in the adiponectin levels and CVD risk factors.	There were no significant differences between the high-and low catechin groups with respect to changes in the serum adiponectin level and any CV risk factors.
Persson et al. [52] Sweden	n=17 healthy adults aged 20-31 years.	3 hr randomized, three-phase, crossover study	400 ml green tea, black tea or Rooibos tea.	ACE activity, NO concentration.	Green tea and Rooibos tea may have cardiovascular effects through inhibition of ACE activity.
Grassi et al. [53] Italy	n=19 healthy men.	5 1-week periods. Randomized, DB controlled, cross-over design	Twice daily intake of black tea (0, 100, 200, 400 and 800 mg tea flavonoids/day)	FMD.	Black tea ingestion dose dependently improved FMD and decreased peripheral arterial stiffness in healthy volunteers.
Inflammation					
Maghsoumi-Norouzabad L et al. [54] Iran	n=36 patients (10 men and 26 women) aged 50-70 years old with knee osteoarthritis	42-day randomized parallel trial.	Received daily 3 cups/d Burdock root tea (each cup containing 2 g/150 mL boiled water) half-hour after the meal. The control group received three cups containing 150 cc boiled water daily.	Inflammatory markers.	Burdock root tea significantly decreased the levels of serum IL-6, hs-CRP and malondialdehyde, while the levels of serum TAC and activities of SOD were significantly increased. GPX activities increased but not significantly.

Mahmoud et al. [55] Kuwait	n=30 patients with T2DM	12-week randomized trial.	3 cups/d (600 mL) of black tea per day; and a Low Intake (LI) group, administered 1 cup (200 mL) per day,	Intracellular cytokine expression, regulatory T cells.	Tea consumption correlated with increased regulatory T cells CD3+ CD4+ CD25+ FOXP3, CD3+ CD4+ IL-10+ cells (an immunosuppressive phenotype), reduced (pro-inflammatory) CD3+ CD4+ IL-17+ cells and reduced Th1-associated CD3+ CD4+ IFN-Y+ cells.
Koutelidakis et al. [43] Greece	n=43 with CAD	Randomized controlled, parallel design with 2 arms,	330 ml water or tea (4.5 g green tea/330 ml, providing approximately 400 mg catechins).	Biomarkers measured hourly up to 5 hrs post ingestion.	Tea consumption did not affect selected biomarkers at any postprandial time point in patients with CAD including CRP.
Bahorun et al. [56] Mauritius	n=232 Susceptible to ischemic heart disease.	12-week randomized controlled study.	9 g (3 cups of black tea) daily followed by a 3-week wash-out (with control group consuming hot water).	CRP.	CRP in the high-risk group >3 mg/L was significantly decreased by 53.4% and 41.1% in men and women, respectively. Tea supplementation-associated decrease in plasma uric acid and CRP levels may benefit humans at high risk of CV events and may augment drug therapy.

Abbrevations: ACE: Acetylcholinesterase, BMI: Body Mass Index, BP: Blood Pressure, BTP: Black Tea Polyphenols, CACs: Circulating Angiogenic Cells, CRP: C-Reactive Protein, CV: Cardiovascular, HDL; high-Density Lipoprotein, LDL: Low-Density Lipoprotein, MetS: Metabolic Syndrome, NO: Nitric Oxide, SOD: Sodium Oxide Dismutase, TAC: Total Antioxidant Capacity.

Table 4: Tea and cardiovascular disease outcomes (RCTs only).

Measure of cardiovascular disease	Strength and amount of evidence	References
Blood Pressure	Strong evidence from meta-analysis that long-term consumption (<12 weeks) and drinking 4-5 cups tea (green and black) daily could reduce SBP and DBP, especially those with blood pressure in pre- and hypertensive ranges.	Greyling et al. [20]; Liu et al. [21]; Yarmolinsky et al. [19]; Hartley et al. [8].
	Emerging meta-analytical evidence that sour tea may reduce SBP and DBP.	Serban et al. [25]
	Growing evidence from RCTs that drinking 2-3 cups black tea may reduce SBP and DBP.	Grassi et al. [28]; Hodgson et al. [29]; Hodgson et al. [31]
	Emerging evidence (3 RCTs) showing that sour tea may reduce BP, especially amongst type 2 diabetics.	Kafeshani et al. [27]; Mozaffari-Khosravi et al. [30]; Mozaffari-Khosravi et al. [33]
	One RCT showed that brewed hibiscus tea daily significantly lowered BP amongst pre- and mildly hypertensive adults.	McKay et al. [32]
Cholesterol and lipids	Strong meta-analytical evidence indicates that green tea and its catechins may have beneficial effects on total cholesterol and LDL reduction.	Yuan et al. [36]; Khalesi et al. [6]; Onakpoya I et al. [7]; Kim et al. [37]; Zheng et al. [38]
	Meta-analytical evidence for black tea is mixed with subjects with higher cardiovascular risk appearing to have most benefit.	Zhao et al. [34]
	Longer-term trials imply that black tea may reduce triglyceride levels, alter body fat distribution and increase fat excretion.	Ashigai et al. [40]; Bohn et al. [6]; Bahorun et al. [44]
	Emerging evidence from RCTs that chamomile and goshi tea could improve blood lipid profiles.	Ishida et al. [39]; Rafraf et al. [41]
Cardiovascular function	Strong meta-analytical evidence indicates that drinking green tea (1-3 cups daily) could reduce MI and stroke risk. Other works shows 2-3 cups of green or black tea daily could improve endothelial function.	Pang et al. [45]; Tang et al. [46]
	Growing evidence from RCTs that black tea could improve flow-mediated dilation and levels of circulating angiogenic cells.	Grassi et al. [48]; Schreuder et al. [49]; Grassi et al. [53]
Inflammation	Meta-analytical evidence looking at tea intake in relation to markers of inflammation is lacking.	Maghsoumi-Norouzabad et al. [54]; Mahmoud et al. [55]; Koutelidakis et al. [43];
	Four RCTs show that certain patient's groups – type 2 diabetics, those with coronary artery/ ischemic heart disease or knee osteoarthritis could benefit from tea drinking (black, green and burdock root tested).	Bahorun et al. [56]

Table 5: Summary of the results of systematic review of tea and cardiovascular disease.

findings for black tea appear reveal that more research is needed. One paper showed favourable effects on serum LDL cholesterol, particularly amongst those with elevated cardiovascular risk [34]. Another reported no effects in relation to total cholesterol, LDL or HDL concentrations [35].

Eight RCTs examined the effects of tea interventions on cholesterol levels, lipid profile and distribution [6,39-44]. In most studies 3 to 5 cups of tea were ingested daily [6,41,42,44]. One trial comprised of two 2-week treatment periods found that amongst borderline hypercholesterolemic subjects 5 cups of tea daily did not alter lipid profiles [42]. A longer 12-week trial providing 3 cups (each 200 ml) of black tea infusate to normal healthy adults showed that triglyceride levels reduced by 35.8%, and LDL/HDL plasma cholesterol ratio reduced by 16.6% [44]. A post-ingestion study discovered that serum triglyceride levels significantly rose 3 hours after breakfast with water but not with tea [43].

Regarding lipid distribution one trial found that drinking black tea over 3 months significantly reduced waist circumference and waist-to-

hip ratio indicating improved body fat distribution [6]. A small trial comprised of two 10-day intervention periods found that the ingestion of black tea polyphenols (55 mg as a beverage) three times daily increased faecal lipid excretion [40]. Other work using Goishi tea (122 mg polyphenols) found this to increase HDL cholesterol and reduce elevations in triglycerides, especially amongst those with a BMI <25 kg/m^2 after 12 weeks of drinking this [39]. Amongst patients with type 2 diabetes chamomile tea (3 g/150 ml hot water) thrice daily after meal over 8 weeks significantly lowered total cholesterol, triglyceride, and LDL levels compared to a control [41]. The overall quality of studies was good with all seven RCTs having a Jadad score of 3 or above. One drawback was that 5 of these did not provide a detailed breakdown of blinding methods used.

Cardiovascular function

Three meta-analysis articles focused on inter-associations between tea drinking and cardiovascular function [45-47]. One meta-analysis focused on green tea concluding that those drinking 1-3 cups per day contributed to reduced myocardial infarction risk (OR=0.81, 95% CI: 0.67-0.98) and stroke (OR=0.64, 95% CI: 0.47-0.86) compared to those who drank <1 cups/day [45]. Pooled analysis from 18 cohorts demonstrated that a one cup per day increment of green tea consumption lowered the risk of CVD mortality by 5% [46]. Other work found moderate consumption of black or green tea (2-3 cups; 500 ml) to enhance endothelial-dependent vasodilation which could provide a mechanistic explanation for the reduced risk if cardiovascular events observed amongst tea drinkers [47].

Six RCTs focused on aspects of CV function [48-53]. A small 8-day trial providing black tea (150 mg polyphenols) twice daily noted improvements in circulating angiogenic cells (CACs) and flow-mediated dilation (FMD), with a maximal response 2 hours after ingestion [48]. A 7-day trial of 20 healthy subjects drinking 3 cups black tea per day also observed improvements in FMD with this appearing to relate to a direct effect of the tea on the endothelium [49]. Similarly, amongst 19 healthy men drinking black tea twice daily over 5 1-week periods showed that the variety of tea providing 800 mg flavonoids significantly improved FMD and reduced peripheral arterial stiffness compared with the control [53].

A small 8-week RCT showed that green tea (4 cups/day) significantly reduced plasma serum amyloid alpha; an independent CV disease risk factor, in obese subjects with metabolic syndrome [50]. Authors from a separate study concluded that green and Rooibos teas may exert their CV effects by inhibiting ACE activity [52]. Other work showed that high versus low catechin green tea had no effect on CV risk factors [51] although this was conducted on healthy adults. Regarding the quality of trials one lacked rigor [52] but the remaining trials were adequately designed.

Inflammation

Focused meta-analytical evidence on tea drinking in relation to inflammation and related markers is lacking. Four trials conducted some research in this field [43,54-56]. With regard to black tea a 12-week trial showed that three cups (600 ml) daily increased regulatory T-cells and reduced pro-inflammatory cells amongst patients with type 2 diabetes [55]. A large Mauritian trial found that CRP levels reduced by 53.4% in men and 41.1% in women at high risk of ischemic heart disease drinking 3 cups of black tea daily over 12-weeks [56].

One small post-ingestion trial observed no links between green tea consumption and CRP levels [43]. However, amongst 36 patients with knee osteoarthritis drinking three cups of Burdock root tea daily (2 g/150 ml boiled water) over 42 days appeared to aid and significantly reduce markers of inflammation (Interleukin-6, high sensitivity-C-reactive protein) and improved levels of oxidative stress [54]. Further adequately designed trials are needed. Only one trial focusing on inflammation was found to be of suitable quality according to the Jadad scale.

Discussion

A summary of the results from this review is given in Table 5. There has been a significant upsurge in the number of scientific articles studying the role of tea in human health [5] (2097 related publications in the last 10 years; PubMed search) – this includes its role in relation to cardiovascular well-being. Tea is one of the most popular and cost-effective beverages consumed after water - renowned for its health promoting properties since ancient times [3]. Alongside this, the market and evidence-based for tea forms other than black and green tea is growing. This is reflected in the present review with evidence for chamomile, sour, hibiscus, goishi and rooibos tea in relation to cardiovascular wellbeing emerging (Table 3).

In relation to measures of cardiovascular health strongest positive effects relate to black and green tea, most consistently in relation to reduced systolic and diastolic pressure [8,19-24]. The totality of the evidence indicates that drinking 4 to 5 cups of black and green tea daily in the longer term (for more than 12 weeks) could help to reduce systolic and diastolic blood pressure [20,21] particularly amongst those at risk of high blood pressure [19]. Given the high prevalence of hypertension in the UK and worldwide these findings have important public health implications [31]. For example, a large proportion of the general population have blood pressure levels within the ranges included in trials i.e. at increased risk of hypertension making results particularly applicable [29,31].

Next, evidence was strongest in relation to cholesterol and lipid levels. Green tea appears to be more strongly related to reduced total and LDL cholesterol, as evidenced by a large number of meta-analytical publications [22,23,36-38]. For black tea those with a higher cardiovascular risk appear to have more benefit [11] with indications from RCTs suggesting that black tea could reduce triglyceride levels, alter body fat distribution and increase fat excretion [6,40,44]. For black tea there is evidence that this can improve FMD and exhibit vascular protective properties that could be of clinical relevance [48,49,53]. Although these effects appear to be modest they could be of importance for cardiovascular health at the population level due to the widespread habitual consumption of tea and high prevalence of cardiovascular risk factors. The number of studies looking at tea in relation to inflammation was small but indicated a positive effect. Some findings suggest that certain populations may benefit such as those with type 2 diabetes [55] or ischemic heart disease [56]. Further studies on healthy populations are needed to better understand how tea drinking could affect inflammation.

In terms of mechanisms, reductions in CVD risk by tea may be attributed to high levels of polyphenols which both green and black tea contain [8]. Polyphenols (as found in tea) when taken in adequate doses can have a positive effect on the prevention of cardiovascular risk and lipid oxidation [57]. These can also increase the endothelial synthesis of nitric oxide yielding vasoprotective effects [58]. It has also been proved that these compounds can alter hepatic cholesterol absorption, triglyceride biosynthesis and lipoprotein secretion, the processing of lipoproteins in plasma, and inflammation [59]. Bearing this in mind the

different dosages of polyphenols used in trials could have contributed to variations in study findings. It would be worth deciphering ideal 'optimal doses' of polyphenols that could influence specific aspects of health such as cardiovascular wellbeing. Tea polysaccharides (TPS) – a group of heteropolysaccharides bound with protein are another component worthy of further investigation [60]. TPS are thought to possess bioactive antioxidant and anti-inflammatory properties with could influence measures of CVD [60]. Finally, it should also be considered that whilst many biologically active compounds in tea have been identified many unidentified compounds remain which could also possess bioactive properties [4].

All the papers reviewed were either meta-analytical or RCTs which makes findings stronger than if they were cross-sectional. It was a strength that the present article focused on the use of teas per se rather than tea extracts. This also makes the findings more applicable to the lay population and lowers costs for the public domain. Regarding future research several suggestions have been put forward. Meta-analysis papers need to 'separate out' green and black tea (and indeed emerging tea forms) so their individual effects can be better deciphered. There is evidence that various types of teas could act synergistically which could have health benefits to humans [7]. However, their individual effects first need to be clearly understood before cumulative effects are studied. It is important that future RCTs should be long enough in duration to be relevant to public health. Smaller studies tend to be less methodologically robust and are more likely to be conducted in selected populations where they can report larger beneficial effects than larger trials [61,62]. Where studies lacked conclusive results, this may have been due to their short duration, small sample sizes or inadequate tea (polyphenol) dosing regimens. The results of the present review need to be interpreted with this in mind.

Conclusion

Moderate intakes of tea (black and green) appear to be linked with blood pressure reductions at around 4 to 5 servings per day. Green tea seems to benefit the lowering of total and LDL cholesterol. Daily tea consumption also appears to have generic extended benefits including improved vascular function and reduced inflammation. Based on the evidence collated it seems plausible that tea consumption could be recommended to the general population or to patients as a strategy to reduce cardiovascular risk. These benefits largely appear to be attributed to the synergistic effects of tea phenolics coupled with its flavonoid elements.

Disclosure

The views expressed are those of the authors alone and personnel from the UK TEA & INFUSIONS ASSOCIATION (UKTIA) had no role in writing this review.

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