Thematic Article

Candidate foods in the Asia–Pacific region for cardiovascular protection: Oriental tea

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Chinese tea and the major health effects include: antimicrobial, anti-ultraviolet radiation, anticancer, lowering blood lipid and glucose, and protecting against coronary heart diseases. In contrast to the extensive studies on the protective effects of tea on cancer, fewer studies on the health effects of tea on cardiovascular diseases (CVD) have been published. This paper summarises the research results on the possible protective effects of tea on CVD available in China. The results from animal studies clearly demonstrated that tea pigments are effective in lowering blood lipid levels and preventing plaque formation in the aorta. However, the evidence of tea pigments in protecting ischemia heart disease (IHD) in humans is less convincing. One large well-designed ecological study reported an inverse correlation between tea drinking and IHD mortality; but the inverse correlation disappeared after controlling possible confounding factors. However, the effects in improving blood lipid levels and rheology biomarkers in hyperlipidemia subjects or CVD patients by tea pigments seem promising. However, these studies were not well-designed, controlled randomized clinical trials. This made the assessment difficult and inconclusive.

Key words: cardiovascular disease, China, Oriental tea.

Introduction

The health effects of tea have been documented in numerous classical books in traditional Chinese medicine and also studied extensively using modern scientific approaches and methods. The major health effects of tea include: antimicrobial, anti-ultraviolet radiation, anticancer, lowering blood lipid and glucose, and protecting against coronary heart diseases. Green tea was used in most experimental studies and in some human studies, black tea and oolong tea were also used. The tea preparations used in the studies include whole water extract of tea, tea polyphenols, individual tea catechins (especially epigallocatechin gallate, EGCG) and tea pigments (the oxidized product of tea polyphenols, containing theaflavins, thearubigins, etc.) (Table 1; Figs 1,2).

In contrast to the extensive studies on the protective effects of tea on cancer, fewer studies on the health effects of tea on cardiovascular diseases (CVD) have been published. Among them, most studies were animal experiments using tea pigments, and there are only a few epidemiological studies and clinical trials. Therefore, the results are far from conclusive. This paper summarises the research results on the possible protective effects of tea on CVD available in China.

Epidemiological studies

The ecological study of 65 rural counties in China (Chen *et al.*) was repeated in 1989 and it was found that the percentages of people drinking green tea daily was inversely correlated with mortality of ischemic heart disease in subjects aged between 35–69**,** with correlation coefficients (r) of -0.27 ($P < 0.05$) for males and -0.17 ($P = 0.17$) for females. However, this correlation was no longer significant in both sexes in further logistic analysis controlling for smoking, alcohol drinking and animal food consumption. This finding is in line with the epidemiological studies on the relationship between tea drinking and cancer mortality, which shows controversial results. As diseases with multiple causes such as CVD and cancers, tea drinking is only one of the lifestyle factors affecting the morbidity and mortality of these diseases. So far, only randomized population-based intervention trials could provide convincing results in assessing the role of tea drinking in the occurrence of CVD and cancers.

Animal studies

Protection against atherosclerosis

Lou *et al.* studied the effects of tea pigments on experimental atherosclerosis in rabbits.[1] Fifty healthy male rabbits were randomly divided into two groups: a control group and a tea pigments (TP) group. In the first 3 months, the TP group was given 50 mg TP (Fig. 2) and 0.5 g cholesterol orally every day, while the control group was given 0.5 g cholesterol only. In the fourth month, the tea pigments groups were given 10 mg/kg of TP intravenously for 1 month. The results

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showed that the percentages of plaque area in the whole area of the aorta in the TP group (2.1 ± 4.7%) were significantly smaller than the control group (5.6 ± 5.9%) ± ($P < 0.05$). The contents of cholesterol in the aorta walls of the TP group (0.7 ± 0.4 mg) were significantly lower than that of the control group (1.4 ± 0.8 mg) ($P < 0.01$) (Table 2).

Xuan *et al.* recently reported the preventive effects of tea pigments on hypercholesterolemia rabbits which showed that by the end of the experiment (8 weeks), the concentrations of plasma endothelin and the relative areas of plaque in the aorta were significantly lower than those of the control group, after being treated with two tea pigments (Tables 3,4).[2] However, the total serum cholesterol and triglycerides levels were not significantly different between the two tea pigments treated groups and the control group (Table 5). In another experiment, two groups of Apo-E-deficient mice were fed with a 'high fat western diet' only or the 'high fat western diet' plus tea pigments (100 mg/kg bodyweight) for 6 weeks. The results showed that the plaque area in the aortic sinuses of the tea pigments treated animals were significantly less than that of the control animals ($P < 0.05$, Table 6). The expression of endothelial nitric oxide synthase (eNOS) in the tea pigments treated group was higher than that of the control group ($P < 0.05$). However, the serum total cholesterol level was again not significantly different between the two groups (Table 7).

Table 1. Composition (%) of tea leaves

Polyphenols	36.0
Carbohydrates	25.0
Protein	15.0
Lignin	6.5
Ash	5.0
Amino acids	4.0
Methylxanthines	3.5
Lipids	2.0
Organic acids	1.5
Chlorophyll, etc.	0.5
Carotenoids	< 0.1
Volatiles	< 0.1

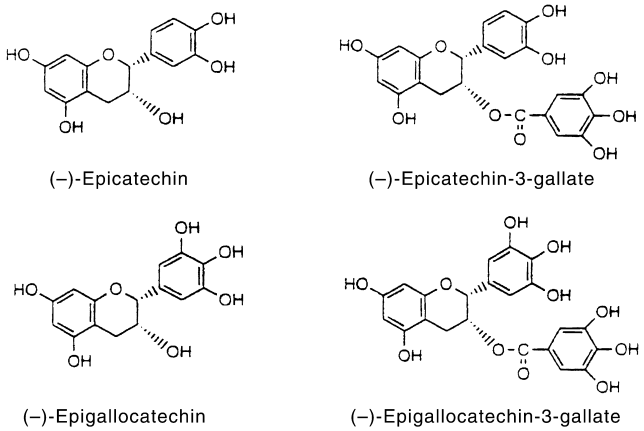

Figure 1. Major components of green tea polyphenols. Taken from Reference 7.

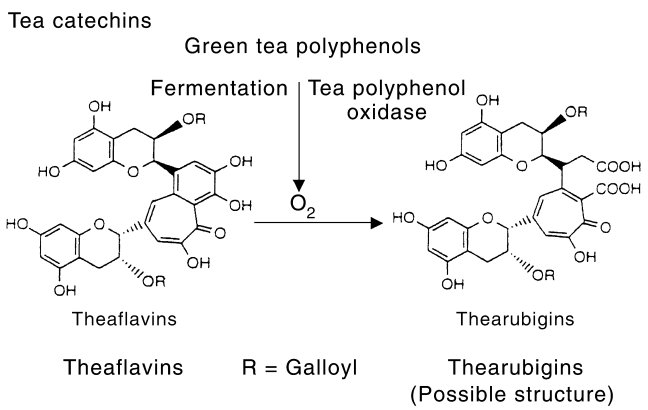

Figure 2. The oxidation of polyphenols to tea pigments. Taken from Reference 7.

Effects of tea flavanols on ischemia/reperfusion dysrhythmias

Ischemia/reperfusion dysrhythmia (RA) and myocardial stunning are the major characteristics of mycocardial reperfusion injury (MRI). In general, it is caused by the sudden increase of oxygen free radicals after mycocardial ischemia during early reperfusion. Peng *et al.* studied the effects of tea flavanols on ischemia/reperfusion dysrhythmias in the isolated perfused rat heart system.[3] Twenty-five Wistar rats were divided into two groups: the control group was given

Table 2. Effects of tea pigments on plaque formation and cholesterol content in aorta of rabbits

	Control	Tea pigments
Cholesterol (mg, dry weight)	1.4 ± 0.8	0.7 ± 0.4
Plaque area/total aorta area (%)	5.6% ± 5.9	2.1% ± 4.7

Table 3. Effects of tea pigments on plasma endothelin in rabbits

Groups	*n*	Endothelin (ng/L)
Control	8	775.6 ± 668.7
Low dose (32 μg/(g ·d))	8	251.7 ± 241.6*
High dose (96 μg/(g ·d))	8	65.4 ± 17.2**

*$P > 0.05$, **$P < 0.01$, compared with the control group. g ·d, grams per day.

Table 4. Effects of tea pigments on aorta plaque formation in rabbits

Groups	Plaque area/ thoracic aorta area (%)	Plaque area/ascendent aorta area (%)
Control	0.793 ± 0.077	0.625 ± 0.206
Low dose (32 μg/(g ·d))	0.588 ± 0.205*	0.326 ± 0.276*
High dose (96 μg/(g ·d))	0.437 ± 0.116*	0.175 ± 0.092**

*$P < 0.05$; **$P < 0.01$, compared with the control group. g ·d, grams per day.

Table 5. Effects of tea pigments on blood lipids in rabbits (mean ± SD, mmol/L)

Groups	0 weeks	4 weeks	8 weeks
Total cholesterol			
Control	1.32 ± 0.29	31.5 ± 6.21*	26.7 ± 6.79*
Low dose (32 μg/(g ·d))	1.29 ± 0.30	28.6 ± 6.32*	24.9 ± 4.82*
High dose (96 μg/(g ·d))	1.35 ± 0.33	27.0 ± 5.88*	23.3 ± 5.00*
Triglycerides			
Control	0.78 ± 0.13	3.81 ± 1.36*	4.32 ± 1.25*
Low dose (32 μg/(g ·d))	0.79 ± 0.11	3.51 ± 1.70*	4.25 ± 1.03*
High dose (96 μg/(g ·d))	0.76 ± 0.12	3.45 ± 1.59*	3.59 ± 1.18*
HDL-C			
Control	0.98 ± 0.16	0.90 ± 0.11**	0.86 ± 0.10**
Low dose (32 μg/(g ·d))	0.92 ± 0.11	0.92 ± 0.14**	0.93 ± 0.13**
High dose (96 μg/(g ·d))	0.94 ± 0.16	0.93 ± 0.12**	0.88 ± 0.10**

* $P < 0.00$; ** $P > 0.05$, compared with the control group. HDL-C, high-density lipoprotein cholesterol.

Table 6. Effect of tea pigment on the area lesions in the aortic sinuses of Apo-E-deficient mice

Groups	*n*	Plaque area (μm^2)	Thoracic aorta area (μm^2)	Ratio
Control	8	124267 ± 47053	477116 ± 75214	0.2595 ± 0.0860
Tea pigment	8	37168 ± 17593**	411195 ± 90385*	0.0913 ± 0.0416**

*$P > 0.05$; ** $P < 0.01$, compared with the control group.

Table 7. Effect of tea pigment on the expression of eNOS in Apo-E-deficient mice (mmol/L)

Groups	*n*	eNOS (relative level)
Control	8	1.885 ± 0.858
Tea pigment	8	4.182 ± 1.701*

*$P < 0.05$, compared with the control group. eNOS, endothelial nitric oxide synthase.

Krebs–Henseleit (KH), while the tea flavanols group was given KH and tea flavanols (68.18 μmol/L as drinking fluid). The results (Table 8) showed that the incidence of reperfusion dysrhythmias in the control group (11/12, 91.7%) was significantly higher than that in the tea flavanols group (3/13, 23.1%) ($P < 0.005$). The duration of reperfusion dysrhythmias was much longer in the control group (27.91 ± 6.94 min) than that in the tea flavanols group (9.83 ± 6.21 min) ($P < 0.01$). These data suggested that tea flavanols could effectively reduce the incidence of reperfusion-induced dysrhythmias in experimental rat heart system, especially ventricular fibrillation.

Effects on platelet functions

Zhang *et al.* studied the effects of tea flavanols on platelet functions.[4] In the in vitro study, the plasma-rich platelet (PRP) that was induced by adenosine diphosphate (ADP), adrenalin or arachidonic acid was separated into two groups. The experimental group was added with TF in the concentration of 1 g/L, while the control group was added with distilled water. The results showed that TF remarkably inhibited human platelet aggregation induced by ADP, adrenalin or arachidonic acid (Table 9).

Clinical trials

Tea flavanols and platelet function

Zhang *et al.* observed the effect of tea flavanols on platelet aggregation in patients who have had myocardial infarction for a long time and is known as a pre-existing condition.[4] Twelve patients (8 males and 4 females) were given TF (750 mg/day) without other treatments for 2 months. The results showed that both platelet aggregation and thromboxane B_2 (TXB_2) levels decreased significantly after 2 months (Tables 10,11).

Effects of tea pigment on the prevention of atherosclerosis

Lou *et al.* was the pioneer in studying the effect of TP on the prevention of atherosclerosis in clinical trials in China.[5] A total of 120 patients with hyperlipidemia accompanied by hyperfibrinogenemia were treated with 0.25 g of TP daily for 2 months. The serum fibrinogen level decreased significantly ($P < 0.01$) and the effective rate was 85.0% (102/120). Another 12 patients with old myocardial infarction and increased levels of platelet aggregation and plasma TXB_2 (thromboxane B_2) were treated with TP (0.25 g) three times daily for 2 months. The levels of platelet aggregation and plasma TXB_2 decreased significantly ($P < 0.01$).

Later on in the 1990s, there were more than 100 clinical trials conducted in hospitals in various parts of China to test the preventive and therapeutic effects of TP on blood lipids, blood rheology and platelet function in patients. However,

Table 8. Effects of tea flavanols on ischemia/reperfusion dysrhythmias in rats

Groups	Reperfusion dysrhythmias (%)	RA duration (min)	Ischemia dysrhythmias (%)
Tea flavanols	23.1 (3/13)*	9.83 ± 6.21*	7.69 (1/13)*
Control	91.7 (11/12)	27.91 ± 6.94	58.33 (7/12)

* $P < 0.005$, compared with the control group. RA, reperfusion arrhythmias.

Table 9. Effects of tea flavanols (1g/L) on in vitro platelet aggregation induced by adrenalin, arachidonic acid and ADP

	1 μmol/L adrenalin ($n = 20$)		0.5 g/L arachidonic acid ($n = 12$)		2.5 μmol/L ADP ($n = 12$)		5 μmol/L ADP ($n = 12$)	
	Min	Max	Min	Max	Min	Max	Min	Max
TF	21.04 ± 1.48	55.18 ± 1.36	5.43 ± 2.20	12.76 ± 1.59	18.43 ± 1.4	28.59 ± 1.67	19.59 ± 1.32	29.34 ± 1.52
Control	20.54 ± 1.29	64.46 ± 1.24	22.56 ± 1.11	55.42 ± 0.22	38.05 ± 1.2	52.82 ± 1.26	43.33 ± 1.17	67.53 ± 1.11
P	> 0.05	< 0.01	< 0.01	< 0.01	< 0.001	< 0.001	< 0.001	< 0.001

TF, tea flavanols; ADP, adenosine diphosphate; min, minimum; max, maximum.

Table 10. Effect of TF on platelet aggregation in patients with old myocardial infarction [$1g^{-1}$ (X ± SD)]

Groups	2.5 μmol/L ADP		1.25 μmol/L ADP		2 μmol/L Adr		1 μmol/L Adr	
	Min	Max	Min	Max	Min	Max	Min	Max
Before treatment	60.52 ± 1.42	63.61 ± 1.41	37.48 ± 1.52	44.58 ± 1.62	31.14 ± 1.67	61.20 ± 1.48	21.78 ± 1.52	61.77 ± 1.29
After 2 months	25.45 ± 1.56	30.54 ± 1.61	19.92 ± 1.44	22.76 ± 1.52	18.31 ± 1.54	37.83 ± 1.99	16.54 ± 1.58	33.80 ± 1.96
P	< 0.001	< 0.01	< 0.01	< 0.01	< 0.05	< 0.01	< 0.05	< 0.05

TF, tea flavanols; ADP, adenosine diphosphate; Adr, adrenalin; min, minimum; max, maximum.

Table 11. Effects of tea flavanols on plasma TXB_2 in patients with old myocardial infarction

Groups	*n*	TXB_2 (ng/L)	*P*
Before treatment	12	157.00 ± 36.37	
After 2 months	12	118.90 ± 26.72	< 0.01

TXB_2, thromboxane B_2.

many of the studies did not include a parallel placebo control group or only had a small sample size; therefore, it is difficult to assess the validity of the reported results. However, as the number of studies was so big and most of the studies have reported protective effects on CVD, some selected results are summarized in Tables 12 and 13. All these clinical trials used the TP capsule produced by the Jiangxi Green Color Pharmaceutical Company (Nanchang City, China) and the original reports are published in the Monograph of Papers on clinical studies on tea pigments in China.[6]

Discussion and conclusion

The results from animal studies clearly demonstrated that TP are effective in lowering blood lipid levels and preventing plaque formation in the aorta. The mechanism of the latter effect may be related to the inhibition of low-density lipoprotein (LDL) cholesterol oxidation by tea pigments (Xuan *et al.*).

However, the evidence of TP in protecting ischemia heart disease (IHD) in humans is less convincing. Only one large well-designed ecological study reported an inverse correlation between tea drinking and IHD mortality; but the inverse correlation disappeared after controlling possible confounding factors. In contrast, the effects in improving blood lipid levels and rheology biomarkers in hyperlipidemia subjects or CVD patients by tea pigments seems promising. However, these studies were not well-designed, controlled, randomized clinical trials. Many of the reported trials used a known drug as control and did not have a placebo control group. This made the assessment difficult and inconclusive.

Tea pigment is the tea component mostly studied in its effects on CVD. In contrast, tea polyphenol was the tea component mostly studied in its effect on cancer. However, not like tea polyphenols and the individual catechins, the composition and chemical structure of tea pigments are not well-established and the analytical methods for thearubigins (a major component of tea pigments) is not available. It is very likely that there were some inconsistencies in the TP samples used in various studies. Therefore, there is an urgent need to identify the composition of TP and develop necessary analytical methods to control the quality of the test samples.

Table 12. Effects of tea pigments on blood lipids in hyperlipidemia subjects*

Authors	*n*	Dose (mg/day)	TC	TG	HDL-C	LDL-C	Apo-B	Apo-A	Page no. of Ref 6
Xie, YR[a]	150	375	< 0.001	< 0.001	< 0.001	< 0.01	< 0.001	< 0.001	p. 32
Mu, NZ[b]	600	375	< 0.05	< 0.01	< 0.05	< 0.05	–	–	p. 50
Tan, ZZ[b]	70	750	> 0.05	< 0.01	< 0.01	< 0.01	–	–	p. 74
Yang, BE[b]	196	750	< 0.01	< 0.01	< 0.01	< 0.01	–	–	p. 124
Sha, M[b]	148	750	> 0.05	> 0.05	> 0.05	< 0.05	–	–	p. 150
Yang, XJ[b]	50	750	< 0.01	< 0.01	< 0.01	< 0.01	–	–	p. 258

* Results are expressed as *P*-values of *t*-test in favour of the treated group as compared with the control group.
a, b: Duration of the study – a, 2 months; b, 1 month.
TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Apo-A, apoprotein A; Apo-B; apoprotein-B.

Table 13. Effects of tea pigments on blood rheology in hyperlipidemia or CVD subjects*

Authors	*n*	Dose (mg/day)	VB	VP	PAD	Fibr	Hematocrit	Page no. of Ref 6
Xie, YR[a]	150	375	< 0.01	< 0.01	< 0.01	–	< 0.05	p. 32
Mu, NZ[b]	600	375	< 0.05	< 0.05	< 0.01	–	> 0.05	p. 50
Mu, NZ[b]	76	375	< 0.05	< 0.05	< 0.01	–	< 0.01	p. 415
Cheng, XH[c]	80	750	< 0.01	< 0.001	–	< 0.005	< 0.01	p. 431
Jiang, XR[d]	30	750	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	p. 478

* Results are expressed as *P*-values of *t*-test in favour of the treated group as compared with the control group.
VB, blood viscosity; VP, plasma viscosity; PAD, platelet aggregation degree; Fibr, fibrinogen.
Duration of the study: a, 2 months; b, 1 month; c, 2 years; d, 15 days.

References

1. Lou FQ, Yang ZC, Yuan WL, Xia SY, Song JF, Zhang MF. Effects of tea pigment on experimental atherosclerosis in rabbits and treating patients of hyperfibrinogenemia. Chin Med J 1983; 10: 632–634.
2. Xuan WL, Wang SW, Han C, Chen JS. Preventive effects of tea pigment on experimental atherosclerosis in hypercholesterolemia rabbits. China J Arterioscler 2000; 8: 131–133.
3. Peng ZP, Huang YW, Hu H. Action of tea flavanols on the ischemia/reperfusion arrhythmias in the isolated perfused rat heart. Chin J Pathophysiology 1993; 9: 401–403.
4. Zhang XG, Lou FQ, Lu JS, Xia SY, Zhang MF. Further studies of the effects of tea flavanols on platelet functions. J Zhejiang Med Uni 1989; 18: 244–247.
5. Lou FQ, Zhang MF, Zhang XG, Liu JM, Yuan WL. Study on the effect of tea pigment on the prevention of atherosclerosis. Proceedings of International Tea Quality Human Health Symposium. November 4–9th, 1987; 268–273.
6. Center for Tea Pigments Promotion. Monograph of Papers on clinical studies on tea pigments in China. Beijing: China Medical and Pharmaceutical Technology Publishing House, 1998; 32–478.
7. Granham HN. Green tea composition, consumption, and polyphenol chemistry. Prev Med 1992; 21: 334–350.