PRINT: ISSN 0972-0073 ONLINE: 2456-6802
Ethno Med, 6(3): 161-166 (2012)
DOI: 10.31901/24566772.2012/06.03.04

The Effect of Tea in Cerebrovascular Disease

Pahari Ghosh[1], Amar Kr Misra[2], Anup Kr Bhattacharya[3], Namrata Triveda[1], Arindam Ghosh[3], Ipsita Ghosh, Tapash Rudra[1], Rakesh Roy[1] and Sanjay De[1]

[1]Ramakrishna Mission Seva Pratishthan, Vivekananda Institute of Medical Science, 99, Sara Bose Road, Kolkata 700 026, West Bengal, India
[2]North Bengal Medical College, West Bengal, India
[3]Mata Gujri Memorial Medical College, Kishanganj, West Bengal, India
[4]NRS Medical College and Hospital, Kolkata, West Bengal, India

KEYWORDS Flavonoids. Ischemia. Hyperglycemia. Cholesterol. Low Density Lipoprotein

ABSTRACT Tea is the most widely consumed human beverage and rich in flavonoids, which causes significant endothelium dependent vasodilatation. Aims are to study the effect of tea drinking in subjects with ischemic stroke and metabolic syndromes. A total of 1100 stroke patients were selected from indoor/ outdoor department of Ramakrishna Mission Seva Pratisthan and other Hospitals of Kolkata from last three years. Individuals between 40 to 80 years of age were recruited. Clinical and biochemical examination were conducted in each case at the onset and every 6 months interval. Individuals stable on existing medications were advised to continue the same unless situation demands dose modification or withdrawal. Methods of tea preparation were detailed to study participants and they were asked to take ≥3 cups (each cup contains 150 ml of tea /day. Out of 1100 participants, 787 were men and 313 were women and the mean age was 61.62±11.02. Tea drinkers constituted 95.09% of total study individuals. At second follow up, 773 subjects were regular in attendance and 9 died. The most preferred type of tea ingested was decoction (53.64%). Significant ($p< 0.001$) decrements were noticed in systolic blood pressure, Body Mass Index (BMI), fasting blood glucose and Low Density Lipoprotein (LDL) level when compared between base line and consecutive visits. Tea consumption of 450 ml or more (≥3cups)/day was associated with reduction of the incidence of recurrent ischemic stroke, significant decrement of systolic blood pressure, better control of fasting hyperglycemia, and lowering down of the level of total cholesterol and Low Density Lipoprotein level in subjects with hypercholesterolemia. Further investigations are needed to corroborate our observations.

INTRODUCTION

Tea is the most widely consumed beverage in the world (Cheng 2004). The polyphenolic flavonoids in tea are thought to have a protective role in cerebrovascular disease (Arab et al. 2009). Daily consumption of either green or black tea equaling three cups per day could prevent the onset of ischemic stroke (Arab et al. 2009). Although experimental studies are supportive of reducing the risk of ischemic stroke, epidemiological evidence is equivocal because of lack of accurate measurements on tea exposure.

Stroke, previously known as cerebrovascular accident, is the rapidly developing loss of brain function(s) due to disturbance in the blood supply to the brain. This can be due to ischemia (lack of blood flow) caused by blockage (thrombosis, arterial embolism), or a hemorrhage (leakage of blood) (Sims and Muyderman 2009). It has been estimated that cerebrovascular diseases (stroke) accounted for 5.5 million deaths worldwide, equivalent to 9.6 % of all deaths (World Health Organization 2002).

Stroke can have a profound influence on individual and their families (Flynn et al. 2008). Till date, there are few known preventive approaches to reduce stroke incidence. Preventive approaches have been shown to powerfully impact disease burden as well as costs (Kahn et al. 2008; Lee et al. 2006). Meta-analysis of the relationship between consumption of black tea and cardiovascular disease risk suggested heterogeneity of results and associated with overall reduced risks (Peters et al. 2001). In addition, flavonoids have consistently been shown to inhibit the development of atherosclerosis in animal models (Hodgson 2008). Animal studies have concluded that "daily intake of green tea catechins / extract efficiently protects the penumbra from irreversible damage due to cerebral ischemia, reduced the formation of post ischemic brain edema and infarct volume and consequent neurological deficits" (Hong et al. 2000; Lee et al. 2004; Suzuki et al. 2004). The observational epidemiological research in humans is strongly

Address for correspondence:
Dr. Pahari Ghosh
Professor
MD, MRCP, FCCP, DM (Neurology)
67, Rash Behari Avenue, Kolkata-700026
Mobile: 9831023296
E-mail: pgstrokeunit@gmail.com,
ghosh.pahari@gmail.com

supportive of the hypothesis that tea consumption, at the level of e"3 cups per day, either as green or black tea, reduces the risk of occurrence of stroke, stroke volume, and mortality from stroke (Delavar et al. 2008; Liang et al. 2009; Reddy et al. 2005).

Catechin is a promising tool against metabolic syndrome. It could decrease fasting blood glucose, triglyceride levels, abdominal fat and insulin (Davies et al. 2003). Catechins may prevent low density lipoprotein from oxidative damage either through their free radical or by recycling other antioxidants (Hodgson et al. 2002; Kakuda 2002; Sato et al; 1989). However, reliable data were lacking. The incidence of cerebral haemorrhage and stroke was two-fold higher in those people who took less than 5 cups of tea than those who took 5 cups or more daily (Keli et al. 1996). An inverse correlation between black tea consumption and the incidence of stroke was also replicated with the Zutphen study in which 552 men aged between 50 and 69 were followed during 15 years (Arts et al. 2000). However this inverse association was not observed in another Netherland based study (Gupta et al. 2011).

There is no observational epidemiological study on effects of tea intake in cerebrovascular disease and metabolic syndromes in Indian subcontinent. However, one recent review article from India has concluded that regular intake of green tea as a beverage has prophylactic potential against stroke incidence (Liang et al. 2009).

Objectives

Under this context, the researchers aimed at determining the effect of tea drinking in cases of proved cerebrovascular disease with or without diabetes mellitus, hypertension, ischemic heart disease and dyslipidaemia as well as to study the effect of tea drinking in cases of diabetes mellitus (DM), hypertension (HTN) and dyslipidaemia.

MATERIAL AND METHODS

Subjects

A total 1100 subjects with stroke from last 3 years were identified with a male- female ratio of 787:313 from in and out patients department of the Ramakrishna Mission Seva Pratisthan (RKMSP) Institute and other Premiere Private Hospitals, Kolkata. Cases were selected based on the following criteria: (i) Cases of established cerebrovascular disease based on World Health Organization stroke defined criteria (with or without neuro-radiological confirmation), age range 40 to 80 yrs and with or without coexisting hypertension, diabetes mellitus, ischemic heart disease and dyslipidaemia. Patients with history of transient ischemic attack were excluded from the study. All volunteers provided written consent for participation in this study. The project was approved by the Institutional Ethics Committee of Ramakrishna Mission Seva Pratisthan.

Study Design

The study is a descriptive longitudinal study over a period of four years. During the study period, subjects were instructed to cease intake of beverages other than tea and not to make any changes to their usual food intake habit and physical activity. Subjects were instructed to drink tea 5 cups per day (150 ml of each). Women were asked not to take hormone replacement therapy. Height was measured at baseline, and body weight was measured at baseline and at successive follow-up.

Tea Preparation

The method of tea preparation was standardized as far as practicable. Tea leaves (2gm approx) were boiled in 150 ml of water for 1 minute, with constant movement. A consistent weight of tea will be achieved by providing subjects with a spoon that, when filled contained 2 gm of tea leaves. Subjects were instructed to use a standard tea cup, which holds approximately 150 ml of water. Subjects were asked not to take tea on the morning before each blood sample in order to avoid the possibility of acute effects.

Data Collection

Detailed history including questionnaire based on stroke, diabetes, hypertension and addiction were carried out. Clinical examination was carried out by competent physician and the neurological counterpart was supervised by a neurologist.

Body weight and height of each participant was measured and recorded at one year interval. BMI (Body mass index) of each individual was calculated and recorded.

Blood pressure was measured using a standard mercury manometer. Subjects rested in the supine position for 5 minutes to cancel white coat effects. Blood pressure was then measured on the right arm. Blood pressure measurements were not disclosed to participants during the study.

Biochemical examination of all these patients at the time of entry and at six months interval was performed from National Accredited Laboratory. Blood biochemistry estimation included fasting (8 hours fasting) and (post prandial) PP glucose, blood urea, creatinine and twelve hours fasting lipid profile high density lipoprotein, low density lipoprotein, very low density lipoprotein and triglyceride. Neuro-imaging (CT scan of brain / MRI of brain), Electro Cardiogram studies were done in all cases. Nerve conduction velocity study and Carotid Doppler were performed in selected cases.

Biochemical examination of fasting blood sugar and PP were done using Standard Hexokinase method, reference ranges were 70 to 100 mg/dl and 80 to 140 mg/dl respectively. Serum cholesterol was measured using standard CHOD PAP method, reference range was < 200 mg/dl. high density lipoprotein cholesterol, very low density lipoprotein cholesterol and low density lipoprotein cholesterol were measured using Direct Enzymatic Method, reference ranges for high density lipoprotein were < 35 mg/dl (male), < 45 mg/dl (female), for very low density lipoprotein were < 40 mg/dl (both male and female) and for low density lipoprotein were < 100 mg/dl (both male and female). Serum triglyceride was measured using the standard GPO- PAP method, reference range was < 200 mg/dl.

Subjects already taking lipid lowering agent, anti-hypertensive, oral or parenteral anti-diabetic and other prescribed drugs were asked to continue the same without dosage modification unless situation demands.

Total patients included in the study were divided in three groups according to their tea intake habits- up to 3 cups (450 ml per day), 4 to 5 cups (600-750 ml per day) and more than 5 cups (more than 750 ml per day).

Besides explaining possible health benefits of liquor tea to the study participants and thereby believing them for prescribed amount of tea intake, they were also asked to communicate to the investigator through telephone, if needed, besides routine follow up visits of the study.

Individual database was maintained for all these subjects at the outset and every six month interval. All the collected data were statistically analysed using paired 't'test and Wilcoxon's matched pairs signed rank test. Comparative study on stroke incidence, changes of blood pressure, Body Mass Index, blood glucose, serum lipid profile were done at the first and subsequent visits. A value of $p < 0.05$ was considered to be statistically significant for all analyses. The data was analysed using Statistica version 6.0.

RESULTS

The researchers screened a total of 1100 patients with ischemic stroke, out of which 787 were men and 313 were women. The mean age of the participants was 61.62 ±11.02. The mean height of the individuals with stroke was 164.6 ±6.72 centimeter and mean weight was 60.95±9.3 kg. The mean body mass index at the entry of study was 22.16 ±3.70 and mean body mass index at the end of one year was 21.96 ±3.51 (3rd visit). A statistically significant decline was noted at < 0.001 level (t=9.45, p=.000).

Out of 1100 subjects, tea drinker constituted 95.09% (n=1046) and rest (4.91%) (n=54) was non tea drinker. The type of tea ingested as reported at the onset of the study was tea with additives (46.36%).

At second visit, 773 subjects were regular and 300 subjects were erratic / absent in attendance as shown in Table 1.

Table 1: Follow-up presentation of the N= 1100 subjects

Baseline	*2nd Visit*	*3rd Visit till date*
Regular follow-up	773	639
Erratic/ Absent group in follow-up	300	11
Migrated	27	-
Death	9	-
Total subjects	1100	

Out of 773 subjects, 724 (93.66 %) subjects with tea drinker, and most common type was decoction, that is, tea without additives (53.64%). Considering the history of amount of tea intake, 450 ml/day is the highest amount taken by 46.64% individuals followed by

Table 2: Second Follow up patients (N=773)

Tea drinker (n=724)	*Non tea drinker (n=49)*	*Death statistics among patients under surveillance (n=9)*	*Break up of death in different groups*	
Tea consumption (150ml/ cup)	No. of patients with repeat attacks (n=138)	19 non-tea drinker have a history of repeated attacks	Non-tea drinker	3
Upto 3 cups	98		Upto 3 cups	5
4-5 cups	24		4-5 cups	1
>5 cups	16		>5 cups	0
Total	19.06%	38.77%	Total	9

33.16% individuals taking 600 to 750 ml/day and 20.20% subjects taking more than 750ml/ day.

The incidence of repeat stroke was 19.06% in tea drinker group and 38.77% in non-tea drinker group. The difference in repeat stroke incidence between these two groups was found to be statistically significant ($p< 0.001$). Second follow up patient's summary is shown in Table 2.

The range of systolic blood pressure among 1100 subjects at the entry visit was 90-230 mm of Hg and the mean was 137.97±20.74. The range of systolic blood pressure among 773 subjects (regular follow-up) after one year follow up was 90-220 mm of Hg and the mean was 135.93±19.84. A statistically significant decline was evident in systolic blood pressure but the quantum of change (95% CI 1.42-8.81) mm Hg is not clinically important. The range of Diastolic blood pressure among 1100 subjects at the entry visit was 60-155 mm of Hg and the mean was 89.41±14.43. The range of diastolic blood pressure among 773 subjects (regular follow-up) after one year follow up was same as entry level (60-220 mm of Hg) and the mean was 90.79±15.38. Comparison between biochemical parameters at first and second visits by Paired t-test were shown in Table 3.

Table 3: Comparison between biochemical parameters at first and second visits by Paired t-test (Wilcoxin's matched pairs signed rank test)

Variables (N1=1100) (n2=773)	*Mean (SD)*	*Range*	*t*	*p value*
FBG_N1	116.95±46.53	50 -420	7.381	**.000**
FBG_n2	105.67±33.28	50 -322		
PPBG_N1	166.91±67.65	69 -432	.094	.926
PPBG_n2	160.24±65.51	71 -374		
TG_N1	145.70±68.82	38 -593	.548	.584
TG_n2	142.94±65.70	13 -593		
TC_N1	180.43±44.68	37 -347	4.229	**.000**
TC_n2	172.28±44.81	18 -329		
LDL_N1	108.99±34.57	18 -248	4.441	**.000**
LDL_n2	102.25±33.94	14 -248		
HDL_N1	49.35±12.79	15 - 90	-1.408	.160
HDL_n2	50.73±17.37	18 -152		
VLDL_NI	24.10±10.12	5 - 77	-2.791	**.005**
VLDL_n2	24.91	8 - 74		
Urea_N1	29.42±15.12	3.5-211	3.293	**.001**
Urea_n2	27.32±13.80	0.9-133		
Cr_N1	1.08±0.37	0.1- 3.9	1.751	.080
Cr_n2	1.06±0.38	0.1- 4.4		

DISCUSSION

The mechanism of protective effect of tea against stroke remains speculative. Experimental studies have suggested that tea consumption may reduce the risk of ischemic stroke. However, epidemiological evidence is mostly equivocal, mainly; due to lack of accurate measurements on tea exposure. A recent meta-analysis has shown individuals ≥3 cups of tea per day appear to reduce risk of a fatal or non-fatal stroke by approximately 21% as compared non drinkers of tea (Arab et al. 2009). A recent case control study from southern China have observed a significant decrease in ischemic stroke risk for drinking at least one cup of tea weekly when compared with infrequent or non drinking (Taubert et al. 2007). The researchers have observed daily black tea consumption of 450 ml or more (≥3/day) was associated with significant reduction in the incidence of a risk of recurrent ischemic stroke.

High blood pressure is the principal strategy in limiting the stroke in humans. Results of population studies suggest that long term regular ingestion of tea may lower blood pressure (Stensvold et al. 1992).

A recent meta- analysis of five controlled trials showed no overall effects of systolic blood pressure or diastolic blood pressure, whereas

analysis of similar number of trials using flavonoids rich dark chocolate did show significant blood pressure lowering (Soares et al. 2002).

The researchers observed a statistically significant decline of systolic blood pressure in our subjects but the quantum of change is not clinically important. In humans, systolic blood pressure levels were inversely related to tea ingestion (Yang et al. 2004).

The ability of the tea flavonoids to activate endothelial NOS and thereby improving NO bioavailability is likely the primary mechanism for reduction of blood pressure observed in different human studies (Actis Goretta et al. 2006; Davies et al. 2003). It is possible that tea flavonoids produced vasodilator function and thereby, reduction of blood pressure on long term use in our subjects. However, further trials are needed to support our observation. Results of *in vitro* studies, animal based studies and population based studies suggest that flavonoids could decrease blood cholesterol concentration (Ikada et al. 1992).

The present study showed that consumption of black tea significantly reduces blood cholesterol and low density lipoprotein cholesterol level. The researcher's observation was found to be consistent with the earlier study where consumption of black tea appreciably reduced total and low density lipoprotein cholesterol in mildly hypercholesterolemic adults (Davies et al. 2003).

Tea catechins were found to produce hypocholesterolemia in rats by reducing cholesterol absorption from intestine *in vivo* and by precipitating cholesterol from micelles *in vitro* (Daniells 2008). Whether similar mechanism is operative in human being is yet to be determined. The researchers studied 1100 subjects with ischemic stroke. They report that regular ingestion of black tea was found to be associated with significant reduction of body mass index. Reduction of body mass index in their subjects seems to be reduction of bodyweight in overweight and obese individuals. This may be related to some unknown biological molecular effects of black tea polyphenols in vivo.

Health benefits of tea are largely due to presence of polyphenols, principally flavonoids. Black tea is not only known for its antioxidants, immune boosting and anti-hypertensive properties, but also found to be useful for controlling diabetes (Chen et al. 2009). Compound in black tea called theaflavins and thearubigins were found to mimic the effects of insulin and help in preventing diabetes (Hodgson 2006; Sabu et al. 2002). Black tea contains a polysaccharide compound that inhibits an enzyme called alpha-glycosidase, which turns starch into glucose (Gomes et al. 1995).

Diabetes related research has shown the potential benefits of green and black teas in glucose and insulin metabolism in rats (Greenberg et al. 2005; Salazar-Martinez et al. 2004), unclear association in cohort studies (Fukino et al. 2005) and inconclusive evidence in trials (Zhong et al. 2006). However, the researchers observed significant decline of fasting blood glucose level in our subjects ($p< 0.001$).

Regular consumption of black tea has been found to be associated with lower risk of type 2 diabetes in Asian men and women in Singapore (Odegaard et al. 2008). There has been no statistically significant change in diastolic blood pressure, high density lipoprotein cholesterol, very low density lipoprotein cholesterol, urea and creatinine in our observational study.

LIMITATIONS

There are limitations in this study which are worth mentioning. These are erratic attendance of large number of patients in follow up. Besides this, a group of subjects with ischemic stroke did not follow the strict methodology of tea preparation and amount of tea intake as advised.

CONCLUSION

The researchers' observation reveals daily tea consumption of 450 ml or more (≥3 cups / day) may reduce the incidence of recurrent ischemic stroke. Besides this, it may give rise to better control of fasting hyperglycemia, lowering of BMI in overweight and obese individuals; decrease the level of total cholesterol as well as LDL cholesterol in subjects with hyper cholesterolemia. However, further study is needed to support our observations. To the best of our knowledge, this is the first prospective observational study of effect of tea in cerebrovascular disease from Eastern India.

REFERENCES

Actis Goretta L, Ottaviani JI, Fraga CG 2006. Inhibition of angiotensin converting enzyme activity by flavonoide rich foods. *J Agric Food Chem*, 54: 229-234.

Arab L, Liu W, Elashoff D 2009. Green and black tea consumption and risk of stroke: A meta- analysis. *Stroke*, 40: 1786-1792.

Arts ICW, Van de Putte B, Hollman PCH 2000. Catechin contents of foods commonly consumed in the Netherlands 2. Tea, wine, fruit juices and chocolate milk. *J Agric Food Chem*, 48: 1752-1757.

Chen H, Qu Z, Fu L, Dong P, Zhang X 2009. Physicochemical properties and antioxidant capacity of 3 polysaccharides from green tea, oolong tea, and black tea. *Journal of Food Science*, 74(6): C469-C474.

Cheng T O 2004. Will green tea be even better than black tea to increase coronary flow velocity reserve? *Am J Cardiol*, 94: 12-23.

Daniells S 2008. Black tea compounds may protect against diabetes. *Aging Cell,* 7: 69-77.

Davies MJ, Judd JT, Baer DJ, Clevidence BA, Paul DR, Edwards AJ, Wiseman SA, Muesing RA, Chen SC 2003. Black tea consumption reduces total and LDL cholesterol in mildly hypercholesterolemic adults. *J Nutr*, 133(10): 3298S- 3302S.

Delavar MA, SannLM, Lin KG, Tajuddin S et al. 2008. Black tea consumption and risk of metabolic syndrome among middle aged women. *Research Journal of International Studies*, 8: 117-124.

Flynn RWV, Mac Walter RSM, Dooney ASF 2008. The cost of cerebral ischemia. *Neuropharmacology,* 55: 250-256.

Fukino Y, Shimbo M, Aoki N et al. 2005. Randomized controlled trial for an effect of green tea consumption on insulin resistance and inflammation markers. *J Nutr Sci Vitaminol (Tokyo),* 51: 335-342.

Gomes A, Vedasiromoni JR, Das M et al.1995. Anti-hyperglycemic effect of black tea in rat. *J Ethnopharmacol*, 45: 223-226.

Greenberg JA, Axen KV, Schnoll R, Boozer CN 2005. Coffee, tea and diabetes: The role of weight loss and caffeine. *Int J Obes*, 29: 1121-1129.

Gupta A, Khurana B, Raheja I 2011. Green tea: A phytopharmaceutical 'wonder' extract for ischaemic stroke. *Research Journal of Pharmaceutical, Biological and Chemical Sciences,* 2(1): 304-312.

Hodgson JM, Puddey IB, Burke V, Watts GF, Beilin LJ 2002. Regular ingestion of black tea improves brachial artery vasodilator function. *Clin Sci (London)*, 102: 195.

Hodgson JM 2008. Tea flavonoids and cardiovascular disease. *Asia Pac J Clin Nutr*, 17(S1): 288-290.

Hodgson JM 2006. Effects of tea and tea flavonoids on endothelial function and blood pressure: A brief review. *Clin Exp Pharma Col Physiol*, 33: 838-841.

Hong JT, Ryu SR, Kim HJ, Lee JK, Lee SH, Kim DB, Yun YP, Ryu JH, Lee BM, Kim PY 2000. Neuroprotective effect of green tea extract in exper-imental ischemia-reperfusion brain injury. *Brain Res Bull*, 53: 743–749.

Ikada I, Imastro Y, Sasaki E, Nakayama M, Nagao H, Takeo T 1992. Tea catechins decrease micellar solubility and intestinal absorption of cholesterol in rats. *Biochem Biophys Acta,* 1127: 141-146.

Kahn R, Robertson RM, Smith R, Eddy D 2008. The impact of prevention on reducing the burden of cardiocvascular disease. *Circulation*, 118: 576-585.

Kakuda T 2002. Neuroprotective effects of the green tea components theanine and catechins. *Biol Pharm Bull,* 25(12): 1513-1518.

Keli S.O, Hertog M.G, Feskens E J et al. 1996. Dietary flavonoids, antioxidant vitamins and incidence of stroke: The Zutphen study. *Arch Intern Med*, 156: 637-642.

Lee H, Bae JH, Lee SR 2004. Protective effect of green tea polyphenol EGCG against neuronal damage and brain edema after unilateral cerebral ischemia in gerbils. *J Neurosci Res*, 77: 892–900.

Lee WC, Christensen MC, Joshi AV, Pashos CL 2006. Long term cost of stroke subtypes among Medicare beneficiaries. *Cerebrovasc Dis*, 23: 57-65.

Liang W, Lee AH, Binns CW, Huang R, Hu D, Zhou Q 2009. Tea consumption and ischemic stroke risk: A case-control study in southern China. *Stroke*, 40(7): 2480-2485.

Odegaard AO, Pereira MA, Koh WP, Arakawa K, Lee HP, Yu MC 2008. Coffee, tea, and incident type 2 diabetes: The Singapore Chinese Health Study. *Am J Clin Nutr*, 88(4): 979-985.

Peters U, Poole C, Arab L 2001. Does tea affect cardiovascular disease? A meta-analysis. *Am J Epidemiol,* 154: 495-503.

Reddy VC, Vidya Sagar GV, Sreeramulu D, Venu L, Raghunath M 2005. Addition of milk does not alter the antioxidant activity of black tea. *Ann Nutr Metab,* 49: 189-195.

Sabu MC, Smitha K, Kuttan R 2002. Anti-diabetic activity of green tea polyphenols and their role in reducing oxidative stress in experimental diabetes. *J Ethnopharmacol*, 83: 109-116.

Salazar-Martinez E, Willett WC, Ascherio A et al. 2004. Coffee consumption and risk of type 2 diabetes mellitus. *Ann Intern Med*, 140: 1-8.

Sato Y, Nakatsuka H, Watanabe T, Hisamichi S, Shimizu H, Fujisaku S et al.1989. Possible contribution of green tea drinking habits to the prevention of stroke. *Tohoku J Exp Med*, 157(4): 337-343.

Sims NR, Muyderman H 2010. Mitochondria, oxidative metabolism and cell death in stroke. *Biochim Biophys Acta,* 1802(1): 80-91.

Soares De Moura R, Costa Viana FS, Souza MA, Kovary K et al. 2002. Antyhypertensive, vasodialator and antioxidant effects of a vinifera grape skin extract. *J Pharm Pharamacol*, 54: 15- 20.

Stensvold I, Tverdal A, Solvoll K, Foss OP 1992. Tea consumption, relationship to cholesterol, blood pressure, and coronary and total mortality. *Prev Med,* 21: 546-553.

Suzuki M, Tabuchi M, Ikeda M, Umegaki K, Tomita T 2004. Protective effects of green tea catechins on cerebral ischemic damage. *Med Sci Monit*, 10: BR166–174.

Taubert D, Rolsen R, Schomig E 2007. Effects of coca and tea intake on blood pressure: A meta analysis. *Arch Intech Med*, 167: 626-634.

World Health Organization. *The World Health Report: 2002: Reducing Risks, Promoting Healthy Life.* Geneva: WHO.

Yang YC, Lu FH, Wu JS, Wu CH, Chang CJ 2004. The protective effects of habitual tea consumption and hypertension. *Arch Intech Med*, 164: 1534-1540.

Zhong L, Furne JK, Levitt MD 2006. An extract of black, green, and mulberry teas causes malabsorption of carbohydrate but not of triacylglycerol in healthy volunteers. *Am J Clin Nutr,* 84: 551–555.