


Green Tea – A Brew of Benefits?

Claire Chan, Pharm.D.
PGY-2 Critical Care Pharmacy Resident
Baptist Hospital of Miami
Clairech@baptisthealth.net



Objectives

- ◆ Describe the chemical components of green tea
- ◆ Provide an overview of green tea's potential health benefits
- ◆ Review and evaluate supporting literature

Overview and History

- ◆ Dried leaves of *Camellia sinensis*
- ◆ First discovered 2737 B.C. by Chinese emperor Shen Nung “Divine Healer”
- ◆ Used for centuries as beverage as well as medicinal agent
- ◆ Least oxidized type of tea
 - Polyphenol oxidase inactivated



Sumpio BE, et al. J Am Coll Surg. 2006;202(5):913-25.
Cooper R, et al. J Altern Complement Med. 2005;11(3):521-8.
Image from <http://shakethepalmtree.files.wordpress.com/2007/09/green-tea-shaded.jpg>

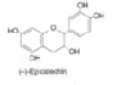
Tea Extraction Process

Catechins		Theaflavins & Thearubigins
White Tea (buds or young leaves)	Steamed (oxidase inactivation)	Dried
Green Tea (mature leaves)	Withered → Steamed or Pan-fired (oxidase inactivation)	Dried
Oolong Tea (mature leaves)	Withered → Bruised → Partially Fermented → Pan-fired	Dried
Black Tea (mature leaves)	Withered → Rolled → Fully Fermented → Fired	Dried

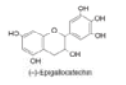
Image adapted from Cooper R, et al. J Altern Complement Med. 2005;11(3):521-8.

Chemical Components

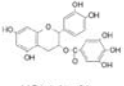
- ◆ Catechins: major polyphenolic compounds
 - 59% (-) Epigallocatechin gallate (EGCG)
 - 19% (-) Epigallocatechin (EGC), 13.6% (-) epicatechin-3-gallate (ECG), 6.4% (-) epicatechin (EC)
- ◆ Also: caffeine, theaflavins, phenolic acids



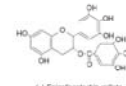
(-)-Epicatechin



(-)-Epigallocatechin



(-)-Epicatechin gallate



(-)-Epigallocatechin gallate

Cabrera C, et al. J Am Coll Nutr. 2006;25(2):79-99.
Image adapted from Cooper R, et al. J Altern Complement Med. 2005;11(3):521-8.

Dose and Composition

- ◆ Dose: 1 gm tea leaves/100 mL water
- ◆ 30-42% catechins, 3-5% caffeine

Compound	Green tea (cup)	Black tea (cup)
Catechins	60–125 mg	30–60 mg
Theaflavins	—	3.0–6.0 mg
Caffeine	20–50 mg	30–60 mg
L-theanine	20–40 mg	20–40 mg

Babu PV, et al. Curr Med Chem. 2008;15(18):1840-50.
Image adapted from Cooper R, et al. J Altern Complement Med. 2005;11(3):521-8.

Pharmacokinetics

- ◆ Low bioavailability
- ◆ Plasma catechins: 0.2-2% ingested amount
- ◆ Peak: 2-4 hours
- ◆ Extensive biotransformation
 - Methylation, glucuronidation, sulfation, ring-fissure metabolism
- ◆ 80% as active conjugates in urine and plasma

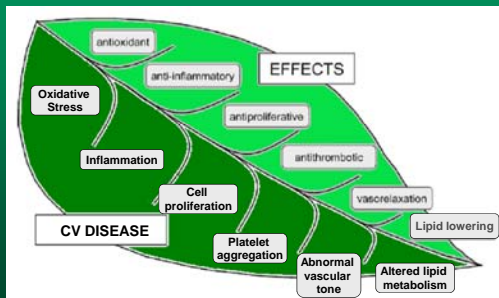
Babu PV, et al. *Curr Med Chem.* 2008;15(18):1840-50.
Khan N, Mukhtar H. *Life Sci.* 2007; 26:81(7):519-33

Proposed Mechanisms

- ◆ Antioxidant
 - Free radical scavenging
- ◆ Lipid-lowering
 - Inhibits cholesterol, fatty acid absorption and synthesis
- ◆ Anti-hypertensive
 - Increased production of nitric oxide, prostacyclin, cAMP
- ◆ Anti-thrombogenic
 - Inhibits platelet aggregation
- ◆ Anti-inflammatory
 - Inhibits leukocyte adhesion
- ◆ Anti-proliferative
 - Decreases remodeling

Babu PV, et al. *Curr Med Chem.* 2008;15(18):1840-50.
Cooper R, et al. *J Altern Complement Med.* 2005 Jun;11(3):521-8.

Cardioprotection - Mechanisms



Adapted from Stangl V, et al. *Cardiovasc Res.* 2007;73(2):348-58.

Anti-Cancer - Proposed Mechanisms

- ◆ Antioxidant activity
- ◆ Angiogenesis inhibition *in vitro*
- ◆ Anticarcinogenic activity
 - Blocks cell membrane receptors, thereby inhibiting cancer cell growth
 - Suppresses CYP enzymes involved in initiation
- ◆ Anti-tumor activity
 - Blocks DNA transcription of genes in cancer cell lines

Cooper R, et al. *J Altern Complement Med.* 2005;11(4):639-52.

Reported Benefits

- ◆ Antioxidant
 - Cardiovascular protection
 - Anti-cancer
- ◆ Anti-carcinogenic
- ◆ Anti-tumor
- ◆ Weight loss
- ◆ Anti-aging
- ◆ Antibacterial
- ◆ Antiviral



Babu PV, et al. *Curr Med Chem.* 2008;15(18):1840-50.
Image from <http://tea-brewery.com/wp-content/uploads/2009/10/green-tea.jpg>

Anti-Cancer

- ◆ Evidence: animal *in vivo* studies and human epidemiologic observations
- ◆ Reported to protect against certain cancers including colon, bladder, breast, lung, prostate

Cooper R, et al. *J Altern Complement Med.* 2005;11(4):639-52.

Anti-Cancer - Literature

- ◆ Review of 43 epidemiological studies, 4 RCTs, and 1 meta-analysis
 - More than half of the studies suggest reduced risk of certain cancers, especially GI (esophageal, stomach, pancreatic, liver, colorectal)
 - Interpretation is a challenge
 - ◆ Heterogeneous study designs, settings, populations, exposures, comparisons, outcomes and potential biases

Liu J, et al. *Chin Med*. 2008;3:12.

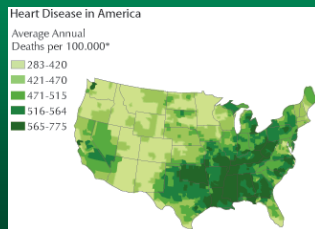
Benefits - Literature

- ◆ Kuriyama, et al. - The Ohsaki Study
 - Population-based prospective cohort study
 - N=40,530 Japanese
 - 11-year follow-up (all cause mortality), 7-year follow-up (cause-specific mortality)
 - Consumption of greater than 2 cups/day decreased risk of death from CVD by 22 - 33% versus consumption of less than half-cup/day
 - No reduction in mortality due to cancer was found

Kuriyama S, et al. *JAMA*. 2006;296(10):1255-65.

Cardioprotection

- ◆ Cardiovascular disease - leading cause of death in U.S.
- ◆ More than 80 million in U.S. have some form of CVD



www.CDC.com Washington, D.C. Preventing Heart Disease and Stroke.
Image from http://www.heartdisease.com/images/map_heart_disease.gif

Maron DJ, et al. *Arch Intern Med*. 2003;163(12):1448-53.

Cardioprotection - Literature

- ◆ Maron, et al.
 - RCT (n=240 Chinese)
 - Mild-moderate hypercholesterolemia on low-fat diet
 - Theaflavin-enriched green tea extract vs. placebo x 12 weeks
 - Significant changes in total cholesterol (11%) and LDL (16%)

Cardioprotection - Literature

- ◆ Yang, et al.
 - Cross-sectional study (n=1507 Taiwanese)
 - Outcome: risk of developing hypertension
 - 120-599 ml/day for ≥ 1 year reduced risk 46%
 - > 600 ml/day reduced risk 65%, compared to < 120 ml/day
- ◆ Hirano, et al.
 - Survey of green tea intake, other factors (n=393 Japanese)
 - No inverse association between green tea intake and CAD prevalence
 - However, green tea inversely associated with MI

Yang YC, et al. *Arch Intern Med*. 2004;164(14):1534-40.

Weight Loss

- ◆ Mice fed green tea: significant suppression of food intake, weight gain, and fat accumulation¹
 - Decreased leptin levels
- ◆ Associated with mild increase in thermogenesis²
 - May be more than that due to caffeine alone, due to COMT inhibition
- ◆ Sayama, et al.
 - RCT (n=10)
 - Green tea extract, caffeine, or placebo
 - Green tea showed significantly increased energy expenditure over 24 h

1. Sayama K, et al. *In Vivo* 2000;14:481-484.
2. Dulloo AG, et al. *Am J Clin Nutr* 1999;70:1040-1045.

Green Tea Extract

- ◆ 4th most commonly used dietary supplement in U.S.
- ◆ Weight-loss product containing green tea suspended in France and Spain due to hepatotoxicity concerns
- ◆ USP reviewed safety information
 - “Unaware of significant safety issues” as long as caution statement included



Sarma DN, et al. *Drug Saf.* 2008;31(6):469-84.
<http://www.nature.com/news/080606green-tea-natural-brand-green-tea-extract-315-mg-08px>

Laxi-Comp, Inc. 2010
Natural Medicines Comprehensive Database

Warnings

- ◆ Increased bleeding due to inhibition of platelet aggregation
 - Discontinue use 14 days prior to dental or surgical procedures
 - Drug interactions with anticoagulant and antiplatelet agents
- ◆ All of the cautions and drug interactions associated with caffeine

Conclusions

- ◆ So...is green tea a brew of benefits?
- ◆ Mixed results from epidemiologic and clinical studies
 - Differing lifestyle factors
 - Inadequate methodology to define intake
- ◆ Fairly free of side effects, potential for a variety of benefits, healthy alternative
- ◆ Consider moderate daily consumption

True/False Test Questions

- ◆ The major polyphenolic compounds in green tea are called catechins.
- ◆ Green tea is reported to have anti-hypertensive, anti-inflammatory, anti-proliferative and lipid lowering effects.
- ◆ The Ohsaki study showed that green tea consumption is associated with reduced mortality due to cancer.

References

- ◆ Bohn P, Liu D. Green tea catechins and cardiovascular health: an update. *Curr Med Chem.* 2008;15(18):1816-20.
- ◆ Bostin K, Koppitt P, Fain F, et al. Green tea (Camellia sinensis) for the prevention of cancer. *Cochrane Database Syst Rev.* 2009 Jul 8;(3):CD002001.
- ◆ Bostman JL. Green tea and cancer in humans: a review of the literature. *Nutr Cancer.* 1998;31(1):151-9.
- ◆ Cabrera C, Anadol R, Gonzalez R. Beneficial effects of green tea—a review. *J Am Coll Nutr.* 2006 Apr;25(2):79-99.
- ◆ Cooper R, Moric DJ, Moric DM. Medicinal benefits of green tea: Part I. Review of noncancer health benefits. *J Altern Complement Med.* 2003 Jun;11(6):221-8.
- ◆ Cooper R, Moric DJ, Moric DM. Medicinal benefits of green tea: part II. review of anticancer properties. *J Altern Complement Med.* 2003 Aug;11(6):539-52.
- ◆ Dalloso MG, Dreyer C, Wolter D, Girardier L, et al. Efficacy of a green tea extract rich in catechin polyphenols and caffeine in increasing 24-h energy expenditure and fat oxidation in humans. *Am J Clin Nutr.* 1999;70(1):10-15.
- ◆ Dalloso MG, Seydoux J, Girardier L, Chantre P, Vandermander J. Green tea and thermogenesis: Interactions between catechin polyphenols, caffeine, and sympathetic activity. *Int J Obes Relat Metab Disord.* 2002;26(2):272-278.
- ◆ Fu J, Li G, Lambert JD, Yang CS. Inhibition of carcinogenesis by tea constituents. *Semin Cancer Biol.* 2007 Oct;17(5):325-302. Epub 2007 Jul 4.
- ◆ Arita N, Mukhtar H. Tea polyphenols for health promotion. *Life Sci.* 2007 Jul 26;81(7):519-33.
- ◆ Kuriyama S, Shimazu T, Ohmori K, et al. Green tea consumption and mortality due to cardiovascular disease, cancer, and all causes in Japanese: Ohsaki study. *JAMA.* 2006 Sep 13;296(10):1233-45.
- ◆ Maron DJ, Li GP, Cai NS, et al. Cholesterol-lowering effect of a flavanol-enriched green tea extract: a randomized controlled trial. *Arch Intern Med.* 2003 Jun 23;163(12):1448-53.
- ◆ Sarma DN, Barrett ML, Chavez ML, et al. Safety of green tea extracts: a systematic review by the US Pharmacopeia. *Drug Saf.* 2008;31(6):469-84.
- ◆ Sayama K, Liu S, Ziegen G, Ogumi I. Effects of green tea on growth, food utilization, and lipid metabolism in mice. *In Vivo.* 2003;17(3):181-184.
- ◆ Sheanonda SM, Vira JA. Effects of flavonoid-containing beverages and EGCG on endothelial function. *J Am Coll Nutr.* 2007 Aug;26(1):266S-572S.
- ◆ Sand V, Dreyer H, Sengel K, Lorenz M. Molecular targets of tea polyphenols in the cardiovascular system. *Cardiovasc Res.* 2007 Jun 15;73(2):348-58. Epub 2006 Sep 1.
- ◆ Yang CS, Mills KT, Meng X. Inhibition of carcinogenesis by tea. *Annu Rev Pharmacol Toxicol.* 2002;42:25-54.
- ◆ Yang SC, Lu FH, Wu BS, Wu CH, Chang CJ. The protective effect of habitual tea consumption on hypertension. *Arch Intern Med.* 2001 Jul 25;161(14):1534-40.