Tea Expert Newsletter

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Scientific update on green tea and weight management

Unilever

Scientific Update on Green Tea and Weight Management

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"From the editor"

Green tea is a natural product that comes from the plant *Camellia sinensis* var. *sinensis*. It is widely consumed across Asia and is growing in popularity in western countries. Green tea can be a great source of hydration, contributing to daily fluid intakes. In addition, green tea is generally drunk without milk and sugar which means it can easily be incorporated into a weight management programme. In previous newsletters we have reviewed the hydrating properties of tea, as well as the scientific findings associated with the use of sugars and sweeteners in some tea based beverage formats in the context of weight management. Over the past decade the potential benefits of green tea, particularly in relation to the unique polyphenols it contains, have been heavily researched. In this issue we build further upon the topic of weight management and present the latest evidence that supports the notion that adding green tea to a healthy lifestyle may provide added benefits in management of weight.

Contents

1. Introduction

Tea is the most widely consumed beverage in the world, second only to water. The different kinds of tea (green, black, oolong, etc) originate from the same plant, *Camellia sinensis*. The plant is a significant source of many polyphenolic compounds, in particular flavonoids known as *catechins*. The sensorial attributes of the different teas are related with the process by which they are produced. For instance, during the production of black tea, most of the catechins are enzymatically oxidised to produce complex polymers responsible for its characteristic flavour and darker colour. Green tea, in contrast, largely retains the original catechins because the fresh leaves are heat-treated shortly after harvest, and enzymatic oxidation is inhibited. Green tea is also consumed in formats other than the traditional tea. Green tea extracts as supplements are popularly consumed.[1] Also, extracts of green leaf tea are used in other beverage formats such as ready-to-drink teas.

Green tea has been a favourite topic of research for those interested in how dietary plant-derived polyphenols may improve human health. The scientific evidence compiled over the years - consisting of *in vitro*, animal and clinical work - has served to generate many hypotheses on potential health benefits of green tea consumption. It is only recently that a stronger picture of association between green tea consumption and certain health benefits in controlled clinical settings is starting to emerge.

In this newsletter we selected recently published papers (2012-2013) on green tea and areas relevant for weight management. Specifically, we discuss the latest scientific evidence on green tea and weight and fat loss; the potential of green tea to support exercise beyond its hydrating properties; the metabolic response to green tea consumption, and the evidence that supports an effect of green tea on fasting blood glucose.

2. GREEN TEA AND WEIGHT MANAGEMENT

2.1 GREEN TEA AND WEIGHT LOSS

Jurgens TM, Whelan AM, Killian L, Doucette S, Kirk S, Foy E.
Green tea for weight loss and weight maintenance in overweight or obese adults.
Cochrane Database Syst Rev. 2012

ABSTRACT

Preparations of green tea are used as aids in weight loss and weight maintenance. Catechins and caffeine, both contained in green tea, are each believed to have a role in increasing energy metabolism, which may lead to weight loss. A number of randomised controlled trials (RCTs) evaluating the role of green tea in weight loss have been published; however, the efficacy of green tea preparations in weight loss remains unclear.

Objective: *To assess the efficacy and safety of green tea preparations for weight loss and weight maintenance in overweight or obese adults.*

Search Methods: *We searched the following databases from inception to specified date as well as reference lists of relevant articles: The Cochrane Library (Issue 12, 2011), MEDLINE (December 2011), EMBASE (December 2011), CINAHL (January 2012), AMED (January 2012), Biological Abstracts (January 2012), IBIDS (August 2010), Obesity+ (January 2012), IPA (January 2012) and Web of Science (December 2011). Current Controlled Trials with links to other databases of ongoing trials were also searched.*

Selection Criteria: RCTs of at least 12 weeks' duration comparing green tea preparations to a control in overweight or obese adults.

Data Collection: *Three authors independently extracted data, assessed studies for risk of bias and quality, with differences resolved by consensus. Heterogeneity of included studies was assessed visually using forest plots and quantified using the I(2) statistic. We synthesised data using meta-analysis and descriptive analysis as appropriate; subgroup and sensitivity analyses were conducted. Adverse effects reported in studies were recorded.*

Main Results: *Due to the level of heterogeneity among studies, studies were divided into two groups; those conducted in Japan and those conducted outside Japan. Study length ranged between 12 and 13 weeks. Meta-analysis of six studies conducted outside Japan showed a mean difference (MD) in weight loss of -0.04 kg (95% CI -0.5 to 0.4; P = 0.88; I(2) = 18%; 532 participants). The eight studies conducted in Japan were not similar enough to allow pooling of results and MD in weight loss ranged from -0.2 kg to -3.5 kg (1030 participants) in favour of green tea preparations. Meta-analysis of studies measuring change in body mass index (BMI) conducted outside Japan showed a MD in BMI of -0.2 kg/m(2) (95% CI -0.5 to 0.1; P = 0.21; I(2) = 38%; 222 participants). Differences among the eight studies conducted in Japan did not allow pooling of results and showed a reduction in BMI ranging from no effect to -1.3 kg/m(2) (1030 participants), in favour of green tea preparations over control. Meta-analysis of five studies conducted outside Japan and measuring waist circumference reported a MD of -0.2 cm (95% CI -1.4 to 0.9; P = 0.70; I(2) = 58%; 404 participants). Differences among the eight studies conducted in Japan did not allow pooling of results and showed effects on waist circumference ranging from a gain of 1 cm to a loss of 3.3 cm (1030 participants). Meta-analysis for three weight loss studies, conducted outside Japan, with waist-to-hip ratio data (144 participants) yielded no significant change (MD 0; 95% CI -0.02 to 0.01). Analysis of two studies conducted to determine if green tea could help to maintain weight after a period of weight loss (184 participants) showed a change in weight loss of 0.6 to -1.6 kg, a change in BMI from 0.2 to -0.5 kg/m(2) and a change in waist circumference from 0.3 to -1.7 cm. In the eight studies that recorded adverse events, four reported adverse events that were mild to moderate, with the exception of two (green tea preparations group) that required hospitalisation (reported as not associated with the intervention). Nine studies reported on compliance/adherence, one study assessed attitude towards eating as part of the health-related quality of life outcome. No studies reported on patient satisfaction, morbidity or cost.*

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Authors' Conclusions: *Green tea preparations appear to induce a small, statistically non-significant weight loss in overweight or obese adults. Because the amount of weight loss is small, it is not likely to be clinically important. Green tea had no significant effect on the maintenance of weight loss. Of those studies recording information on adverse events, only two identified an adverse event requiring hospitalisation. The remaining adverse events were judged to be mild to moderate.*

SUMMARY

This meta-analysis included 18 randomized controlled trials (15 weight loss and 3 weight maintenance studies), with a duration of 12 weeks.[2] Nine of the 18 studies took place in Japan (all weight loss studies, 1 combined with physical activity) and four were conducted in the Netherlands (1 on weight loss and 3 on weight maintenance), while the rest took place in Australia (1), China (1), Taiwan (1), Thailand (1), and US (1) (all weight loss studies, 2 combined with physical activity). Several clinical trials included dose-response protocols (2 in Japan and 1 in China), but for the purpose of this analysis, the multiple intervention groups in each of these three studies were pooled within each study, creating one green tea group and one control group for each study (different doses from the same paper were pooled and treated as one). Therefore, only one observation per study was included in the overall analysis, and potential dose-effect responses were not analysed.

Of the 18 studies, 14 had sufficient data for weight loss analysis. The first observation derived from this meta-analysis revealed a significant heterogeneity among the studies. Studies conducted in Japan seem to 'differentiate' with respect to the rest of the evidence, which includes studies conducted in other Asian and Caucasian populations (with the same duration of intervention). This observation may not be so surprising, given the fact that they seem to be more consistent in protocols, namely in the dose, form and time of administration, and typically the same green tea composition is used. A more uniform outcome is expected when the conditions of intervention are tightly controlled and reproduced. Therefore, the authors decided to separate the analysis between Japanese vs. non-Japanese studies.

Inside Japan, the analysis showed an overall positive effect. Outside Japan, the studies showed higher variation in clinical design and composition of the green tea preparations used in the trials. Outside Japan, the meta-analysis of weight loss studies included 6 studies (3 in other Asian populations, 3 in Caucasian populations, 2 of which combined green tea with physical activity) and no effect was observed. Inconsistency in the product content may also account for the variation in results obtained. Also, the form of administration (drink vs. capsules/supplements or other) is also different and it is not clear whether it may have an impact in the final outcome (all the Japanese studies involved green tea as beverage and consistent green tea composition). To improve quality, future studies should provide a complete quantitative description of the chemical composition of the green tea preparations, establish a standard dose of green tea (with a standardized content of catechins and caffeine), and include additional outcomes such as health-related quality of life and adverse effects.

Overall, taking all the evidence together the conclusion of this meta-analysis was that the consumption of green tea preparations only led to small (non-statistically significant) effect on weight loss.

INTERPRETATION

In this meta-analysis, the authors involved in the prestigious Cochrane collaboration have addressed the question on whether consumption of green tea has a significant effect on weight loss and weight maintenance, by looking at the available relevant evidence. The matter is pertinent, considering the potential impact of a simple dietary intervention in the context of the present obesity epidemic and public health. As the authors state, green tea has a long history of many uses, one of which is helping overweight people to lose weight and/or maintain weight loss. Weight loss has been included (either as primary or secondary outcome) in most of the human study interventions testing green tea, irrespectively of the dose or duration of the study. Typically, green tea preparations for weight loss are extracts of green tea that contain a higher concentration of ingredients (catechins and/or caffeine) than the regular green tea beverage prepared from a teabag.

This paper is not the first meta-analysis that has systematically looked at the effect of green tea on weight loss and weight maintenance. Two fairly recent systematic reviews and meta-analysis have also been published.[3,4]

2.1

Hursel *et al*'s review (2009) included a meta-analysis of 11 randomized clinical trials on green tea in weight loss, using only PUBMED as database, collecting information until 2008. They included Asian and non-Asian studies in the overall analysis, and considered more than one observation per study when a dose-response was conducted (resulting in 11 and 4 observations in Asian and non-Asian populations, respectively). Their overall conclusion was that green tea had a small but significant effect on weight loss and weight maintenance. Hursel *et al* noted that all the Asian studies had a low habitual caffeine intake and nearly all Caucasian studies had a high habitual caffeine intake. It is not clear whether habitual caffeine intake play a role in the efficacy of green tea.

Phung *et al* (2010) conducted their review using a more comprehensive search strategy, using MEDLINE, EMBASE, CENTRAL, and the Natural Medicines Comprehensive Database, leading to the inclusion of 15 randomized clinical trials. Phung *et al* only included studies on weight loss (not on weight maintenance) and conducted an analysis on different anthropometric measures. However, the authors did not set the length of intervention as inclusion criteria, and included studies ranging from 3-24 week interventions. To resolve heterogeneity this review looked at the evidence considering whether the green tea effect was compared to either a caffeinated or non-caffeinated control. The strongest effects were seen in studies in which the effect of green tea (catechins plus caffeine) was compared to a caffeinated control. They concluded that green tea catechins with caffeine may have a small but positive effect on reduction in weight loss, BMI and waist circumference.

The body of evidence on green tea and weight loss available in the public domain has not changed much since the reviews conducted by Hursel *et al* and Phung *et al*. Every meta-analysis has different limitations, and typically raises different questions: whether the database was exhaustive enough, whether the inclusion/exclusion criteria were appropriate, whether literature in non-English language should have been included, whether the doses and composition of the green tea material should have been considered.

So, what is the contribution of this Cochrane review to the existing evidence? With a different approach, this Cochrane review identified the relevant articles using an exhaustive search strategy that is not limited by language and on a clearly defined study population, with an also well-defined duration of the interventions (12 weeks). This review is strict in the analysis of potential bias. The authors made also an attempt to relate one catechin (EGCG) with the effect. It is worth mentioning that this review includes studies that combined green tea interventions with exercise or exercise program (Takashima *et al*, in Japan, and Maki *et al*, and Hill *et al*, in US and Australia, respectively).[5-7] Exercise has already a significant effect on weight loss in overweight populations, and a synergy between green tea and exercise cannot be ruled out. The question is whether articles including exercise should have been excluded from the overall analysis, although their exclusion would probably not have affected the overall outcome.

One interesting point that this study makes clear is that the evidence seems to be stronger for Japanese populations. As analysed in this publication, the risk of bias in the selected Japanese studies is not different from the studies conducted elsewhere (only one study, by Tsuchida *et al*, was removed due to high risk of bias).[8] The question that remains unanswered is whether there is indeed a stronger effect in Japanese populations (due to, for instance, a low habitual dietary intake of caffeine, other diet background, or just ethnicity) or the observation has something to do with a more consistent clinical design or execution. Studies conducted in China (the cited Wang *et al*, and a more recent one, not included in this meta-analysis, Zhang *et al*)[9,10] appear to be very well in agreement with the Japanese studies. In contrast, little evidence has been compiled from Caucasian populations using a similar protocol for a valid comparison.

Finally, the outcome of this meta-analysis is in line with previous reviews on the same topic. Although the effect on weight loss is small - and probably time and dose dependent-, it may still be relevant if the loss is in body (intra-abdominal) fat. Paralleling the implications of small reductions in blood pressure for primary prevention (that is, a reduction as little as 2 mmHg could have a great public health impact),[11] the small reductions by green tea consumption in weight loss may still have a positive impact at a population level in the longer term. What dose and for how long are questions that remain to be answered.

2.2

2.2 GREEN TEA AND BODY COMPOSITION

Zhang Y, Yu Y, Li X, Meguro S, Hayashi S, Katashima M, Yasumasu T, Wang J, Li K. Effects of catechin-enriched green tea beverage on visceral fat loss in adults with a high proportion of visceral fat: A double-blind, placebo-controlled, randomized trial. Journal of Functional Foods, 2012; 4(1): 315-322

ABSTRACT

The effects of catechin-enriched green tea on Chinese adults with a high proportion of abdominal visceral fat were evaluated. Subjects (118) were randomly assigned to consume daily a beverage containing 609.3 mg catechins and 68.7 mg caffeine or a control beverage for 12 weeks. Abdominal fat area, body weight and composition were measured at week 0, week 8, and week 12. One hundred and four subjects completed the trial. Average visceral fat area, body weight, and body fat were reduced significantly by catechin-enriched green tea treatment but these effects were not seen in the control group with per-protocol sets analysis. The decrease at week 12 in the visceral fat area in the catechin group was greater than that in the control group (P = 0.04). Thus, consumption of the catechin-enriched green tea beverage for 12 weeks induced visceral fat loss in Chinese adults with a high proportion of abdominal visceral fat.

SUMMARY

The aim of this study by Zhang *et al* was to evaluate the effect of green tea on body composition, especially on visceral fat, without any additional diet or exercise intervention.[10] In this randomized double blind controlled trial, subjects were recruited from the Beijing area and selected not only on the basis of their BMI (which classified them as 'obese') but also by accumulation of fat in the abdominal area (measured by waist circumference, inclusion criteria of ≥80 cm for women, ≥90 cm for men). After passing the inclusion/exclusion criteria, 118 volunteers joined the trial. Anthropometric measures (body height, weight, waist and hip circumference, and fat mass) were measured at week 0, 8, and 12. Abdominal computed tomography scans (CT scans) were performed to evaluate abdominal fat at week 0 and 12 (primary outcome of the study).

In this study, the control drink had a composition similar to the regular green tea sold in China (86.2 mg catechins and 40.4 mg caffeine), meanwhile the test drink was a catechin-enriched green tea beverage, with a slightly higher caffeine content (609 mg catechins and 68.7 mg caffeine). The treatment was administered as a beverage (350 ml, containing catechins and caffeine) and the volunteers were instructed to drink it after lunch time, within 30 min, daily for 12 weeks.

To monitor for potential confounding factors associated to lifestyle, in particular habitual diet and physical activity, subjects were asked to record their dietary intake and physical activity score, physical condition and the eventual use of any medicine. Compliance and blindness was also tested and evaluated at the end of the study.

A number of 104 subjects completed the trial, 65 females and 39 males (53 and 51 subjects in the control and test group, respectively). Compliance was calculated as higher than 90% and similar in both groups. Body weight, BMI, and body fat mass all decreased significantly at week 12 compared to baseline in the test group. At week 12 there was a significant difference between control and test groups in visceral fat area. The green tea group showed a reduction of 6% in visceral fat after 12 weeks, 10 times greater than the control.

INTERPRETATION

It has been long hypothesized that regular consumption of green tea, or green tea extracts, may beneficially influence body composition (most remarkably, reduce intra-abdominal visceral fat). Consistent evidence for beneficial effects of catechin-enriched green tea consumption on body composition has been collected primarily from clinical trials conducted in Japan.[8,12-14] The effect appears to be time and dose dependent and the trials generally showed statistically significant and physiologically relevant reductions in visceral fat after 12 weeks of green tea consumption, in doses around 500 - 600mg catechins, with caffeine. All these Japanese studies used a consistent green tea composition. Importantly, the participants in these studies (which included overweight/obese males and females) were instructed to follow their habitual patterns of food intake and exercise,

so the effects were measured against their dietary background and usual levels of physical activity. The experimental design and the daily doses, frequencies of intake, and beverage forms of catechins consumed have typically reflected a realistic consumer situation.

The contribution of this recent paper adds to -and strengthens- the evidence in Chinese populations. A previous study conducted in Shanghai reported the effect of green tea on body composition after a 12-week intervention.[9] Participants (205 subjects) received one of four conditions (as drinks): a low-catechin low-caffeine control (30 mg catechins), 2 conditions providing around 460 mg catechins (which differed in the way the dose was administered during the day), and a condition providing 886 mg catechins. All catechin-enriched conditions showed reductions greater than the control. Intra-abdominal fat was significantly reduced in the highest catechin-containing beverage (886 mg), compared to control (reduction of 7% intra-abdominal fat). The conditions using 460 mg catechin showed reductions of 4.6-5.0%.

How does the paper by Zhang *et al* compared to previous evidence? The authors also reported a significant reduction of visceral fat (compared to control) after a 12 week intervention. The reduction can be calculated as 6% for a dose of 609 mg catechins, which is well in agreement with the paper by Wang *et al*, if the dose of catechins is considered. This observation strengthens the idea that there is not only a time- but also a dose-dependence in the effect of green tea catechins. This study was not an exercise intervention but recorded the daily physical activity of the participants. The authors found no correlation between the changes in body composition with changes in physical activity in this study, concluding that the changes in visceral fat were due to green tea consumption and not physical activity.

The effect of green tea on visceral fat appears to correlate with the dose of catechin ingested. It is not clear what role caffeine plays in this effect, if it is needed at all, or whether there is an optimal caffeine-to-catechin ratio. Zhang *et al* used a dose of 68 mg caffeine in the test group (vs. 40 mg in control) in contrast to Wang *et al*, who used 100-200 mg in their test groups (vs. 10 mg in control group). Caffeine is very well known for its acute effects on energy metabolism, increasing energy expenditure, and thus it may synergize with the effect of the catechins in the long term. As all clinical trials evaluating body composition (visceral fat) have tested green tea containing both catechins and caffeine, a catechin-caffeine interaction cannot be ruled out.

2.3

2.3 GREEN TEA AND EXERCISE

Randell RK, Hodgson AB, Lotito SB, Jacobs DM, Boon N, Mela DJ, Jeukendrup AE No Effect of 1 or 7 d of Green Tea Extract Ingestion on Fat Oxidation during Exercise. Med Sci Sports Exerc. 2013;45(5):883-91.

ABSTRACT

Purpose: *The aim of this study was to investigate the effects of 1 and 7 d of green tea extract (GTE) ingestion on whole body fat oxidation during moderate-intensity exercise.*

Methods: *Thirty-one men completed two exercise trials (60-min cycle, 50% Wmax). After the baseline trial (day 0), subjects were randomly assigned to one of three conditions involving a week supplementation of the following: 1) 7 d of placebo, 2) 6 d of placebo followed by 1 d of GTE (GTE1), and 3) 7 d of GTE ingestion (GTE7). The morning after the supplementation week, subjects consumed an additional supplement and completed a second exercise trial (day 8). V˙O2 and V˙CO2 measurements were taken during exercise to calculate whole body fat oxidation rates. Blood samples, for analysis of plasma fatty acids (FA), glycerol, and epigallocatechin gallate, were collected at rest and during exercise.*

Results: *On day 8, the plasma kinetics and maximal plasma concentrations of epigallocatechin gallate were similar in the GTE1 and GTE7 group (206 ± 28 and 216 ± 25 ng·mL, respectively). One day of GTE ingestion did not affect markers of lipolysis during the exercise bout. Seven days of GTE ingestion significantly increased plasma glycerol during exercise (P = 0.045) and plasma FA during exercise (P = 0.020) as well as at rest (P = 0.046). However, fat oxidation did not change in any of the groups.*

Conclusions: *There was no effect of 1 d of GTE ingestion on markers of lipolysis or fat oxidation during exercise. Seven days of GTE ingestion increased lipolysis, indicated by increased plasma FA and glycerol concentrations, but did not result in significant changes in fat oxidation.*

SUMMARY

Randell *et al* investigated the effect of green tea on fat oxidation during moderate exercise.[15] This study was conducted in healthy young males (normal range of BMI) who regularly train 3-5 times a week, 30-90 min/session (fit individuals and athletes).

The study followed a parallel-design, so subjects were allocated to only one of the 3 groups. To ensure that the physical effort involved was similar to all participants, the exercise test conditions were set up for each one of the subjects. One week previous to the start of the study, the Wmax for each individual was measured (workload at which the subject reaches exhaustion) and the 50% Wmax was calculated and subsequently used in the exercise tests. There were 2 exercise test days (day 0 and day 8) and participants received a standardised diet 24-h previous each exercise test, to control for energy intake.

The study evaluated the effect of green tea after 1 or 7 days of daily consumption. The green tea was administered as 2 drinks per day. Each drink provided 559mg catechins and 120mg caffeine. The participants also received one drink 2 h before the exercise challenge, to ensure that the peak of catechins in plasma coincided with the start of the exercise test. Acute EGCG bioavailability was virtually identical regardless whether the subjects were pre-exposed to the green tea preparation for 1 or 7 days. No plasma catechins were detected in the placebo group.

This study showed no effect of green tea supplementation on fat oxidation rates during exercise compared to the effect of exercise alone, after 1 or 7 days of daily ingestion. However, a significant increase in plasma glycerol and free fatty acids was observed after 7 days (but not after 1 day of intake), which may be indicative of a green tea-driven effect on lipolysis. The physiological relevance of this finding needs to be elucidated.

INTERPRETATION

For the correct interpretation of this paper by Randell *et al* it is necessary to discuss the context in which this research was conducted. The hypothesis was that green tea has an effect on fat oxidation *during exercise*, compared to exercise alone, and therefore, green tea has the potential to improve endurance or performance. The intended population for this effect is *athletes*, and the trial was therefore conducted in young subjects that regularly train 3-5 times/week, for 30-90 min each session.

2.3

The research hypothesis by Randell *et al* is a valid one. Green tea is one of the most widely used dietary interventions in the sports community, based on the belief of its 'fat burning' properties (reviewed by Jeukendrup and Randell).[1] Considering that green tea appears to have an effect on fat oxidation under resting conditions *and* in healthy (not overweight) people, it is reasonable to speculate on the potential of a combination green tea and exercise.[16-18] Without any doubt, any intervention aiming to increase the capacity of skeletal muscle to oxidise fats during exercise – and thus, spare the use of glycogen stores and delay the onset of fatigue - is clearly advantageous for athletes.

Only a few papers have studied the combined effect of a green tea intervention with exercise in healthy athletes. The design and doses used in the different studies largely vary. Venables *et al* found an increase in fat oxidation during exercise after the intake of 810 mg catechins for just one day.[19] Eichenberger *et al* found no effect of green tea on respiratory exchange ratio (RER) in endurance-trained men challenged with a 2-h cycling exercise.[20] Despite being a 3-week intervention, it can be argued that the dose used by Eichenberger *et al* was too low (159 mg catechins/day). In contrast, Ota *et al* and Ichinose *et al* found a positive effect of 570 mg green tea catechins (combined with exercise) on fat oxidation (at 8 weeks) and RER (at 10 weeks), respectively.[21,22]

How does Randell *et al* compare to the existing evidence? This paper found no effect of green tea on fat oxidation during exercise, using a total dose of 1119 mg catechins (559 mg twice daily, with caffeine) in a 7-day intervention. Although there were two exercise test days in this study (day 0 and day 8), exercise was not restricted between test days, so the participants went on with their individual exercise routines, together with the green tea intervention. The participants had a relatively high level of training at the start of the study. It can be speculated that 7 days of additional training in combination with green tea may not be enough to make a significant difference, and longer interventions are needed. In contrast, 7-day intervention was enough to show increased lipolysis (measured as plasma glycerol and free fatty acids). It is very well known that caffeine increases lipolysis, and caffeine in the preparation may have accounted for this effect. Interestingly, the increase in free fatty acids was not enough to drive the increase in fat oxidation rates, indicating that availability of fuel was not a limiting factor for fat oxidation rates in these subjects. Also, the level of fitness and/or fat oxidation rates of the participants at start are aspects that need to be considered in the design of future research. The efficacy of green tea may be greater in those with lower fat oxidation rates in which small changes may make a significant difference.

Finally, it is important to highlight that the findings of this paper apply to this particular population (athletes), where the purpose of increasing fat oxidation is to enhance endurance and/or performance. When looking at exercise for the purpose of weight and fat loss, the outcome and efficacy of green tea may be different, because the population is also different. Exercise is an effective means to increase fat oxidation with the aim of burning fat in overweight/obese people, considering that during moderate intensity exercise, the metabolism is elevated up to 10 fold compared to resting conditions. Some evidence supports the potential of green tea combined with an exercise-induced weight loss program. For instance, in a Japanese study looking at catechin-enriched green tea intervention and visceral fat loss Kataoka *et al* showed that those who engaged in regular light physical activity benefited with greater fat loss when combined with the green tea beverage.[23] In a pilot study Takashima *et al* reported an increase in fat oxidation during exercise in overweight subjects after a 3-month combined programme of exercise and catechin-enriched green tea consumption.[5] Similarly, in the US, Maki *et al* showed that the intake of a catechin-enriched beverage together with a regular exercise regime led to a greater body weight and fat loss than exercise alone.[6] Together, these studies support the hypothesis that catechin-enriched green tea may potentiate the effects of physical activity on fat loss, probably due to increase fat oxidation rates during the exercise, in a susceptible population (overweight/obese). This aspect of green tea and exercise for weight/fat loss was not the objective of Randell *et al* but it is a promising area for potential health benefits of green tea.

2.4

2.4 METABOLIC RESPONSE TO GREEN TEA

Hodgson AB, Randell RK, Boon N, Garczarek U, Mela DJ, Jeukendrup AE, Jacobs DM. Metabolic response to green tea extract during rest and moderate-intensity exercise. J Nutr Biochem. 2013;24(1):325-34.

ABSTRACT

Background: *Green tea catechins have been hypothesized to increase energy expenditure and fat oxidation by inhibiting catechol-O-methyltransferase (COMT) and thus promoting more sustained adrenergic stimulation. Metabolomics may help to clarify the mechanisms underlying their putative physiological effects.*

Objective: *The study investigated the effects of 7-day ingestion of green tea extract (GTE) on the plasma metabolite profile at rest and during exercise.*

Methods: *In a placebo-controlled, double-blind, randomized, parallel study, 27 healthy physically active males consumed either GTE (n=13, 1200 mg catechins, 240 mg caffeine/day) or placebo (n=14, PLA) drinks for 7 days. After consuming a final drink (day 8), they rested for 2 h and then completed 60 min of moderate-intensity cycling exercise (56% ± 4% VO(2)max). Blood samples were collected before and during exercise. Plasma was analyzed using untargeted four-phase metabolite profiling and targeted profiling of catecholamines.*

Results: *Using the metabolomic approach, we observed that GTE did not enhance adrenergic stimulation (adrenaline and noradrenaline) during rest or exercise. At rest, GTE led to changes in metabolite concentrations related to fat metabolism (3-β-hydroxybutyrate), lipolysis (glycerol) and tricarboxylic acid cycle (TCA) cycle intermediates (citrate) when compared to PLA. GTE during exercise caused reductions in 3-β-hydroxybutyrate concentrations as well as increases in pyruvate, lactate and alanine concentrations when compared to PLA.*

Conclusions: *GTE supplementation resulted in marked metabolic differences during rest and exercise. Yet these metabolic differences were not related to the adrenergic system, which questions the in vivo relevance of the COMT inhibition mechanism of action for GTE.*

SUMMARY

In this placebo-controlled, double-blind, randomized parallel study, Hodgson *et al* investigated the metabolic response (at rest and during moderate exercise) to 7-day daily supplementation with a catechin-enriched green tea beverage.[24] The subjects enrolled in this intervention were young males, who exercised 3-5 times a week. Subjects received a total dose of 1119 mg green tea catechins, 240mg caffeine per day, administered as drinks (2 cans daily). Subjects were instructed to consume 2 cans every day, 1 hour before breakfast and 1 hour before dinner.

The plasma metabolic profile was measured before (day 0) and after 7-day supplementation (day 8), before (time 0) and at regular intervals during a 60-min exercise test (time 120-180 min). At day 8, subjects received 1 can (559 mg catechins, 120 mg caffeine) 2 hours before starting the exercise. The exercise consisted of a moderate cycling test for 60 min. Therefore, this study design included the 7-day ('chronic') supplementation as well as the single bolus ('acute') intake the day of the exercise.

Exercise induces massive changes in metabolism, when compared to resting conditions. It is known that exercise induces significant increases in markers of glycolysis (lactate and pyruvate), indicators of lipolysis (glycerol), tricarboxylic acid cycle (TCA) intermediates, indicators of adenine catabolism (uric acid), indicators of hormonal activity (cortisol), catecholamines, certain fatty acids, phospholipids, and amino acids, amongst others.

When looking at the effect of green tea (vs. placebo) on exercise, the metabolite changes induced by the green tea intervention were weak. Nevertheless, some significant metabolite changes by the green tea intervention were seen (malate, lactate, pyruvate, certain cholesteryl esters, and alanine, and a reduction in 3-hydroxybutyrate), but no effect was seen on exercise-induced catecholamines.

The metabolic response to green tea was also evaluated under resting conditions, after the 7-day intervention (day 8 vs. day 0, at time 0). Caffeine (present in the

supplement) and hippuric acid, homovanillic acid, and 3,4-dihydroxyphenylacetate (known gut microflora metabolites of catechins) were elevated post-supplementation. Green tea intervention also induced decreases in triacylglycerides, certain fatty acids and amino-acids, and increases in certain cholesteryl esters, 3-hydroxybutyrate, citrate, lactaldehyde and glycerol.

INTERPRETATION

This paper by Hodgson *et al* provides insights on the metabolic changes induced by a 7-day intervention with a catechin-enriched green tea beverage, during exercise and under resting conditions, in healthy young males. Using a metabolomic approach, the authors targeted metabolites related with energy metabolism (carbohydrate and lipid) and metabolites related with adrenergic stimulation (catecholamines).

During exercise, no effect of green tea on fat oxidation-related metabolites was detected, which is in full agreement with the physiological findings of this study.[24] To complement the physiology, this paper generates plausible hypothesis regarding factors that might mitigate any effects of GT on fat oxidation during exercise. For instance, an increase in lactate was detected, compared to exercise alone; lactate is known to limit lipolysis and fat oxidation during exercise.

The authors detected an increase in fat oxidation-related metabolites under resting conditions. They used green tea containing caffeine. Is the effect of green tea on fat oxidation at rest due to catechins, caffeine or the combination of both? This question remains to be answered. It has been long hypothesized that green tea ingestion may affect thermogenesis and fat metabolism/oxidation. Dulloo *et al*, clearly showed a positive effect of a mix of caffeine and catechins on both energy expenditure and fat oxidation over the effect of caffeine alone.[16] Berube-Parent *et al* also reported increases in energy expenditure for mixtures of caffeine (600 mg) and catechins (270-1200 mg) but fat oxidation was only slightly increased at low or high doses of catechins, not significantly different from a caffeinated control.[25] Other reports (such as those by Rumpler *et al* and Rudelle *et al*) found increases in energy expenditure of caffeinated mixtures of green tea or green tea catechins, relative to decaffeinated controls, but no additional effect on fat oxidation was seen.[17,18] Gregersen *et al* only found small (but not statistically significant) increases in energy expenditure (1.4-2.3%) by mixtures of caffeine alone (150mg) and with EGCG (645mg), EGC (684mg), or catechins (total 494mg), in comparison with decaffeinated control.[26] It is known that caffeine increases energy expenditure at rest. The interpretation of the totality of the evidence has been difficult due to the different study designs, the variation in caffeine and catechin dosages, and whether caffeinated-controlled placebo or non-caffeinated beverages were used for comparison. The dietary background of caffeine may also be a factor that affects the results. A more recent meta-analysis by Hursel *et al* - which included reports on effects of green tea but also studies on caffeine alone- found a positive overall effect of combinations of caffeine and green tea catechins on fat oxidation.[27]

One of the most important contributions of this paper is that, despite detecting an increase in markers of fat oxidation and lipolysis under resting conditions, these effects do not appear to be mediated by catecholamines, challenging the hypothesis of catechol-O-methyltransferase (COMT) inhibition by green tea catechins. It has been suggested that green tea extract ingestion may shift fuel utilization, from carbohydrates to fat oxidation, at rest. Dulloo *et al* suggested that the effect may be mediated by catecholamines.[16] It has been long speculated that EGCG may inhibit COMT, an enzyme that degrades catecholamines such as noradrenaline, and thus, may enhance lipid catabolism by prolonging and augmenting sympathetic stimulation. This would result in more available circulating free fatty acids for potential oxidation. This paper however, indicates that green tea may increase fat oxidation through a mechanism not related to catecholamines.

In summary, this paper shows that green tea has differential metabolic effects under resting vs. exercise conditions, using a metabolomics approach. This work adds to the evidence that green tea affects fat oxidation and lipolysis under resting conditions. The metabolomics approach can be potentially more sensitive in capturing early changes at a stage at which physiological changes are not evident yet (by standard lab techniques). In future work it will be interesting to correlate the observed changes in metabolomics (glycerol, 3-hydroxybutyrate) with changes in physiological measures of fat oxidation (not measured in this paper). It will be also interesting to elucidate dose- and time-responses for the effects of green tea, whether the observations reported in this paper are due to the catechins or caffeine (or both), as well as the mechanism involved.

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2.5 GREEN TEA AND GLYCEMIC CONTROL

Zheng XX, Xu YL, Li SH, Hui R, Wu YJ, Huang XH.
Effects of green tea catechins with or without caffeine on glycemic control in adults: a meta-analysis of randomized controlled trials. Am J Clin Nutr. 2013;97(4):750-62.

ABSTRACT

Background: *The effect of green tea catechins (GTCs) with or without caffeine on glycemic control is controversial.*

Objective: *We aimed to identify and quantify the effects of GTCs or GTC-caffeine mixtures on glucose metabolism in adults.*

Design: *A comprehensive literature search was conducted to identify relevant trials of GTCs with or without caffeine on markers of glycemic control [fasting blood glucose (FBG), fasting blood insulin (FBI), glycated hemoglobin (Hb A1c), and homeostatic model assessment of insulin resistance (HOMA-IR)]. Weighted mean differences were calculated for net changes by using fixed-effects models. Prespecified subgroup analyses were performed to explore the influence of covariates on net changes in FBG and FBI concentrations.*

Results: *Twenty-two eligible randomized controlled trials with 1584 subjects were identified. Pooled analyses showed that FBG (-1.48 mg/dL; 95% CI: -2.57, -0.40 mg/dL) decreased significantly with GTCs with or without caffeine, whereas FBI (0.04 μU/mL; 95% CI: -0.36, 0.45 μU/mL), Hb A1c (-0.04%; 95% CI: -0.15, 0.08%), and HOMA-IR (-0.05; 95% CI: -0.37, 0.26) did not. Subgroup analyses indicated that the glucose-lowering effect was apparent when the duration of follow-up was over a median of 12 wk. Overall, no significant heterogeneity was detected for FBG, FBI, Hb A1c, or HOMA-IR.*

Conclusions: The meta-analysis showed that the administration of GTCs with or without caffeine resulted in a significant reduction in FBG. The limited data available on GTCs did not support a positive effect on FBI, Hb A1c, or HOMA-IR. Thus, more large and well-designed trials are needed in the future. This trial was registered at http://www.crd.york.ac.uk/prospero as CRD42012002139.

SUMMARY

In this meta-analysis Zheng *et al* included 22 randomized controlled studies which looked at the effect of green tea on fasting blood glucose and insulin, and insulin resistance.[28] The compiled studies included different doses of green tea, mostly covering regular conditions of use (260-661mg green tea catechins/day, equivalent to 3-6 cups) but also including studies with high doses (800+mg catechins/day). Length of intervention ranged from 3 to 24 weeks (< 1 to 6 months), with most of the studies conducted for 8 to 12 weeks.

Out of the 22 studies, 25 observations could be used to evaluate the effect on fasting blood glucose, as some of the studies provided information for consumers with high and low habitual caffeine intake. The available evidence for the effect of green tea on glycated haemoglobin and insulin sensitivity evaluation is much more limited (6 studies, 6-7 observations). The authors found that the consumption of green tea catechins with or without caffeine significantly reduced fasting blood glucose concentrations, but did not affect glycated haemoglobin and HOMA-IR.

INTERPRETATION

The meta-analysis by Zheng *et al* shows a reduction in fasting blood glucose after consumption of green tea. How are these findings relevant in the context of weight management? It is important to highlight that the inhibition of glucose absorption is not a direct therapeutic target of choice in weight management, due to its association with the expected (unpleasant) gastrointestinal side-effects (this is one of the side effects of the clinical use of acarbose, a well known inhibitor of amylase used in diabetes). In other words, in order to have a significant direct impact on weight loss, the inhibition of glucose absorption should be too high to induce a significant energy loss (negative energy balance), and at this level of inhibition the side effects would be too unpleasant to justify it as a therapeutic target.

However, it is known that a reduced ability to handle postprandial glucose is a major, early metabolic risk related to obesity. If a safe dietary intervention (such as consumption of green tea) had the potential to *modulate* postprandial glycaemia (and improve glycemic control), such dietary intervention would have –in the long term- a

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significant beneficial impact in reducing the risk of metabolic syndrome and obesity. It is clear then that it is not about the *inhibition* of carbohydrate absorption to induce a net negative energy balance, but the *modulation* of postprandial glycaemia that in the long term may be associated with lower metabolic risks that lead to obesity. In this context, the findings by Zheng *et al* become highly relevant for weight management, as their results suggest that the consumption of green tea may lead to better glycemic control.

The compiled literature includes studies conducted in Asian and Caucasian populations, using different doses of green tea catechins, with and without caffeine, for different periods of time. The authors conclude that time of exposure (length of intervention) was a critical (significant) variable for the effect of green tea, whilst dosage, presence of caffeine in the green tea preparation, and habitual caffeine intake were not (statistically) significant effect modifiers. However, based on the available evidence, the effect of green tea seems to be greater in trials using green tea preparations containing caffeine, in subjects with a low habitual caffeine intake. As suggested for other effects of green tea, it is possible that the mix of catechins and caffeine act somehow synergistically, and both are necessary for the effect. Interestingly, for the effect on fasting blood glucose, ethnicity does not seem to play a role, as the effect was clearly similar in Caucasian and Asian populations.

In terms of plausible mechanism of action, it has been long hypothesized that green tea catechins can (potentially) interact with carbohydrate-related enzymes (such as amylase or α-glycosidase), largely based on *in vitro* observations (for a recent paper, see Yilmazer-Musa *et al*).[29] In this context, it can be speculated that by interacting with the carbohydrate digestive enzymes, for instance, green tea may slow the postprandial digestion and absorption of carbohydrates, and this may result in better glycemic control and a lower fasting glucose in the long term. Although this hypothesis, direct postprandial modulation by green tea catechins is valid, it definitely needs further *in vivo* testing, as the studies conducted so far have led to inconsistent results (see Park *et al*, Josic *et al*).[30,31]

In summary, the key message of this paper is that consumption of green tea has a small but significant effect on fasting blood glucose, and this may positively contribute towards an overall healthful profile in the long term.

3. CONCLUDING REMARKS

FROM THIS OVERVIEW OF THE RECENT SCIENCE, SEVERAL KEY MESSAGES EMERGE:

- Catechin enriched green tea has a small effect on weight loss in overweight/obese population when consumed for 12 weeks. The effect seems to be greater in Asian (Japanese, Chinese) populations than in Western populations. Recent evidence strengthens the effect on a Chinese population, particularly on reduction of visceral fat, while the evidence in Caucasians is still scarce. Green tea may be more effective in combination with exercise, in reducing visceral fat.

- Despite being widely used by the sport community, there is no new evidence to support an effect of green tea during exercise in athletes. The value of green tea to help optimize 'performance' is still uncertain and not consistently supported.

- Green tea appears to have an effect on fat oxidation at rest in healthy individuals, measured by changes in the metabolite profile (metabolomics). This is in agreement with existing evidence showing enhanced fat oxidation in resting conditions, measured in metabolic chambers. Considering that small effects may become physiologically meaningful if sustained over time, metabolomics may represent a useful tool to capture early changes in energy metabolism before the physiological measures are able to detect them.

- Consumption of green tea with or without caffeine resulted in a significant reduction of fasting blood glucose concentrations. Small reductions may still have a great public health impact. Given the association between impaired glucose handling and risk of obesity, these observations add to the positive impact of green tea consumption in the context of weight management.

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6. NOTES

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