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THE ROLE OF SELECTED BIOACTIVE COMPOUNDS IN TEAS, SPICES, COCOA AND COFFEE IN BODY WEIGHT CONTROL

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Abstract: The prevalence of obesity and its associated complications, in the form of metabolic disorders, are a major public health problem. Taking into consideration that obesity is a risk factor for chronic diseases such as type 2 diabetes, cardiovascular disease and cancer, which are an increasing public health concern, the search and use of dietary agents for the prevention and management of obesity would be of tremendous benefit. Recently, natural bioactive phytochemicals present in foods have been found to provide health benefits and have effects on the prevention of several chronic non-communicable diseases including obesity. Naturally-occurring bioactive compounds present in teas, spices, cocoa and coffee, such as catechins, capsaicinoids, capsinoids, ginerols, and methylxanthines have been shown to modulate physiological and molecular pathways that are involved in energy metabolism, adiposity, and obesity. These compounds play an important role in weight control by decreasing appetite, increasing fat oxidation, augmenting thermogenesis, elevating energy expenditure and diminishing substrate absorption. The main objective of the present review is to present the impact of bioactive compounds found in teas, spices, cocoa and coffee on body weight control with the provision of mechanisms of actions.

Key words: Catechins, capsaicinoids, gingerols, satiety, appetite, energy expenditure, weight control

Introduction

Obesity, defined as an excess of adipose tissue when body mass index is >30 kg/m^2, is due to an imbalance between energy intake and energy expenditure. Obesity is a major health problem in the industrialized world, and it has reached epidemic proportions globally. The World Health Organization estimates that worldwide, obesity has more than doubled since 1980. In 2014, more than 1.9 billion adults, 18 years and older, were overweight. Of these, over 600 million were obese. 39% of adults aged 18 years and over were overweight in 2014, and 13% were obese. Overall, about 13% of the world's adult populations (11% of men and 15% of women) were obese in 2014. Most of the world's populations live in countries where being overweight and obese kill more people than being underweight. 42 million children under the age of 5 were overweight or obese in 2013 [1,2]. Moreover, its prevalence is likely to increase as a result of changes in lifestyle, decreased physical activity, and socioeconomic development, among others.

In addition, obesity is a complex multi-factorial and chronic disease that is considered to be a risk factor for the genesis or development of various diseases including hypertension, type 2 diabetes, coronary heart disease, cancer, respiratory complications and osteoarthritis. Despite the current intensive efforts to reduce obesity by diet, exercise, education, drug therapies and surgery, an effective long-term solution to this problem has yet to be provided.

Obesity, once developed, is difficult to reverse [3]. This is not only caused by biological resistance to weight loss in the form of a decrease in energy expenditure [4] and an increase in appetite, but also because the large behavior changes needed to sustain weight loss [5] are difficult for most people to sustain in what is termed a toxic environment, that is, where food is abundant and where little physical activity is required in daily living [6].

Excess fat mass develops over time from a very small positive energy imbalance. In general, the average weight gain per year is small, approximately 0.5 kg across all race, economic, and sex groups [7,8]. Studies have estimated that by affecting energy balance by approximately 100 calories per day through some combination of reductions in energy intake and increases in physical activity weight gain could be prevented in most of the population [9]. Others have verified that the degree of positive energy balance that causes weight gain in other populations is small [7]. Thus, small changes that reduce the small positive energy balance in the population should be more feasible to sustain over time and should be sufficient to prevent further weight gain.

There are many dietary, and to a lesser extent, pharmacological strategies which have been shown to affect energy balance in a manner that results in successful weight reduction [10]. Such therapies typically affect one or more aspects of energy balance including appetite, nutrient absorption, substrate oxidation and thermogenesis.

Scientists in various fields are constantly looking for new molecules that could be used as dietary functional ingredients in the prevention and management of excess weight and obesity and studies with flavonoids, including the different categories of catechins have shown promising results.

Epidemiological evidence and several randomized controlled intervention trials have shown an inverse relationship between habitual tea consumption, primarily green tea and levels of body fat and waist circumference [11–13]. While tea, particularly green tea contains an array of compounds, the putative anti-obesity effects have been most commonly attributed to the polyphenols of green tea, specifically the catechins [14]. The catechins present in tea may affect different aspects of energy balance that, in total bring about body weight and fat loss.

Generally, it is believed that spices and herbs are used to give flavour to foods and drinks without adding any calories. However, consumption of foods with added spices and herbal drinks result to an increase in energy expenditure and decrease in energy intake. Capsaicinoids found in chilli peppers have bioactive properties which help to support weight management [15, 16].

Methylxanthines, especially caffeine, which are present in teas, cocoa and coffee have been reported to have thermogenic effects and can stimulate fat oxidation in vitro, partly by the sympathetic activation of the central nervous system [17, 18]. In humans, caffeine has been shown to stimulate thermogenesis and fat oxidation [18].

In this paper, a review of the significance of bioactive compounds present in teas, spices, cocoa and coffee are presented, with emphasis laid on the their mechanisms of action.

A Brief Description of Bioactive Components Present in Teas, Spices, Cocoa and Coffee and Their Relationship with Body Weight Control

Tea Consumption and Weight Management

Tea is one of the beverages most consumed worldwide. Black tea represents approximately 72% of total consumed tea in the world, whereas green tea accounts for approximately 26% [19]. Freshly harvested tea leaf is processed differently in different parts of the world to give oolong tea, green tea or black tea. Green tea is prepared from the fresh tea leaf and widely consumed in Japan and China. Americans and Europeans prefer black tea, which is prepared through the oxidation, curing process of maceration and exposure to atmospheric oxygen [20]. The consumption of oolong tea is confined mainly to China and Taiwan while roasted tea is consumed mostly in Japan. Green and roasted teas are steamed, respectively, to avoid enzymatic oxidation; oolong tea is semi-fermented to permit a moderate level of enzymatic oxidation during processing [20]. Because of limitations set in the author's guidelines in this journal, in this review, emphasis will be laid only on black and green, whose compositions are presented in Table 1 below.

Table 1: The Major Components of Black Tea and Green Tea [21]

Component	**Black tea (% weight extract solids)**	**Component**	**Green tea (% weight extract solids)**
Catechins	3-10	Catechins	30-42
Theaflavins	3-6	Flavonols	5-10
Thearubigens	12-18	Other flavonoids	2-4
Flavonols	6-8	Theogallin	2-3
Phenolic acids and depsides	10-12	Other depsides	1
Amino Acids	13-15	Ascorbic Acid	1-2
Methylxanthines	8-11	Gallic Acid	0.5
Carbohydrates	15	Quinic acid	2
Protein	1	Other organic acids	4-5
Minerals	10	Theanine	4-6
Volatiles	<0.1	Other amino acids	4-6
		Methylxanthines	7-9
		Carbohydrates	10-15
		Minerals	6-8
		Volatiles	0.02

Fresh tea leaf is rich in water soluble polyphenols, particularly flavanols, flavanol gallate and flavanol glycosides [22, 23]. The major tea catechins: α-epigallocatechin-3-gallate (EGCG), α-epigallocatechin (EGC), α-epicatechin-3-gallate (ECG), α-epicatechin (EC), α-epicatechin-3-gallate (ECG), α-epicatechin (EC), α-gallocatechin and β-catechin constitute 30% to 42% of the green tea solids by weight. The concentration of different categories of catechins in green tea infusions is presented in Table 2 below.

Apart from green tea, catechins can also be found in other common foods, such cocoa, chocolate, black tea, red wine etc (for details see Table 3 below).

Recent studies have demonstrated the effects of catechins found in black, green and oolong teas on weight con-

Table 2: Catechin Concentrations of Green Tea Infusions [22]

Catechin in Green Tea Infusion	Catechin Concentration (mg/L)*	Catechin Concentration (mg/8 fl oz)*
Epigallocatechin-3-gallate (EGCG)	117-442	25-106
Epigallocatechin (EGC)	203-471	49-113
Epicatechin-3-gallate (ECG)	17-150	4-36
Epicatechin (EC)	25-81	6-19

*mg = milligram; L = liter; fl oz = fluid ounce
(1 US fluid ounce = ~30 ml)

Table 3: Catechin Content of Some Selected Common Foods (data source presented below the table)

Food	Catechin (mg/100g)	Epicatechin (mg/100g)	Epigallocatechin, Epicatechin Gallate, & Epigallocatechin Gallate (mg/100g)
Apples	0.9	6.1	0.6
Blackberries	37.1	4.7	0.8
Black Grapes	10.1	8.7	2.8
Brewed Black Tea	1.5	2.1	23.1
Brewed Green Tea	2.6	8.3	114.3
Cherries	1.3	7.0	0.4
Cocoa	0.00	26.2	0.00
Dark Chocolate	12.0	41.5	0.00
Fava Beans	8.2	7.8	4.7
Milk Chocolate	2.1	6.3	0.00
Pears	0.3	3.8	0.8
Raspberries	1.6	4.1	1.0
Red Table Wine	7.0	3.3	0.1

Source: Nutrient Data Laboratory US Department of Agriculture. USDA Database for the Flavonoid Content of Selected Foods. US Department of Agriculture, Agricultural Research Service, 2011.

trol and prevention of obesity. It has been found that teas, especially green tea possess several physiologic effects in vivo, including reduction in body weight and fat mass, and suppression of blood cholesterol, glucose, and triglyceride levels [18]. A recent meta-analysis of 11 trials with green tea catechins reported an average body weight loss of 1.31 kg for subjects in the treatment groups as compared to control groups, with most intervention periods being approximately 12 weeks [23]. The results of this meta-analysis showed that the average effect of green tea extract on body weight loss was larger for Asian participants (-1.51 kg) versus Caucasian participants (-0.82 kg), which indicates that the Asian population may benefit more from tea consumption.

Recently, Jurgens et al. [24] assessed the efficacy and safety of green tea preparations for weight loss and weight maintenance in overweight or obese adults using RCTs of at least 12 weeks' duration. These authors concluded that green tea preparations appear to induce a small, statistically non-significant weight loss in overweight or obese adults. However, 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.

Epidemiologic studies have shown that increased consumption of black tea (>480 mL/d) was linked with lower levels of serum glucose [25], which suggest the possibility that black tea may prevent obesity. Recently, Satoshi et al. [13] examined the effectiveness of oral administration of black tea polyphenols extract (BTPE) in vitro and in vivo experiments. BTPE suppressed increases in rat plasma triglyceride levels in a dose-dependent manner after oral administration of a lipid emulsion. In addition, administration of 5% BTPE suppressed significantly increases in body weight ($P < 0.05$), parametrial adipose tissue mass, and liver lipid content (reduced to 56.9% and 81.7% of control mice, respectively, $P < 0.05$) in mice fed a high-fat diet. Therefore, it can be concluded that BTPE may prevent diet-induced obesity by inhibiting intestinal lipid absorption.

Kovacs et al. [26] examined whether green tea had any effect on weight maintenance in subjects who had previously lost weight. A total of 104 overweight and moderately obese male and female subjects participated. The study consisted of a very-low-energy diet intervention of 4 weeks followed by a weight-maintenance period of 13 weeks in which the subjects received green tea or placebo. The green tea contained caffeine (104 mg/d) and catechins (573 mg/d, of which 323 mg was epigallocatechin gallate). Green tea appeared to have no effect on weight maintenance following weight loss on the low energy diet compared to the placebo.

The catechins in green tea may stimulate thermogenesis and fat oxidation through inhibition of catechol O-methyltransferase (COMT), an enzyme that degrades norepinephrine (NE) [18]. Green tea extract appeared to increase sympathetic nervous system (SNS) activity acutely, and increases EE and fat oxidation in humans in the short-term [27]. Green tea extract also contains caffeine, which has been shown to stimulate thermogenesis. The fact that a green tea extract stimulates thermogenesis cannot be completely attributed to its caffeine content because the thermogenic effect of green tea is greater than an equivalent amount of caffeine [27]. Thus green tea may act at different steps of NE modulatory pathways and in this way exert a thermogenic and possibly an anti-obesity effect [18].

Cocoa contains about 380 known chemicals, 10 of which are psychoactive compounds. In their natural state, cocoa beans are virtually inedible because of their high concentration of polyphenols, which gives them an extremely bitter flavor. In a final cocoa product such as chocolate, polyphe-

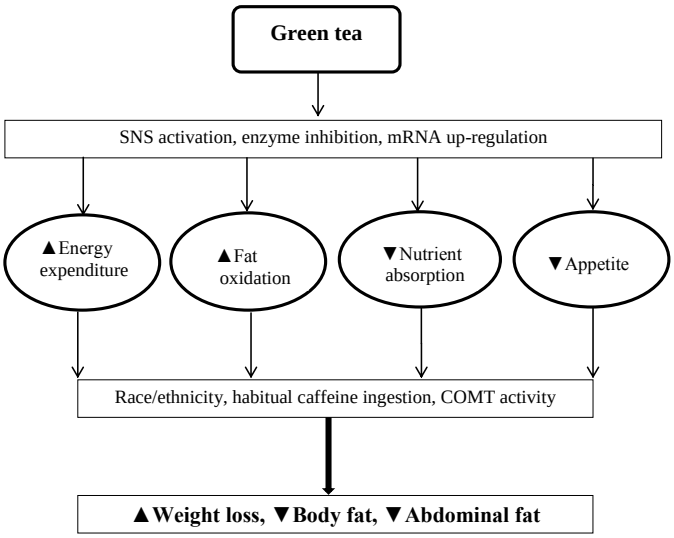

Fig. 1: Mechanisms, Whereby Green Tea Consumption Affects Body Weight [22]

nol content might decrease from 100% to 10% throughout the different manufacturing processes [28].

There are 3 groups of polyphenols in cocoa beans, namely: catechins, which constitute about 37% of the polyphenol content in the beans, anthocyanidins (about 4%), and proanthocyanidins (about 58%). Of the catechins, (-)-epicatechin is the most abundant (up to 35%), while (+)-catechin, (+)-gallocatechin, and (-)-epigallocatechin are present in smaller quantities [29].

Only a few studies have investigated the feasibility of the use of cocoa products, including dark chocolate in weight control. For example, Ferrazzano et al. [30] found that rats fed a cocoa-enriched diet experienced a reduction in body weight, most likely due to lower adipose tissue synthesis. These investigators hypothesized that the polyphenols contained in cocoa may have anti-obesity effects due to their ability to suppress fatty acid synthesis while stimulating cell energy expenditure in the mitochondria.

Furthermore, it has been found that cocoa consumption may also have beneficial effects on satiety, cognitive function, and mood, all which may help in the prevention of weight gain [31].

Capsaicinoids and Capsinoids and Weight Management

Capsicum species, or hot peppers, are used worldwide as food and spices. When it comes to taste, the **Capsicum** family offers probably the widest spectrum of possibilities of any food family, ranging from meek bell peppers to roaring habaneros, Trinidad Moruga Scorpion and Carolina Reaper (the world's hottest pepper) that taste like fire.

That burning sensation comes from a group of compounds called capsaicinoids. Capsaicin (8-methyl-N-vanillyl-6-nonenamide) is the most prevalent capsaicinoid in hot peppers, and also the most widely studied of chilli's medicinal compounds, having been linked with a wide range of potential health benefits, including anti-obesity [16, 32].

When consumed, the capsaicinoids in hot peppers produce the burning sensation by binding to TRPV1 pain receptors. Capsaicinoids with shorter chain lengths hit the front of the tongue, and burn for shorter times while capsaicinoids with longer chain lengths may reside in the receptor longer, burn longer and tend to hit the back of the palate [33, 34].

Capsaicin and its non-pungent counterpart, capsiate (found in sweet pepper) bind with high affinity to the TRPV1 receptor and are passively absorbed, with greater than 80% efficiency, in the stomach and upper portion of the small intestine [35]. Once released in the circulation, albumin transports capsaicin to the adrenal gland where it stimulates the release of catecholamines, which increase thermogenesis [36]. The increase in thermogenesis induced by capsaicin is probably based on ß-adrenergic stimulation.

Generally, capsaicinoids and capsinoids increase energy expenditure (EE) by stimulating thermogenesis as well as enhancing core body and skin temperature [37]. Additionally, both capsaicinoids (capsaicin) and capsinoids (capsiate) have also been reported to influence substrate oxidation [38, 39].

The effects of capsaicin on EE in overweight and obese individuals have been inconsistent. During the 13 weeks following a 4-week weight loss intervention in overweight and obese individuals, a study in the Netherlands found that when 135 mg/day capsaicin was consumed in capsules with meals, resting EE was increased by 119 kcal/day compared with placebo [40]. In a study carried out in Australia it was found that EE was suppressed following consumption of a 33 mg/day capsaicin spice blend for 4 weeks in overweight and obese men and women, but did not vary in lean men and women [41]. Matsumoto et al. [42] conducted a study Japan and reported that EE was augmented in lean women following a 3 mg capsaicin breakfast, but did not vary in overweight and obese women matched for age and height. Therefore, it seems that the effects of capsaicin may be blunted in individuals at high weights.

Capsainoids and capsinoids may prevent weight gain via appetite suppression. In a recent meta-analysis performed by Whiting et al. [16] it was found that taking capsaicinoids prior to a meal reduced ad libitum energy intake by 393.95 KJ (94.09 Kcal) $p<0.001$ during the following meal, but the results should be viewed cautiously as heterogeneity was high ($I2 = 80\%$). The results of this research are interesting,

since it has been shown that even small reductions in body weight (5%) can reduce obesity co-morbidities [43]. It is worth mentioning that larger and longer studies are needed, but there does appear to be some potential for capsaicinoids to be used as a natural weight-loss aid, particularly when used together with diet and exercise programmes.

Ginger and Its Bioactive Components and Weight Control

Originating in Asia, ginger the rhizome of the perennial plant Zingiber officinale Roscoe is widely used in Asian and Indian cuisine as well as in West Africa and the Caribbean. Ginger is thought to have several beneficial health properties, including analgesic, sedative, antipyretic, antibacterial and anti-obesity [44]. Ginger has three main active components: gingerols, zingerone, and shogaols. The characteristic pungent taste of ginger is attributed to the gingerols (6-gingerol, 8-gingerol and zingerone). Other compounds of ginger include volatile oil, aryl alkenes, diarylheptanoids and starch [45].

Because of their structural similarity to capsaicin, 6- and 8-gingerols are relatively potent agonists of TRPV1, which may contribute to the medicinal properties of ginger [44]. Zingerone, a product of gingerol degradation, is only a weak TRPV1 agonist, which is the result of the absence of the side chain [46]. Kadnur and Goyal [8] demonstrated that methanolic extracts of dried ginger prevented fructose-induced elevation of serum cholesterol, triglycerides, glucose, insulin, and gain in body weight in rats. Ginger extracts containing gingerol were also found to enhance adipocyte differentiation [47] and insulin-sensitive glucose uptake, thus suggesting its potential for the prevention and management of both obesity and diabetes. Zingerone was found to suppress the inflammatory responses of adipose tissue in obesity by suppressing the inflammatory action of macrophages and release of MCP-1 from adipocytes [48]. Similar to capsaicin, bioactive components derived from ginger are known to induce sympathetic nervous system–mediated thermogenesis [49]. Others reported the influence of ginger on appetite; however, the evidence is still very preliminary [49]. All these studies suggest that ginger possesses the potential for the prevention of obesity and obesity-linked metabolic effects.

Methylxanthines and Weight Management

Methylxanthines are the secondary plant metabolites derived from purine nucleotides. The most well known methylxanthines are caffeine (1,3,7-trimethylxanthine) and theobromine (3,7-dimethylxanthine), which occur in tea, coffee, cacao and a number of other non-alcoholic beverages of plant origin. Methylxanthines have been found in nearly 100 species in 13 orders of the plant kingdom [50]. Compared with other plant alkaloids, such as nicotine, morphine and strychnine, purine alkaloids are distributed widely throughout the plant kingdom although accumulation of high concentrations is restricted to a limited number of species, including Coffea arabica, Coffea robusta (coffee), Camellia sinensis (tea) and Theobroma cacao (cocoa). Coffee and tea also contain other dimethylxanthines as well as theophylline, which has similar properties to caffeine and theobromine, which pharmacological actions is far less potent than caffeine and theophylline. This review focuses on the main representative of methylxanthines, namely caffeine, which content in commonly consumed foods and beverages is presented in Table 4 below.

Table 4: Caffeine Content of Commonly Consumed Foods and Beverages [51]

Food or beverage	Typical caffeine content (mg/serving)	
	Typical	Range*
Coffee (8 oz. cup) Brewed, drip method	85	65-120
Instant coffee	75	60-85
Decaffeinated coffee	3	2-4
Espresso (1 oz. cup)	40	30-50
Teas (8 oz. cup), brewed, major U.S. brands	40	20-90
Brewed tea, imported brands	60	25-110
Instant tea	28	24-31
Iced tea	25	9-50
Soft drinks (Cola – 12 oz. serving)	40	30-60
Energy drinks (Approx 250 ml. – 8.3 oz. serving)	80	50-160
Cocoa beverage (8 oz. serving)	6	3-32
Chocolate milk beverage (8 oz. serving)	5	2-7
Solid Milk chocolate (1 oz. serving)	6	1-15
Solid Dark chocolate, semi-sweet (1 oz. serving)	20	5-35
Baker's chocolate (1 oz. serving)	26	26
Chocolate flavored syrup (1 oz. serving)	4	4

*Due to brewing method, plant variety, brand, formulation etc.

Caffeine is the most widely consumed stimulating substance in the world. As shown in table 4 above, it is found in coffee, tea, soft drinks, chocolate, and many medications. Caffeine is rapidly and almost completely absorbed in the stomach and small intestine and distributed to all tissues, including the brain. Caffeine metabolism occurs primarily in the liver, where the activity of the cytochrome P450 isoform CYP1A2 accounts for almost 95% of the primary metabolism of caffeine. Caffeine is metabolized into more than 25 metabolites in humans, mainly paraxanthine (representing 72-80% of caffeine metabolism), theobromine, and theophylline [52].

Overall, there is little evidence of health risks and some evidence of health benefits for adults consuming moderate

amounts of coffee (3-4 cups/d providing 300-400 mg/d of caffeine) has been demonstrated in many studies. A review of the effects of caffeine on human health commissioned by Health Canada also concluded that moderate caffeine intake up to 400 mg/d is not associated with adverse health effects in healthy adults [53].

Many studies conducted both in animals and humans have shown caffeine to be effective in weight control by stimulating resting energy expenditure (REE) in both the post-absorptive and postprandial states in lean, obese and post-obese subjects [6], which is often linked to increases in circulating free fatty acid and fat oxidation [18, 54].

Recently, Belza et al. [55] investigated the effects of three different food ingredients tyrosine, green tea extract (GTE) and caffeine on resting metabolic rate and haemodynamics, as well as on ad libitum energy intake (EI) and appetite in 12, normal weight men (age: 23.7 ± 2.6 years, mean ± s.d.). Caffeine induced a thermogenic response of 6% above baseline value (72 ± 25 kJ per 4 h, mean ± s.e.) compared to placebo (P<0.0001). The thermogenic responses to GTE and tyrosine were not significantly different from placebo. Tyrosine tended to increase the 4-h respiratory quotient by 1% compared to placebo (0.01±0.005, P=0.05). Ad libitum EI was not significantly different between treatments but was reduced by 8% (-403 ± 183 kJ), 8% (-400 ± 335 kJ) and 3% (-151 ± 377 kJ) compared to placebo after intake of tyrosine, GTE and caffeine, respectively. No significant difference in haemodynamics was observed between treatments.

The relative importance of the mechanisms by which caffeine exerts its various effects is not fully clarified. Caffeine is a non-selective competitive inhibitor of the phosphodiesterase enzymes. These enzymes have the capacity to degrade the phosphodiesterase bond in cAMP and cyclic guanosine monophosphate (cGMP). One of the main enzymes inhibited by caffeine is 3'-5' AMP phosphodiesterase whose function is to degrade cAMP, causing its local accumulation. The accumulation of cAMP brings about antagonizing of adenosine receptors that have a negative effect on increased noradrenaline (NA) release. Thus, the net result of caffeine is an increased concentration of cAMP, and, in this way, the amount of NA available for stimulation of the adrenoceptor is increased and sustained [56].

The metabolic effects of caffeine depend on the dose and can act synergistically with other stimulants, such ephedrine/ephedra or nicotine. For example a study by [57] demonstrated that 100 mg of caffeine increased REE by 3-4% over 150 min, whereas research conducted by Collins et al. [58] showed that 200 mg of caffeine elevated REE by 5-8% over 3 hrs. When 100 mg of caffeine was combined with nicotine (1 mg), REE increased by 8.5% over a 3-hr period [59]. REE increased to 9.8% over a 3-hr period when 2 mg of nicotine were combined with 100 mg of caffeine.

Although caffeine increases thermogenesis acutely, there are limited data supporting its long-term effects on weight maintenance. Only one study reported that caffeine alone significantly reduced weight gain in participants who increased their caffeine consumption compared with subjects who decreased caffeine intake over a 12-year period [60]. It could be postulated that the lack of research supporting the effectiveness of caffeine for long-term weight regulation is most likely a result of the development of caffeine tolerance [61].

Hursel et al. [62] conducted a meta-analysis to elucidate whether catechin-caffeine mixtures and caffeine-only supplementation indeed increase thermogenesis and fat oxidation. They found that catechin-caffeine mixtures and caffeine-only supplementation increased energy expenditure significantly over 24 h (428.0 kJ (4.7%); $P < 0.001$ and 429.1 kJ (4.8%); $P < 0.001$, respectively). However, 24 h fat oxidation was only increased by catechin-caffeine mixtures (12.2 g (16.0%); $P < 0.02$ and 9.5 g (12.4%); $P = 0.11$, respectively). A dose-response effect on 24 h energy expenditure and fat oxidation occurred with a mean increase of 0.53 kJ mg^{-1} ($P < 0.01$) and 0.02 g mg^{-1} ($P < 0.05$) for catechin-caffeine mixtures and 0.44 kJ mg^{-1} ($P < 0.001$) and 0.01 g mg^{-1} ($P < 0.05$) for caffeine-only. These authors concluded that catechin-caffeine mixtures or a caffeine-only supplementation stimulates daily energy expenditure dose-dependently by 0.4–0.5 kJ mg^{-1} administered. Compared with a placebo, daily fat-oxidation was only significantly increased after catechin-caffeine mixtures ingestion.

Quercetin present in vegetables, tea and condiments, such as okra has also been found to possess anti-obesity, anti-diabetic and anti-hypertensive properties. Table 5 below presents selected sources of quercetin.

Table 5: Quercetin Content of Selected Foods (Source: USDA Database for the Flavonoid Content of Selected Foods, Release 3.1 (2014)

Food	Quercetin Content (mg/100 g)
Capers	233
Onions	22
Okra	21
Cocoa powder	20
Cranberries	14
Lingonberries	7.4
Apples	4.57
Green tea	2.69
Black tea	1.99
Ketchup	0.86

Results of in vitro studies have demonstrated that apart from the indirect effects of quercetin in lipogenesis through the action of insulin, this flavonoid can also diminish or

inhibit this metabolic pathway by acting directly on the expression of genes controlling this metabolic route. The results of studies by Ahn et al. [63] revealed that quercetin decreased the expression of sterol regulatory element-binding proteins (SREBP)-1 and fatty acid synthase (FAS), and by increasing acetyl-CoA carboxylase (ACC) phosphorylation. This research group also showed that quercetin attenuated adipogenesis as a consequence of the decrease in the expression of CCAAT/enhancer binding protein α (C/EBPα), and peroxisome proliferator-activated receptor γ (PPARγ).

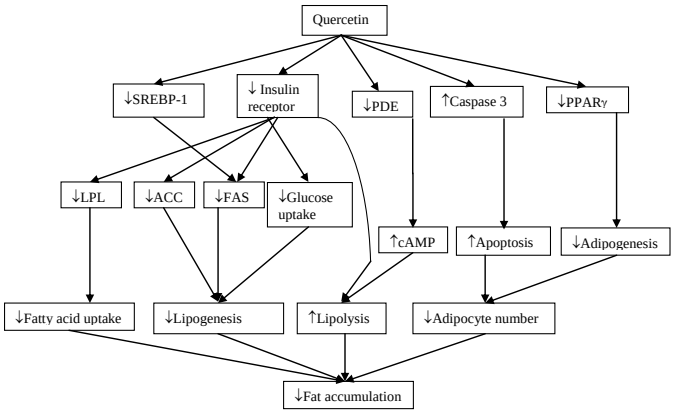

Fig. 2: Proposed Mechanisms for Body Fat Lowering Effects of Quercetin in Adipose Tissue

Quercetin has been shown to be a potent inhibitor of the stimulating effect of vanadate on lipoprotein lipase (LPL) activity. It is worth mentioning that vanadate shows insulin-mimetic effects, such as increases in LPL and suppression of hormone-dependent lipolysis, in isolated rat adipocytes. Consequently, the inhibition of vanadate action leads to inhibition of LPL and thus to the incorporation of fatty acids which circulate as triacylglcyerols in lipoproteins to adipocyte triacylglycerols [64].

Besides the effects on metabolic pathway involved in triacylglycerol accumulation, quercetin has been demonstrated to stimulate lipid mobilization. Studies by Kuppusamy and Das [65] demonstrated that quercetin induced a dose- and time-dependent increase in lipolysis, which was synergic with epinephrine-induced lipolysis. Thus, it can be said that this flavonoid produces a competitive phosphodiesterase (PDE) inhibition. The competitive nature of the kinetics suggests that quercetin could compete with cAMP for the same binding sites in the adipocyte PDE, thus increasing the concentration of cAMP, being an activator of protein kinase A (PKA), which in turn activates the hormone sensitive lipase (HSL).

An increase in adipocyte apoptosis due to a down-regulation of Poly(ADP-ribose) polymerases (PARPs) was demonstrated by Hsu and Yen [66]. PARPs are a set of protein that has several roles in cellular processes, most notably in DNA repair and programmed cell death), Bcl-2 proteins (apoptosis regulator proteins), Bax, and Bak proteins. The activation of caspase-3 and 9, as well as the inhibition of adenosine monophosphate-activated protein kinase (AMPK) pathway, also play a role in the induction of apoptosis (see Fig. 2 and Fig. 3 for mechanisms of actions of quercetin).

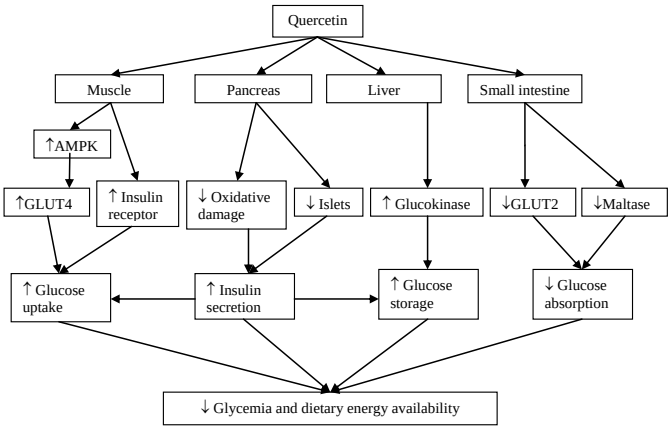

Fig. 3: Proposed Mechanisms for Antidiabetic Effects of Quercetin

Steward et al. [67] conducted an in vivo study in C57BL/6J mice fed a high-fat diet supplemented with quercetin (0.8%) for 3 and 8 weeks. Dietary supplementation with this quercetin produced a transient increase in energy expenditure, which diminished after 8 weeks. A decrease in circulating quercetin levels between 3 and 8 weeks indicated a metabolic adaptation. Furthermore, quercetin, at the concentrations provided, was effective in reducing circulating markers of inflammation, including IFN-γ, TNF-α, IL1 and IL4) after 8 weeks of treatment.

Kobori et al. [68] performed in vivo studies, during which they fed C57/BL6J mice a Western-style diet. They found that chronic dietary intake of quercetin reduced body weight gain, as well as visceral and liver fat accumulation, and improved systemic parameters related to metabolic syndrome (hyperglycemia, hyperinsulinemia and dyslipidemia), probably by decreasing oxidative stress and increasing PPARα expression. In addition, quercetin suppressed the expression of PPARγ and CD36, as well as SREBP-1c and its target fatty acid synthase (FAS) in the liver. The reduction in PPARγ expression suggests a reduction in adipogenesis, because genes involved in this process are controlled by this transcriptional factor. However, the reduction in SREBP expression, as well as the gene of the lipogenic enzyme FAS, indicate a decrease in the de novo lipogenesis in liver. Consequently, a reduced amount of triacylglycerols in plasma, coming from liver and available for adipose tissue uptake, can be expected.

Not all studies have demonstrated favourable effects of quercetin on body weight and fat. For example, in an experiment carried out by [69] in db/db mice treated with quercetin (100 mg/kg of body weight/d) for 7 weeks, this flavonoid led to a reduction in plasma glucose without changes in body weight. In another experiment performed in Wistar rats treated with 25 mg of quercetin/kg body weight/d and fed high-fat diet, body weight also remained unchanged [70].

Unfortunately, there is a scarcity of data on the effects of quercetin on humans. The only published study carried out in humans revealed that nutritional status, namely: body weight, waist circumference, fat mass and fat-free mass remained unchanged in participants with a body mass index between 25 and 35 kg/m2, who consumed 15 mg/d of quercetin for 6 weeks [71].

Several in vivo studies with the use of quercetin have been performed in animal models with diabetes. For example, Kim et al. [69] found a reduction in serum glucose concentrations and blood glycated haemoglobin in C57BL/KsJdb-db mice fed with a diet supplemented with 0.08% quercetin for 7 weeks. The decline in serum glucose concentrations and blood glycated haemoglobin was attributed to the inhibition of small intestine maltase activity without changes in serum insulin levels. Mechanisms of the antidiabetic effects of quercetin are shown in Fig. 3.

Alpha-glucosidase and α-amylase inhibitors help retard post-prandial blood glucose increase. Food compounds with such properties include tannins, anthocyanins, chlorogenic acid and many other polyphenols, including quercetin present in okra [72]. Recently, Rifaai et al. [73] showed that quercetin exerted a protective effect against β-cell damage by its anti-inflammatory, anti-apoptotic, antioxidant and regenerative effects in rats with experimentally induced diabetes.

Wein et al. [70], in a study carried out on male Wistar rats fed with a high-fat diet supplemented daily with 25 mg quercetin/kg body weight, showed an increase in adiponectin expression in white adipose tissue and its circulating concentration, despite an inhibition of PPARγ expression. The authors concluded that the effects of quercetin on adiponectin were PPARγ independent. Taking into account that adiponectin is an adipokine that facilitates insulin action, the authors proposed that the increase in adiponectin levels was involved in the improvement in insulin sensitivity induced by quercetin.

However, Steward et al. [74] induced insulin resistance in rats by feeding animals on a high-fat diet. They noticed that at the dose of 0.8% in the diet, quercetin exacerbated diet-induced insulin resistance at 3 weeks. After 8 weeks, insulin resistance in the quercetin supplemented group was not worse, when compared with animals fed on high-fat alone. These results suggest that the inhibitory effect of insulin signaling at 3 weeks was further eliminated by an adaptive increase hepatic metabolism and/or excretion of the compound between 3-8 weeks. At the doses used, quercetin inhibited insulin-dependent activation of PI-3K.

Concluding Remarks

The studies presented in this manuscript show the complexity and importance of studying bioactive compounds in teas, coffee and spices. These compounds have the potential to produce significant effects on metabolic targets such as satiety, thermogenesis, fat oxidation and overall energy expenditure, when they are examined in a standardized laboratory context. The potential for natural products as sources of nutraceuticals for the management of body weight is now being realized with the involvement of catechins, capsaicin, methylxanthines (caffeine), gingerols, glabridin, etc. Theses natural products have been shown to be effective and safe on body weight management in both human and animal studies. A number of intervention trials have demonstrated a reduction in body weight and fat after chronic consumption of tea catechins with caffeine. Early mechanistic work suggested that tea catechins may increase energy expenditure, stimulating thermogenesis to a greater degree than caffeine alone. Further studies need to be conducted to investigate the mechanism of action, metabolism, long term safety and side effect of bioactive compounds in teas, spices and coffee as well as interactions between these compounds with dietary components. In addition, the impact of the dose, the method of intake (e.g., empty or full stomach, supplement, brewed beverage, etc.), duration of intake, sex, the degree of adiposity and the potential positive interaction with physical activity warrant further research in both mechanistic studies and randomized, controlled intervention trials.

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