



Research review

Capsaicinoids and capsinoids. A potential role for weight management? A systematic review of the evidence

Stephen Whiting, Emma Derbyshire*, B.K. Tiwari

Manchester Food Research Centre, Manchester Metropolitan University, Hollings Faculty, Old Hall Lane, Manchester M14 6HR, UK

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ABSTRACT

Capsaicinoids are a group of chemicals found in chilli peppers, with bioactive properties. The purpose of this study is to systematically review research investigating the potential benefits capsaicinoid compounds may have in relation to weight management. Medical databases were searched and 90 trials found, 20 of which were selected for inclusion, involving 563 participants. Three main areas of potential benefit for weight management were found: (1) increased energy expenditure; (2) increased lipid oxidation and (3) reduced appetite. Trial duration, dosage and sized varied, though trials were generally of high quality with a low risk of bias. It was observed that consumption of capsaicinoids increases energy expenditure by approximately 50 kcal/day, and that this would produce clinically significant levels of weight loss in 1–2 years. It was also observed that regular consumption significantly reduced abdominal adipose tissue levels and reduced appetite and energy intake. The mechanism of action is not presently fully understood, although it is well accepted much of the effects are caused by stimulation of the TRPV1 receptor. While capsaicinoids are not a magic bullet for weight loss, the evidence is that they could play a beneficial role, as part of a weight management program.

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Introduction

Capsaicinoids are a group of molecules unique to fruits of plants from the genus *Capsicum* (chilli peppers). They are responsible for the fruit's pungent sensation and display potentially valuable pharmacological properties (Thiele, Mueller-Seitz, & Petz, 2008).

This sensation occurs as capsaicin binds to the same group of nociceptors which also leads to the sensation of pain from heat and acid (Sanatombi & Sharma, 2008).

The basic chemical structure (Fig. 2) of the compounds is an acid amide of vanillylamine combined with a fatty acid (Aza-Gonzalez, Nunez-Palenius, & Ochoa-Alejo, 2011). Although more than 10 structures exist, the most prominent forms are

* Corresponding author.

E-mail address: e.derbyshire@mmu.ac.uk (E. Derbyshire).

capsaicin and dihydrocapsaicin, accounting for almost 90% of capsaicinoids (Meghvansi et al., 2010). It is thought these chemicals are created by the plant as a defence mechanism against mammalian herbivores and fungi (Tewksbury, Manchego, Haak, & Levey, 2006). Although traditional native to South America, chilli peppers are now grown and consumed worldwide (Mongkolporn & Taylor, 2011). They are integral to many traditional cuisines, such as Mexico, India (the world's largest producer), Thailand, Korea and Indonesia. Not featuring prominently in the traditional European and North American diet, consumption rates tend to be much lower (Ludy & Mattes, 2011).

In addition, overweight and obese populations represent a rapidly growing threat to the health of many societies. In 2008, 1.5 billion adults (20 and older) were overweight; of these around 500 million were obese (World Health, 2011). Reversing the nutrition transition has, however, proven difficult. It is widely accepted that increasing energy expenditure and reducing energy intake form the basis for management of this problem. Human and animal intervention studies using capsaicinoids over the past decades have been found to increase energy expenditure (Imaizumi et al., 2011) and affect appetite (Westerterp-Plantenga, Smeets, & Lejeune, 2005), thereby reducing energy intake.

A similar, but independent group of compounds named capsinoids (naturally occurring from the pepper 'CH-19 Sweet'), have also been the subject of a number of research trials and seem to have similar effects to capsaicinoids, without the pungency (Hursel & Westerterp-Plantenga, 2010). Due to their slightly different structure, they do not stimulate receptors in the mouth, but do in the intestines (Fig. 2). This is seen as a particularly valuable attribute, as many people struggle to consume capsaicinoids due to their 'spiciness' (Luo, Peng, & Li, 2011).

More recently, a number of potential health benefits of consuming chillies have been investigated. Clinical trials suggest capsaicinoids have anti-cancer (Yang et al., 2010), anti-inflammatory (Choi et al., 2011) and antioxidant (Henning et al., 2011) properties.

This review aims to systematically evaluate clinical research into capsaicinoid and capsinoid compounds and establish whether

regular ingestion could have a potential role in weight management strategies. We reviewed randomised, control trials in humans, which investigated capsaicinoid and capsinoid compounds' effects on energy expenditure, lipid oxidation and appetite. The quality and weight of evidence will be examined as will the efficacy of different capsaicinoid compounds.

Methods

Search strategy

Studies were identified by searching Web of Knowledge, PubMed and Scopus (1990-Present). The initial search was performed on 19th July 2011 and updated on 14th October 2011.

The following search terms we used in all databases: 'capsaici', 'capsinoid*', 'chilli*', 'chili*' (alternative spelling). These four terms were combined (using Boolean 'AND') with 'weight loss', 'satiety', 'thermogenesis' and 'energy expenditure', in turn. Trials were initially selected based on their abstract; full content was then reviewed to determine final inclusion. The search strategy was developed by all researchers and carried out by one (SW).

Inclusion and exclusion criteria

Inclusion was based on the following criteria: human, randomised, intervention trials, in English using 'healthy' volunteers, compared to themselves, or a matched control group. Healthy meaning free of disease, but was inclusive of overweight and obese participants.

Identification of relevant studies

A total of 90 clinical trials were identified from the database searches. Searching references lists identified another 11 trials. Sixty-eight trials were excluded for being duplicates and a further 13 were excluded for methodical reasons (Fig. 1), leaving a final total of 20 trials.

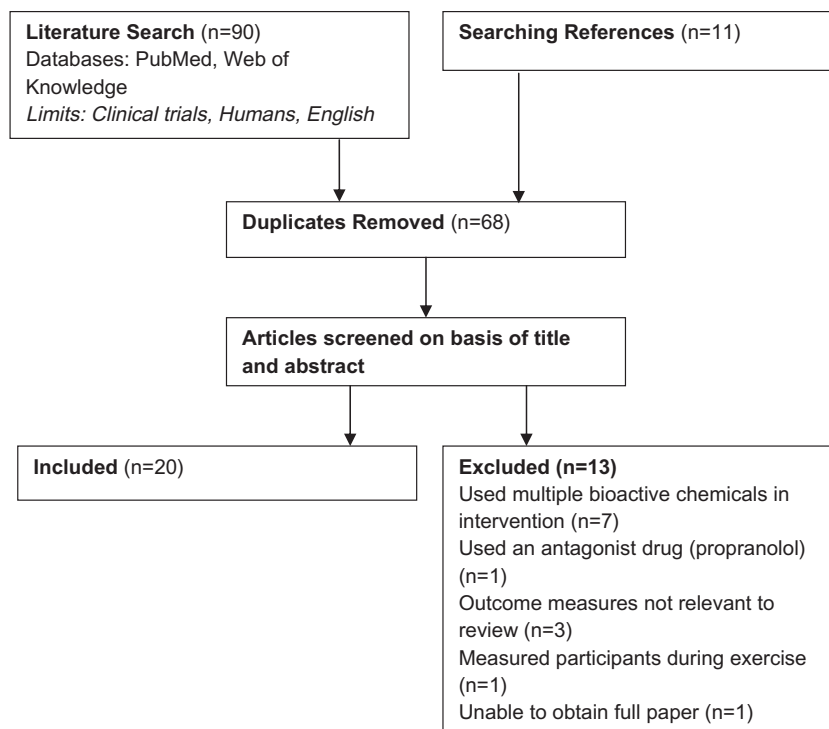


Fig. 1. A flow chart showing the results and exclusions of literature search.

Data extraction

Data extracted from the trials included: characteristics of participants (sex, age, weight, number of participants), intervention used (supplement or actual chilli pepper, comparison to a control group or crossover design and dosage used), type of outcome measure (effect on appetite, energy expenditure/intake, thermogenesis, hormones).

Assessment of bias

The studies were assessed for bias (quality) using similar approaches as previous reviews (Chrubasik, Duke, & Chrubasik,

2006; Chrubasik, Li, & Chrubasik, 2010; Chrubasik, Roufogalis, Muller-Ladner, & Chrubasik, 2008; Chrubasik, Roufogalis, Wagner, & Chrubasik, 2007; Gagnier, Chrubasik, & Manheimer, 2004; Vlachojannis, Cameron, & Chrubasik, 2009), using the following criteria:

- (i) Experimental protocol described.
- (ii) Specified criteria for participant inclusion.
- (iii) Appropriate randomisation.
- (iv) Appropriate blinding.
- (v) Baseline groups' characteristics similar.
- (vi) Participant dropout described.
- (vii) Sample size based on a priori power calculation.

Name	Chemical Structure	Chemical Formula
Capsaicin		C ₁₈ H ₂₇ NO ₃
Dihydrocapsaicin		C ₁₈ H ₂₉ NO ₃
Nordihydrocapsaicin		C ₁₇ H ₂₇ NO ₃
Capsiate		C ₁₈ H ₂₆ NO ₄
Dihydrocapsiate		C ₁₈ H ₂₈ NO ₄
Nordihydrocapsiate		C ₁₇ H ₂₆ NO ₄

Fig. 2. Chemical structures capsaicinoid and capsinoid compounds.

- (viii) Dosage stated.
- (ix) Comparator (control) appropriate.
- (x) Outcome measures described.
- (xi) Outcome measures relevant.
- (xii) Intervention given at an appropriate time.

An overall score was then given out of 12, high scores having a low risk of bias. While a 'no' for some questions might indicate an increased risk of bias, in some cases this would be inherent in the study design. For example if a meal was given containing chilli powder, it would not be possible to blind the control meal (i.e. make it spicy), without the use of another food with a potentially bioactive effect (e.g. black pepper), thus affecting the results.

It was hypothesised that earlier trials would have a higher risk of bias. This is because the first trials in a particular area tend to be more 'exploratory'. That is, they determine relevant conditions, study design and sample size needed to show an effect.

Results

Study lengths were varied; 10 of the 20 studies' intervention involved a single meal, with effects measured in the following few hours. Three trials lasted between 1 and 8 days and the remaining six lasting multiple weeks (the longest being 4 months (Lejeune, Kovacs, & Westerterp-Plantenga, 2003)). The single meal trials tended to be the older studies, with eight of them being 2004 or older.

With regard to sample size, populations varied from 7 (Kawabata et al., 2006) to 91 (Lejeune et al., 2003), with a number of studies employing a crossover design; participants being their own control. Four trials had 10 participants or less, 10 had between 11 and 30, with the remaining five trials having 31 or more. The newer trials (2005 or later) tended to have larger populations although the difference was not pronounced.

In terms of dosage, there was a large variance employed in the studies, ranging from 1 mg/day (Galgani, Ryan, & Ravussin, 2010) to 135 mg/day (Lejeune et al., 2003). Most of the capsaicinoid trials employed between 10 and 36 mg/day, while most of the capsinoid trials used less than 10 mg/day. Ten of the trials gave chilli pepper as a food (usually dried and sprinkled over a meal), with seven opting to use supplements and two using both. Twelve trials investigated the effects of capsaicinoid compounds (from a traditional chilli pepper), with eight using capsinoid compounds (from the CH-19 sweet pepper).

Table 4 shows the results of the assessment of quality. Scores were generally high, showing a low risk of bias (range 7–11 out of 12). As expected, the more recent studies have tended to have the higher scores. The major criticism would be very few of the trials stated that they used a priori power calculation to develop their sample size. Participant drop-out was also not described in the number of studies, especially the older trials.

The intervention of initial studies in this area all consisted of a single meal (the first 7). With all these trials reporting positive results, the first large scale, long duration, high dosage trial was conducted in 2003 (Lejeune et al., 2003). There has been concern expressed that compliance may be an issue, particularly among western populations, due to capsaicinoid's pungency (Hursel & Westerterp-Plantenga, 2010). As such, there has more recently been increased emphasis on investigating the effects of the CH-19 sweet pepper's capsinoid compounds, which do not cause the sensation of heat (of the 8 capsinoid studies, 7 are post 2006).

As stated earlier this review will focus on three areas of weight management, namely: (1) energy expenditure, (2) lipid oxidation, and (3) effect on appetite. The results of these areas and key findings of the studies are reported in Tables 1–3. Fifteen trials reported results of investigations into the effect on energy

expenditure, 11 reported results for lipid oxidation and seven into the effects on appetite.

Energy expenditure

Of the 15 trials measuring effects on energy expenditure post consumption, 13 reported an increase (Table 1). This effect was seen in several capsaicin trials including both single meal (Ludy & Mattes, 2011; Matsumoto et al., 2000; Yoshioka, St-Pierre, Suzuki, & Tremblay, 1998; Yoshioka et al., 1995) and longer term studies (Lejeune et al., 2003). It was also observed in two lengthy trials using dihydrocapsiate (Galgani & Ravussin, 2010; Lee, Li, Zerlin, & Heber, 2010), which found significant increases in energy expenditure after supplementation with capsules ($p = 0.04$ and $p < 0.05$, respectively). Dihydrocapsiate and capsiate (like dihydrocapsaicin and capsaicin) form the bulk of capsinoid molecules found in CH-19 sweet peppers (Kobata, Todo, Yazawa, Iwai, & Watanabe, 1998).

Effects observed include increased metabolic rate (Inoue, Matsunaga, Satoh, & Takahashi, 2007), increases in body temperature (Ohnuki et al., 2001) and increases in oxygen consumption (Josse et al., 2010). Evidence for how long the effects last post-prandial, is provided from several single meal trials, however results varied. An increase in energy expenditure was observed for 30 min post ingestion, but then returned to normal levels in two trials (Lim et al., 1997; Yoshioka et al., 1995). However, increases in body temperature and oxygen consumption were observed for 180 min in different trial (Yoshioka et al., 1998) ($p < 0.05$) and were still evident when monitoring ceased after 60 min in another study (Ohnuki et al., 2001) ($p = 0.01$).

Three studies made calculations for the amount of calories the increase in energy expenditure they observed, would equate to. An increase of around 50Kcal/day were suggested by two trials (Galgani & Ravussin, 2010; Snitker et al., 2009), whilst the third calculated the increase would be around 100 kcal/day for a 100 kg individual. Whether this small increase in calories expended will make a significant difference to an individual's weight is open to some debate. It has been suggested that a positive energy balance of 50 kcal/day may have triggered the general increase in body weight observed in the United States over the past 2–3 decades (Hill, 2006). It was concluded that an increased expenditure of 50 kcal/day, would produce medically significant weight loss 1–2 years of supplementation (Snitker et al., 2009). However, it was argued that 50 kcal/day is within the natural variability of resting metabolic rate variability, and that this is not conclusive evidence of an effect (Galgani & Ravussin, 2010).

Evidence for a dose-dependent effect on energy expenditure is provided by three trials (Inoue et al., 2007; Lee et al., 2010; Ludy & Mattes, 2011). The only other trial to test multiple dosages failed to find an effect at any dosage tested (Galgani et al., 2010). Although this was a relatively short trial, with a random dosage being given on five consecutive days. All these trials featured relatively low dosages of capsaicinoids or capsinoids (highest dose 12 mg/day), studies testing higher dosages may be more informative on this point.

Lipid thermogenesis

Eleven trials investigated the effect of capsaicinoids/capsinoids on lipid oxidation and adipose tissue (see Table 2). Seven trials found beneficial effects, including increased lipid oxidation (recorded by measuring respiratory gases) or a decrease in fat stores. Two large, lengthy trials both observed this effect. One trial ($n = 91$, lasting 4 months) found a significant increase in lipid oxidation among participants taking capsaicin supplements ($p < 0.05$) (Lejeune et al., 2003). Another ($n = 80$, lasting 12 weeks), observed a nearly significant ($p = 0.06$) difference in lipid oxidation and a

Table 1
Details of trials investigating effects on energy expenditure.

Paper number	Author	Intervention used	Dose (mg/day)	Sample size (n)	Duration	Effect	Key findings
1	Yoshioka et al. (1995)	Capsaicinoid rich red pepper	30	8	Single meal	↑	Increase in energy expenditure (EE) for 30 min (significance not stated)
2	Lim et al. (1997)	Capsaicinoid rich red pepper	Not stated	8	Single meal	↑	Increase in EE of 10% for 30 min (not significant)
3	Yoshioka et al. (1998)	Capsaicinoid rich red pepper	30	14	Single meal	↑	Increase in EE ($p < 0.05$) for 180 min
6	Matsumoto et al. (2000)	Capsaicinoid containing meal	3	16	Single meal	↑	Significant increase seen in lean ($p < 0.01$) but not obese group
7	Ohnuki et al. (2001)	CH-19 Sweet pepper	0.03–0.1 per kg of bodyweight	11	Single meal	↑	Increases in body temperature ($p < 0.01$) and oxygen consumption ($p < 0.03$)
7	Lejeune et al. (2003)	Capsaicin supplement [^]	135	91	4 months	↑	Significant increase in resting energy expenditure ($p < 0.005$)
12	Inoue et al. (2007)	Capsinoid supplement*	3 and 10	44	4 weeks	↑	Dose responsive increase in EE (not significant)
13	Smeets and Westerterp-Plantenga (2009)	Capsaicinoid containing meal	Not stated	30	Single meal	X	No effect on EE. Changes in gut-derived hormones detected
14	Snitker et al. (2009)	Capsinoid supplement*	6	80	12 weeks	↑	EE 54 kcal/d higher in treatment group (not significant)
15	Galgani and Ravussin (2010)	Dihydrocapsiate supplement*	3 & 9	78	4 weeks	↑	Increased in EE ($p = 0.04$), around 50 kcal/d
16	Galgani et al. (2010)	Capsinoid supplement*	1, 3, 6 and 12	13	5 days	X	No effect on energy expenditure found
17	Josse et al. (2010)	Capsinoid supplement*	10	12	Single meal	↑	Increases in EE ($p < 0.05$)
18	Lee et al. (2010)	Dihydrocapsiate supplement*	3 and 9	33	8 weeks	↑	Increase in EE at high dosage ($p < 0.05$). Dose dependant effect observed
19	Ludy and Mattes (2011)	Cayenne Red Pepper (Capsaicinoid)	Variable	25	6 days; not consecutive	↑	Significant increase in EE at higher dose ($p = 0.013$). Sensory effect required to obtain full benefit
20	Yoneshiro et al. (2012)	Capsinoid supplement*	9	18	2 days; not consecutive	↑	Significant increase in EE only in group with brown adipose tissue ($p < 0.01$)

Key: ↑, Increase; ↓, Decrease; X, No Effect. *Supplement extracted from CH-19 sweet pepper. *Supplement synthesised using enzymes. ^Supplement origin not stated.

Table 2
Details of trials investigating effects on lipid oxidation and fat loss.

Paper number	Author	Intervention used	Dosage (mg/day)	Population size (n)	Duration	Effect	Key findings
1	Yoshioka et al. (1995)	Capsaicin rich red pepper	30	8	Single meal	X	Decrease in lipid oxidation (significance not stated)
2	Yoshioka et al. (1998)	Capsaicin rich red pepper	30	14	Single meal	↑	Increase in lipid oxidation ($p < 0.05$) for 180 min
8	Lejeune et al. (2003)	Capsaicin supplement [^]	135	91	4 months	↑	Lipid oxidation increase ($p < 0.05$), No significant effect on weight
11	Kawabata et al. (2006)	CH-19 Sweet pepper	1 per kg of bodyweight	7	2 weeks	↑	Decrease in bodyweight ($p < 0.05$) and fat accumulation
12	Inoue et al. (2007)	Capsinoid supplement*	3 and 10	44	4 weeks	↑	Increased lipid oxidation ($p < 0.05$), significance only reached in group with BMI >25
13	Smeets and Westerterp-Plantenga (2009)	Capsaicinoid containing meal	Not Stated	30	Single meal	X	No effect on lipid oxidation. Changes in gut-derived hormones detected
14	Snitker et al. (2009)	Capsinoid supplement*	6	80	12 weeks	↑	Abdominal fat decreased ($p = 0.049$). Lipid oxidation increased ($p = 0.06$)
15	Galgani and Ravussin (2010)	Dihydrocapsiate supplement*	3 and 9	78	4 weeks	X	No changes in lipid oxidation or body fat detected
16	Galgani et al. (2010)	Capsinoid supplement*	1, 3, 6 and 12	13	5 days	X	No effect on lipid oxidation found
17	Josse et al. (2010)	Capsinoid supplement*	10	12	Single meal	↑	Increases lipid oxidation, decrease in blood free fatty acids and glycerol (all $p < 0.05$)
18	Lee et al. (2010)	Dihydrocapsiate supplement*	3 and 9	33	8 weeks	↑	Increase in fat oxidation ($p < 0.05$)

Key: ↑, Increase; ↓, Decrease; X, No Effect. * Supplement extracted from CH-19 sweet pepper. *Supplement synthesised using enzymes. ^Supplement origin not stated.

significant loss of abdominal fat in the capsinoid consuming participants ($p = 0.049$) (Snitker et al., 2009). This was seen even though dosage was relatively low (6 mg/day). It should be noted however, that in both trials despite the increased fat oxidation in participants, body weights did not vary between control and intervention groups.

A significant decrease in abdominal fat was seen in a second trial (Kawabata et al., 2006), with an approximately 20% decrease observed between treatment and control groups ($p < 0.05$). In a more recent trial (Yoneshiro, Aita, Kawai, Iwanaga, & Saito, 2012), the participants were divided into those with brown abdominal tissue (BAT) and those without. Energy expenditure

Table 3
Details of trials investigating effects on appetite.

Paper number	Author	Intervention Used	Dosage (mg/day)	Sample Size (n)	Duration	Effect	Key Findings
4	Yoshioka et al. (1999)	Capsaicin rich red pepper	30	11	Single meal	↓	Decrease in ad libitum energy intakes ($p < 0.05$)
5	Yoshioka et al. (1999)	Capsaicin rich red pepper	18	10	Single meal	↓	Decrease in ad libitum energy intakes ($p < 0.05$), changes in nervous system detected
9	Yoshioka et al. (2004)	Capsaicin supplement or meal	3	16	Single meal	↓	Decrease in ad libitum energy intakes ($p < 0.09$)
7	Lejeune et al. (2003)	Capsaicin supplement	135	91	4 months	X	Participant rated appetite scores were lower in both intervention and placebo groups
10	Westerterp-Plantenga et al. (2005)	Capsaicin supplement or drink	2.25	24	8 days	↓	Decrease in energy intake ($p < 0.01$), increase in satiety ($p < 0.01$)
13	Smeets and Westerterp-Plantenga (2009)	Capsaicin containing meal	Not Stated	30	Single meal	X	No effect on appetite observed. Changes in gut-derived hormones detected
19	Ludy and Mattes (2011)	Cayenne Red Pepper	Variable	25	6 days; not consecutive.	↓	Desire to eat and pre-occupation with food reduced. Desensitisation may occur with regular use

Key: ↑, Increase; ↓, Decrease; X, No Effect. ^Supplement origin not stated.

Table 4
Assessment of risk of bias in all trials.

Paper number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Experimental protocol described	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Specified criteria for participant inclusion	x	x	x	x	x	x	x	✓	x	✓	✓	✓	x	✓	✓	✓	✓	✓	✓	x
Appropriate randomisation	x	✓	✓	✓	✓	n/a	x	✓	✓	✓	x	✓	✓	✓	✓	✓	✓	✓	✓	✓
Appropriate blinding	x	x	x	x	x	n/a	✓	✓	✓	✓	x	✓	✓	✓	✓	✓	✓	✓	✓	✓
Baseline groups' characteristics similar	✓	✓	✓	✓	✓	✓	x	x	✓	x	x	x	x	x	x	x	x	x	x	x
Participant dropout described	x	x	x	x	x	x	x	x	x	x	✓	x	x	x	x	x	x	x	x	x
Sample size power calculation used	x	x	x	x	x	x	x	x	x	x	✓	x	x	x	x	x	x	x	x	x
Dosage stated	✓	x	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	x	✓	✓	✓	✓	✓	✓	✓
Comparator (control) appropriate	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Outcome measures described	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Outcome measures relevant	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Timing appropriate	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Total score (12)	7	7	8	8	7	7	7	10	9	9	9	10	8	10	10	10	10	11	11	8

✓, Yes; x, No or information not stated in text; n/a, category not applicable due to nature of the trial.

was measured and a significant increase ($p < 0.01$) was observed only in the BAT group, so it may well be the case that abdominal fat plays a pivotal role in capsaicinoids and capsinoids biological function.

It may be that capsaicinoid/capsinoid treatment is more beneficial, for those with higher levels of adipose tissue. Fat oxidation was significantly correlated with BMI in a 4 week trial (Inoue et al., 2007). The detected increase in fat oxidation was only significant when analysis was performed on subjects with a BMI greater than 25.

Appetite

Of the seven trials investigating capsaicin's effect on appetite, five found potentially beneficial effects for weight management (see Table 3). Reductions in energy intakes were observed after participants consumed capsaicin containing foods and were then given the chance to eat meals *ad libitum* (Yoshioka et al., 1999, 2004; Westerterp-Plantenga et al., 2005). A capsaicin containing breakfast significantly reduced participants rating of their hunger and their desire to eat before lunch (Yoshioka et al., 2004). Satiety was also observed to be significantly increased ($p < 0.01$) after a capsaicin rich meal (Westerterp-Plantenga et al., 2005).

The effect would seem to be in part (but not entirely) sensory, with three trials investigating whether the effect requires oral stimulation ('heat' sensation in the mouth) from capsaicin (Ludy & Mattes, 2011; Westerterp-Plantenga et al., 2005; Yoshioka

et al., 2004). All three studies found a decrease in appetite independent of whether participants received an oral or non-oral exposure of capsaicin, however, the effect was greatest following oral exposure. No studies were found that investigated the long-term effects on appetite; four of the seven studies were single meal trials.

It has also been proposed that individuals may become desensitised to capsaicin with effects diminishing over time. This was observed in one 6 day trial where the population was divided into those that regularly consume capsaicin versus low consumers. It was observed that there was less of an effect on appetite amongst those that were consuming capsaicin prior to the trial (Ludy & Mattes, 2011).

Discussion

In conclusion there is evidence that capsaicinoids and their sister compounds, capsinoids could play a beneficial role in weight management. Increasing a person's energy expenditure, lipid oxidation and reducing their appetite could be of great assistance in helping and maintaining weight loss.

The weight of evidence is largest for an effect on energy expenditure. The vast majority of studies investigating this area found an effect (13 of 15). The effect, however, seems to be marginal (around 50 kcal/day), and whether this is enough to make a worthwhile impact has been questioned (Galvani & Ravussin, 2010). It may well be the case that longer intervention periods are needed to produce meaningful effects.

It is well accepted that the mechanism of action for this effect is caused by activation of the TRPV1 (transient receptor potential vanilloid type-1) calcium channel, of which capsaicin is a potent antagonist (Tominaga & Tominaga, 2005). A 2009 study found that capsinoids increased the energy metabolism in wild-type mice, but not in TRPV1 knockout mice (Kawabata et al., 2009). It seems TRPV1 activation cause the release of catecholamines, which stimulates the sympathetic nervous system via Beta-adrenoceptors (Hursel & Westerterp-Plantenga, 2010). In another trial, the use of Beta-adrenergic blocker propranolol abolished the increase in thermogenesis in human subjects (Yoshioka et al., 1995). There are also suggestions capsaicinoids/capsinoids may have an effect on other intestinal receptors (Luo et al., 2011).

Evidence also suggests that capsaicinoids have beneficial effects on lipid oxidation and centrally stored adipose tissue; with effects being more pronounced in individuals with a high BMI. High body fat levels are associated with adverse health outcomes including cardiovascular disease and metabolic syndrome (Laurson, Eisenmann, & Welk, 2011). Regular consumption could therefore have major health benefits for takers, even without major weight change. An effect on central adipose tissue could offer particular health benefits, as it plays an important role in the development of cardiovascular diseases, as well as insulin resistance and type II diabetes (Gustafson, 2010). Statistically significant effects on these outcomes were observed in 7 of the 11 trials investigating this area. Like energy expenditure, it may be that longer intervention periods are required to produce significant clinical effects.

The mechanism of action for increasing lipid oxidation and reducing fat tissue may also be due to activation of the TRPV1 channel. Evidence suggests that capsaicin promotes calcium entry that is necessary to prevent preadipocyte-to-adipocyte differentiation. TRPV1 activation may ultimately reduce the number and size of fat cells, and therefore reduce the propensity for obesity to develop (Zhang et al., 2007).

Fewer trials have studied the inter-relationship between capsaicinoid compounds and appetite. Effects observed include reducing energy intake and increased satiety. The results from these trials are consistent, providing evidence for beneficial appetite outcomes. Although all the trials were relatively short (the longest being 8 days) and there is concern effects may be only last in the short term. All studies involved capsaicinoids, no trials were found that investigated the effect of capsinoids on appetite.

Although an effect on appetite has been observed in several trials, the mechanism of action for this is not understood. Consumption has been shown to cause an increase in gut derived hormones, which may be affecting hunger (Smeets & Westerterp-Plantenga, 2009). It may be that the release of catecholamines caused by capsaicin, is influencing appetite. Stimulation of the noradrenergic receptors, to produce feelings of satiety, is the target of most appetite suppressant drugs (Bray, 1993). Although concern about side-effects have meant the withdrawal of such drugs from the market (Khan et al., 1998).

It is possible that capsaicinoids have synergistic weight loss effects with bioactive ingredients. For example, significant weight loss was observed in an 8-week trial combining capsaicin with catechins, tyrosine and caffeine (Belza, Frandsen, & Kondrup, 2007). Equally, the combined effects of capsaicin and green tea supplements reduced appetite and energy intake in a 6-week trial (Reinbach, Smeets, Martinussen, Moller, & Westerterp-Plantenga, 2009). Evidence suggests that both types of compound have similar potency in stimulating the TRPV1 receptor (Iida et al., 2003; Sasahara et al., 2010). However, due to their structure capsinoids cannot reach TRPV1 receptors in the mouth.

Another key factor in the influence of these compounds may well be the dosage given. Although it is not clear from this evidence what would be an optimum level would be. Further

investigation in this area would be very informative. In particular, the dosages used in capsinoid trials have tended to be low (highest 12 mg/day) in comparison to capsaicinoids trials.

Finally, one of the main problems of weight loss using only diet and exercise, is a reduction in resting metabolic rate (Curioni & Lourenco, 2005). This has been successfully counteracted by the use of bioactive compounds that increase metabolism (Coffey, Steiner, Baker, & Allison, 2004), however, their side-effects have meant that they are generally not recommend for widespread use (Josse et al., 2010). Capsaicinoid and capsinoid compounds may provide a safe alternative, suitable for long-term use.

Although effects observed in this body of work are subtle, they should not be interpreted as insignificant. Small dietary changes exert small effects on energy balance, but cumulatively, they may contribute to weight loss or maintenance (Hill, Wyatt, Reed, & Peters, 2003). They could play a key role as part of a weight management programme.

On the whole, there is evidence that capsaicinoids and capsinoids can play an active role in increasing energy expenditure. There is also evidence that these compounds may help to promote lipid oxidation but the effects on appetite are less clear. Capsaicinoids and capsinoids may have a role to play in weight management problems, alongside the use of diet and exercise but clearly longer, well-designed trials are needed. Further clarification is needed in terms of the specific 'doses' needed to yield the desired health benefits.

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