Table 1. Overview of rodent studies, clinical trials and *in vitro* assays addressing BAT-mediated thermogenesis by phytochemicals and their impact on energy expenditure and weight control.

Pterostilbene	blueberries, berries, wine, wine grapes, sorghum[1]			
Reference and model	Design	Sex and N	Treatment	Outcome
[2] Golden Syrian Hamsters	DI	male n=8-10 per group	2.5 mg/kg BW/d in HFD 3 weeks	-BW plasma ↓C, ↓LDL, ↓LDL:HDL
[2] rat hepatic H4IIEC3 cells		male	1,10,100 or 300 µM PTS 30 min	↑PPARα reporter activity
[3] Zucker fa/fa rats	DI	male n=10 per group	15 mg/kg BW/d in HFD 6 weeks	↓BW, ↓fat mass plasma ↓C, ↓insulin
[4] Wistar rats	DI	male n=9 per group	15 or 30 mg/kg BW/d in HFHS 6 weeks	↓BW gain, ↓total fat mass, ↓vWAT, ↓sWAT ↑hepatic CPT1α and ACOX activity
[5] Zucker fa/fa rats	orogastric catheter	male n=10 per group	0, 15 or 30 mg/kg BW/d in chow diet, 6 weeks	↓BW, ↓AT weight ↑iBAT mRNA/protein: NRF1, UCP1, PPARα ↑iBAT CPT1b activity
[6] OLETF rats	DI	male n=6 per group	300 mg/kg BW/d in chow 4 weeks,	-BW, ↓abdominal WAT, ↓total WAT ↓RER, ↑FO, ↑EE ↓WAT FAS mRNA
[7] C57BL/6 mice	DI	male and female n=8 per group/sex	90 mg/kg BW/d in HFD 30 weeks	↓BW, ↑glucose tolerance (after 18 weeks) ↑iWAT thermogenic genes (PPARγ, PGC1α, SIRT1, CIDEA, TBX1), ↑iWAT UCP1 protein ➢ effects in m+f, stronger than in f vs m
[7] 3T3-L1 adipocytes	acute	male	5 µM PTS for 24 hours, d12	↑UCP1 protein, ↑CIDEA, FGF21 mRNA

[8] hypercholesterolaemic Caucasian, AA	placebo parallel	male and female 100 mg/d, n=20 (m5/f15) 250 mg/d, n=20 (m6/f14) placebo, n=20 (m7/f13)	100 or 250 mg/d 6-8 weeks	-BMI (if stratified for C medication ↓BMI) plasma ↑total C, ↑LDL, -HDL
Resveratrol	peanuts and peanut products, grapes, red wine, soy, herbal remedies[9]			
[10] C57Bl/6J mice	DI	male n=8-10 per group	400 mg/kg BW/d in HFD 15 weeks	↓weight gain, ↓final BW, ↓WAT mass ↑VO_2, ↑cold-resistance (rectal T) ↑iBAT mito content, ↑iBAT thermogenic genes (UCP1, PGC1α, PPARα) ↑mito gene enrichment in muscle, ↑IS
[11] C57BL/6NIA	DI	male n=6-9 per group	22.4 mg/kg BW/d in HFD middle aged mice, for 55 weeks	-fat distribution, -BW (trend for↓), ↑IS, -BT ↑survival plasma -TAG, ↑C, ↓GLC, ↓insulin
[12] grey mouse lemur (*Microcebus murinus*)	DI Before-after	male n=6	200 mg/kg BW/d 4 weeks	↑RER, ↓weight gain vs baseline week ↓food intake, -locomotor activity
[13] mice (strain unknown)	DI	male n=8 per group	0.4% w/w in chow diet 8 weeks	↓WAT mass, -BW, ↑VO_2, -locomotor activity ↑iBAT thermogenic genes (UCP1, PRDM16, SIRT1), plasma -C, -TAG, -GLC
[14] CD-1 mice	DI	female n=6 per group	0.1% w/w in HFD 4 weeks	↓BW gain, ↑VO_2, ↓RER, ↑EE (p=0.065), ↑UCP1+ in iWAT sections, ↓iWAT adipocyte size ↑pAMPK, UCP1, PRMD16 protein in iWAT plasma ↓insulin, ↓TAG, -GLC

[14] SVF from iWAT of CD-1 mice	long-term	unknown	10 µM RSV during differentiation with brown adipogenic cocktail	↑thermogenic genes (UCP1, ELOVL3, PGC1α, CIDEA, PRDM16), ↑UCP1, PRDM16 protein ↑respiration, ↑pAMPK ➢ effects AMPK-dependent
[15] CD-1 mice	DI	female	0.1% RSV w/w in HFD 4 weeks	↓BW gain, ↑BA number in iBAT sections ↑iBAT UCP1. PRDM16 and pAMPK protein
[16] Spargue-Dawley rats	DI	male n=8 per group	30 mg/kg BW/d in HFHS 6 weeks	-BW, ↓fat mass ↑BAT thermogenic genes (UCP1, PGC1α, TFAM) ↑iBAT UCP1 protein, ↓acetylated PGC1α (muscle)
[17] obese, healthy (BMI>30) Denmark	placebo parallel	male n=12 per group	500 mg RSV or placebo tablet/d 4 weeks	-BW, -total fat mass, -vWAT mass, plasma –GLC, -C, -TAG,-ALT, -HbA1c -acetylated lysine, pAMPK in muscle
[18] non-obese, normoglycaemic Caucasian	placebo parallel	female RSV n=15 placebo n=14	75 mg RSV/d 12 weeks	-BW, -fat mass, -sWAT mass, -vWAT mass plasma -leptin,-C, -TAG, -NEFA, -GLC -REE, -BP, -IS -WAT microarray: -mito function, -FO genes -muscle SIRT1 activity
[19] older adults with IGT US	before-after	male n=3 female n=7	1, 1.5 or 2 g RSV/d 4 weeks	-BW, -fat mass, -BP plasma –C, -TAG, -insulin, -ALT, -insulin ↓post-meal GLC, ↓post-meal insulin
[20] obese, healthy men	placebo crossover	male n=11	150 mg RSV/d (resVida) or placebo, 30 days per treatment	-BW, -fat mass ↓SEE (caloric restriction), ↑diurnal RER muscle ↑pAMPK, ↑mito activity, ↑SIRT1, PGC1α protein
Quercetin	apples, onions, black currants, red wine, black tea, nuts, seeds, shallots[21]			
[22]	DI	male	0.36% or 0.72% w/w OPE in	↓BW, ↓intra-abdominal fat mass

Sprague–Dawley rats		n=7 per group	HFD, 8 weeks	
[23] Wistar rats	DI	male n=12 per group	185, 270, 925 mg/kg BW/d in HFD 8 weeks	↓BW gain, ↓total fat mass, ↓vWAT plasma ↓TAG, ↓NEFA, -C, ↓GLC at high dose ↓hepatic fat content, ↑fecal lipids ↑PPARα, ↑SIRT1, ↓ACC, ↓FAS mRNA (WAT)
[24] Zucker fa/fa rats	oral gavage	male n=7 per group	10 mg/kg BW/d RSV or vehicle with HFD 10 weeks	↓BW gain plasma ↓TAG, ↓C, ↓GLC, ↓insulin, ↓HOMA-IR ↓TNFα production, iNOs protein in vWAT
[25] C57BL/6	DI	male n=6 for OPE n=9 for control	0.5% w/w OPE in HFD 8 weeks	-BW gain, -eWAT mass, -rWAT mass ↑thermogenic genes (UCP1, PRDM16, CIDEA, PGC1α) in rWAT
[25] 3T3-L1 adipocytes	long-term	male	100 µM quercetin at d5, 7, 9	↑ UCP1, SIRT1, PGC1α mRNA and protein ↑pAMPK, pHSL, ↓lipogenic genes (FAS, ACC)
[26] C57BL/6	DI	male n=8-10 per group	0.1% w/w quercetin in HFD 8 weeks	-BW, -fat mass, -EE, -RER, -FO, -CHO, ↓plasma TAG ↑sWAT thermogenic genes (UCP1, ELOVL3) ↑UCP1+ cells in sWAT, ↑FA uptake in sWAT -mito content sWAT, -BAT morphology/genes
[27] C57BL/6J	DI	male n=8 per group	0.8% w/w in HFD 8 weeks	-BW, -adiposity, -EE, -RER ↓plasma inflammatory cytokines (INFγ, IL1, IL4)
[28] C57BL/6	DI	male n=6 per group	0.05% w/w quercetin in HFD 9 weeks	-BW, ↓WAT adipocyte size ↑UCP1+ cells, ↑UCP1, ↑PGC1α protein in iWAT ↑iWAT thermogenic genes (UCP1, PRDM16, MEM26, NRF-1) ↑PKA, pAMPK protein in iWAT ↑plasma NE, ↑iBAT UCP1

(29) isolated Wistar rat adipocytes	acute	male	0, 1, 10, 100 or 250 µM quercetin, 15 min	↑PDE activity, ↑cAMP, ↑epinephrine-stimulated lipolysis
(30) C57BL/6	DI	male n=8 per group	0.1% w/w quercetin in HFD 12-17 weeks	↓BW, ↓sWAT mass, ↓eWAT mass, ↓eWAT cell size, plasma ↓leptin, ↓insulin, ↓TNFα, ↓IL6 ↓mast cell infiltration eWAT ↓eWAT TNFα, IL6 ↑eWAT SIRT1, pAMPK protein ↑iBAT UCP1 mRNA,
(31) university students healthy Korean	placebo crossover	female n=12	100 mg/d quercetin or placebo capsule for 2 weeks each	-BW, -fat mass, -WHR, -BMI, -SBP, -DBP plasma –TAG, -C, -LDL
(32) overweight/obese subjects (BMI>23 kg/m^2) Korean	placebo crossover	female quercetin n=18 placebo n=19	100 mg/d quercetin or placebo capsules 12 weeks	-BW, -fat mass, -BMI plasma –ALT,-leptin, ↑adiponectin, -TNFα, -IL4
(33) overweight/obese subjects Korean	placebo crossover	male n=5 female n=31	100 mg/d quercetin or placebo capsules 12 weeks	-BW, -fat mas, -BMI, -WC, -RER, -REE plasma –GLC, -C, -LDL, ↓TAG, -leptin -before-after effects on REE, BW, RER, BMI within quercetin group
(34) Meta-analysis	9 RCTs	male=189 female=336	100 to 1000 mg/d 2 to 12 weeks	-BW, -WC, -WHR, -BMI
Luteolin	peppers, carrots, cucumber, pomegranate, herbal spices, cabbage, broccoli, medicinal herbs (sage)[35]			
(36) C57BL/6	DI	male n=8 per group	0.01% w/w in HFD 12 weeks	↓BW, ↓sWAT mass, ↓vWAT mass, ↓BAT mass ↓eWAT adipocyte size, ↑IS ↓mast cell infiltration eWAT plasma –insulin, ↓leptin, ↑adiponectin

(37) C57BL/6	DI	male n=13 per group	0.005% w/w in HFD 16 weeks	↓BW, ↓sWAT mass, ↓vWAT mass plasma ↓TAG, ↓C, ↓NEFA, ↑IS ↑eWAT FAO genes (PGC1α, ADRB3, CPT2, PNP2, ACAD)
(38) C57BL/6	DI	male n=8 per group	0.01% w/w in HFD 20 weeks	↓BW, ↑IS ↓plasma MCP1, IL6, TNFα ↓macrophage infiltration vWAT, ↓M1/M2-ratio
(39) C57BL/6	DI	male n=12 per group	0.01% w/w in HFD 12 weeks	↓BW, ↓weight gain, ↓fat mass ↑VO_2, ↑CO2, ↑RER, ↑BAT UCP1 protein ↑UCP1+ cells in sWAT, ↑thermogenic genes (PGC1α, UCP1, SIRT1, PPARα, ELOVL3) ↑SIRT1, pAMPK, pACC protein in BAT, sWAT
(39) primary subcutaneous and brown adipocytes	acute	unknown	24 hours of 100 nM luteolin on differentiated cells	↑SIRT1, UCP1, PGC1α protein ↑pAMPK, ↑pACC ↑thermogenic genes (UCP1, PRDM16, ELVOL6, PPARα) ➢ effects AMPK-dependent
Catechins	grapes, apples, strawberries, apricots, broad beans, cocoa-products, green/black/oolong tea[40,41]			
(42) Sprague-Dawley rat	DI	male n=8 per group	2% w/w green tea extract in HFD, 2 weeks	-BW, ↓fat mass, ↑BAT weight ↑BAT DNA/protein content ↑EE, propranolol prevented ↑EE
(43) Sprague-Dawley rat	DI	male n=8 per group	0.5% w/w catechins in chow 8 weeks	-BW ↑BAT mass, ↓pWAT mass, ↓eWAT mass ↑BAT UCP1 expression plasma ↓TAG, GLC, leptin
(44) New Zealand black mice	gavage short-term	male n=6 per group	3x 500 mg/kg EGCG or placebo, chow diet	-BW, -fat mass -EE, ↓RER (p=0.053), -activity

[44] New Zealand black mice	DI	male n=11 per group	0.1% w/w EGCG in HFD DIO 4 weeks, DI 4 weeks	↓BW, ↓fat mass, -food intake, ↓eWAT weight plasma ↓TAG, -NEFA -UCP1 mRNA in BAT
[45] iBAT depots from Sprague-Dawely rat	acute	male	100 or 200 µM green tea extract for 40-90 min	↑iBAT respiration (100 µM) ↑norepinephrine (0.1 µM) stimulated respiration at 100 or 200 µM
[46] healthy men Geneva, CH	placebo crossover	male n=10	3x daily capsule with 50mg caffeine and 80 mg EGCG, 50 mg caffeine or placebo	↑diurnal EE, ↑total EE, -nocturnal EE ↓total, diurnal and nocturnal RER ↑FO, ↑urinary norepinephrine excretion
[47] young, healthy subjects Lausanne, CH	placebo crossover	male n=15 female n=16	3x daily beverage with 100 mg caffeine and 180 mg catechins or placebo, 3 days	↑total EE, diurnal EE, nocturnal EE -substrate oxidation -catecholamine secretion
[48] healthy men (BMI 23-27 kg/m^2) Laval University, CA	placebo crossover	male n=14	3x daily capsule with 200 mg caffeine plus 90, 200, 300 or 400 mg EGCG or placebo	↑total EE, -SEE -RER,-FO -catecholamine secretion
[49] overweight/obese men (BMI=31 kg/m^2) Berlin, DE	placebo crossover	male n=10	300 or 600 mg EGCG or placebo capsule for 3 days	-EE (pre- and post-meal) ↓post-meal RQ, ↑post-meal FO (300 mg), ↓post-meal CHO (300 mg) plasma -NEFA,-insulin, GLC
[50] Meta-analysis effect of EGCG on EE or anthropometric measures	8 RTC	n=268	EGCG: 300 or 600 mg/d for 2-3 days 300 to 800 mg/d for 2-12 weeks	↑EE, ↓RER, -FO, - BMI, ↓WC, -fat percentage
[51] healthy men Japanese	placebo crossover	male n=15 low BAT activity (mean SUV=1.9)	615 mg catechins plus 77 mg caffeine or placebo (81 mg caffeine), 2x daily as beverage for 5 weeks	-BMI, -fat mass, -WC, -EE ↑cold-induced thermogenesis, ↑cold-induced FO

[51] healthy men Japanese	acute crossover	male n=15	615 mg catechins plus 77 mg caffeine or placebo (81 mg caffeine), single beverage	↑post-drink EE, ↑EE in high BAT (SUV>2) vs low BAT subjects, pre-assessed by 2 hours cold-exposure
[52] healthy university students Japanese	placebo parallel	female catechin n=10 placebo n=11	640 mg catechins/d or placebo, beverage 12 weeks	-BMI, -fat mass, -BW ↑BAT density in supraclavicular region neg. correlation between EMCL and BAT density
[53] overweight/obese children Japanese	placebo parallel	catechin group (m21, f5) placebo group (m13, f6)	576 mg/d catechins or placebo (75 mg/d catechins), as Oolong tea, 12weeks	-no changes in anthropometric or metabolites in catechin vs control ↓WC, ↓SBP, ↓LDLC in catechin group when stratified to baseline values
[54] normal to overweight men Japanese[36]	placebo parallel	male catechin group n=17 placebo group n=19	690 mg/d catechins or placebo (22 mg/d), as Oolong tea, 12weeks	↓WC, ↓skinfold thickness, ↓total fat area ↓visWAT and sWAT area plasma –NEFA, -TAG, -C, -GLC, -insulin
[55] obese adult Thais (BMI>25kg/m^2)	placebo parallel	catechin group: (m21, f9) placebo group: (m21, f9)	3x daily 250 mg catechins or placebo in capsule 12 weeks	↓BMI, ↓BW, ↓fat mass, ↓WC, -HC ↓RER, ↑REE
[56] overweight/obese adults (BMI >25-32 kg/m^2) Caucasian	before-after	female n=63 male n=7	270 mg/d EGCG in capsule	-BW, ↓WC -SBP, -DBP plasma -C
[57] Meta-analysis effect of green tea extracts on anthropometry	15 RTCs	n=1243	catechin intake combined with caffeine intake (141 up to 1207 mg/d) 8 to 24 weeks	↓BMI, ↓BW, ↓WC, -WHR when compared to caffeine-intake only
Phytoestrogens	kidney beans, mung bean sprouts, Japanese arrowroot, soybean, soy products (tofu, soy milk, soy flour, soy sauce)[58]			

(59) C57/B6J mice	DI	male n=7-8	5% isoflavone-rich fraction of *Puerariae* flower in HFD, 7 weeks	↓BW, ↓WAT mass, ↓BAT mass -food intake, -fecal lipid content ↑VO_2, -RER, ↑UCP1+ cells in BAT sections
(60) CD-1 mice	DI	male n=12 female n=12	25% w/w soy-rich diet (150 pmm daidzein, 190 ppm genistein) vs soy-free diet 16 weeks	↓BW, ↓intra-abdominal fat mass, ↓iWAT, ↓eWAT/ovWAT, ↓WA adipocyte size ↓BAT mass (male), ↑brown appearance, ↓lipid droplet size ↑cold-resistance (rectal T), ↑VO_2, ↓RER (only male data available)
(61) Sprague-Dawley rats	ovx DI	female n=10 per group	isoflavone-rich (200 µg/g) or isoflavone-free diet 13 days	↓BW gain, ↓abdominal fat mass ↓serum leptin
(62) Long-Evans rats	DI	male	isoflavone-rich (600 ppm) or isoflavone-free (10-15 ppm) diet up to 75 days of age	↑food intake, ↓BW gain, ↓WAT mass, ↓BAT mass plasma ↑T3, ↓insulin, leptin ↑UCP1 protein in BAT
(63) Wistar rats	DIO with DI	male n=16 per group	50 mg/kg BW daidzein or vehicle, i.p. DIO 10 weeks, 14 d treatment	↓caloric intake, ↓BW gain ↓hepatic liver content plasma ↓TAG, -C, ↑GLC, -ALT ↑UCP1 protein in BAT
(64) ICR mice	DIO with gavage	male	0, 25, 50 or 100 mg/kg BW DIO 8 weeks, 30 d treatment	↓BW. ↓vWAT mass, ↓sWAT mass plasma ↓C, ↓LDL, ↓NEFA, -TAG, ↑HDL
(64) primary adipocytes differentiated from eWAT SVF	acute	male	0, 1, 3, 16, 64 µM daidzein 24 hours	↑glycerol release (dose-dependent)

[65] adipocytes from Wistar rats	acute	male	0.01, 0.1 or 1 mM daidzein	↑basal lipolysis (dose-dependent) ↑epinephrine-stimulated lipolysis (0.1 mM) ↓lipogenesis from GLC (0.1 and 1 mM)
[66] C57BL/6	DI	female n=8 per group	0.25% w/w genistein in HFD 8 weeks	↓BW, -sWAT weight, -vWAT weight ↓BAT weight (ns), ↑IS plasma –TAG, -C, HDL-, ↓LDL, ↓NEFA ↑iWAT browning (UCP1, CIDEA mRNA) ↑ hypothalamic UNC3 mRNA
[67] C57BL/6	DI	male n=7-8 per group	0.2% w/w genistein in casein diet or casein only (control) 60 days	-BW, ↑glucose tolerance ↑thermogenic genes in sWAT (UCP1, PGC1α) ↑UCP1 protein in sWAT,-BAT ↑EE, ↑VO_2, ↑cold-resistance (rectal T), -RER plasma –TAG, ↓GLC, ↓insulin
[67] primary adipocytes from iWAT of mice	acute	unknown	0, 5, 15, 30 µM genistein for 1 hour	-basal respiration ↑maximal respiration
[68] immortalized brown adipocytes	long-term	unknown	0, 0.1, 1 or 40 µM of genistein on differentiated adipocytes, 3 days treatment	↑UCP1 promoter activity (luciferase) ↑UCP1 activity (immunofluorescence intensity)
[69] C57BL/6	oral gavage	male and female	50 to 200 mg/kg BW genistein or vehicle for 15 d	↓BAT mass, ↓eWAT (m), ↓abdominal WAT (f) plasma ↓TAG, ↓C for 50 mg/kg BW
[70] postmenopausal women (BMI=23.6 kg/m^2) Chinese, equol-producer	placebo parallel	female n=90 per group	40 g soy flour, 40 g low-fat milk powder with 63 mg daidzein, 40 g low fat milk powder (placebo) daily, 6 months	-BW, -BMI, -WC, -HC, -WHR, -fat mass

(71) adolescent males Tasmania	placebo parallel	male isoflavone n=69 placebo n=59	50 mg isoflavone equivalents or placebo tablets daily 6 weeks	-BW
(72) obese women (20-65 yrs) (BMI 30-40 kg/m^2) USA	placebo parallel	female soy group n=22 casein group n=21	3x daily soy (50 mg isoflavone) or casein (3.5 mg isoflavone) shake, 16 weeks	-WC, -weight loss, -fat mass, -truncal fat -SBP, -DBP
(73) impaired glycemic control Chinese women (30-70 yrs)	placebo parallel	female daidzein n=55 genistein n=56 placebo n=54	10 g soy protein with no addition, 50 mg daidzein or 50 mg genistein 24 weeks	-BMI, -WC, -fat mass -IS
(74) patients with NAFLD Iranian (16-69 yrs)	placebo parallel	genistein group (m30, f11) placebo group (m31, f10)	250 mg daidzein or placebo capsules 8 weeks	-BW, ↓fat percentage, ↓WHR, ↓WC, -BMI plasma ↓TAG, -C, -LDL, -HDL, ↓insulin ↓HOMA-IR
(75) postmenopausal women (BMI>30 kg/m^2) Caucasian or AA	placebo parallel	soy group (n=17) 8 AA, 9 Caucasian placebo (n=16) 8 AA, 8 Caucasian	soy protein with isoflavones (160 mg) or placebo casein, shake 3 months	-BW, -total fat, -lean mass ↓abdominal, ↓subcutaneous abdominal fat, ↓vWAT for AA: weight loss more than for Caucasian for Caucasian: vWAT loss bigger than for AA plasma ↓IL6, -CRP, -TNFα, -leptin, -HDL, -LDL, -C, -TAG
(76) postmenopausal women (mean BMI=30.5) Caucasian	placebo parallel	female soy group n=9 placebo n=6	soy protein with isoflavones (160 mg) or placebo casein, shake 3 months	-BMI, -BW, -total fat mass, -IS ↓subcutaneous abdominal fat, ↓intra-abdominal fat plasma -GLC, -insulin

(77) Meta-analysis Effect of soy-isoflavones on BW in non-Asian, postmenopausal women	9 RCTs	isoflavones n=272 placebo n=256	40 to 160 mg/d of isoflavones 8 weeks to 1 year	↓BW with isoflavone intake <100 mg or <6 months more effective more effective with BMI<30 kg/m^2
(78) Meta-analysis effect of soy and isoflavones on anthropometric measures	24 soy RTCs 17 isoflavones RTCs	soy: f1265, m45 (1 RTC) m/f =74 (mixed) isoflavones: f1177, m0	soy protein: 7.5 to 116 mg/d 4 weeks to 2 years isoflavones: 33.3 to 300 mg/d 8 weeks to 2 years	soy: -BW, >40 g/d ↑BW, 1-3 months ↑weight gain -WC, -fat mass isoflavones: ↓BMI for postmenopausal and Caucasian women <100 mg and 2-6 months more effective -fat mass, -WC
Capsaicinoids	chili, bell peppers, jalapenos, habaneros, cayenne pepper, red pepper[79,80]			
(81) Std ddY mice	intragastric tube	unknown n=6-8	vehicle, 10 mg/kg BW capsaicin or 10, 50 mg/kg BW capsiate, 2 weeks	↓BW (ns), -food intake -BAT mass, ↓eWAT for capsiate, ↓pWAT for capsaicin and 50 mg/kg capsiate
(81) Std ddY mice	intragastric tube, acute	unknown n=6-8	Vehicle, 10 mg/kg BW capsaicin or 10 mg/kg BW capsiate, 3 hours	↑VO_2 for capsaicin and capsiate, ↑serum adrenaline plasma ↑NEFA, ↓TAG
(82) C57BL/6 or TRPV1 -/- mice	intragastric tube, acute	male n=5-18	vehicle, 10 mg/kg BW capsaicin or 10 mg/kg BW capsiate, 3 hours	↑VO_2 (capsaicin, capsiate at 10 mg/kg BW) ↑FO (capsaicin, capsiate at 10 mg/kg BW), ↓CHO ↑BAT and colonic T (50 mg/kg capsinoids, 10 mg/kg capsaicin) ↓T increase after denervation of jejunal nerves at 50 mg/kg capsinoid - effects in wt but not TRPV-/- mice
(83) TRPV1 -/- or wt mice	DI	male	0.01% w/w capsaicin in HFD 32 weeks	↓weight gain, ↓BW, ↑BAT UCP1, BMP8b protein

B6.129X1				↑activity, ↑RER, -food intake, ↓BAT TAG content, ↑BAT glycerol release (basal or forskolin-stimulated) ↑TRPV1 protein in BAT ↑Ca^{2+} influx in isolated BA (2 µM CAP) ↑pAMPK, pSIRT1 in BAT ↓PRDM16, PPARγ acetylation (HEK293 1 µM CAP), ↑PRDM16 and PPARγ interaction in BAT lysate ➢ effects blunted in TRPV-/- vs wt mice
[84] TRPV1 -/- or wt mice B6.129X1	DI	male n=40 per group	0.01% w/w capsaicin in HFD 26 weeks	↓weight gain, ↑TRPV1 mRNA in iWAT, eWAT ↑EE, ↑activity, -fecal lipid content, ↑RER, ↑VO_2 ↑UCP1, BMP8b, PPARα/γ protein in s/eWAT, ↑sWAT lipolysis (basal, forskolin-stimulated) ↓PRDM16, PPARγ acetylation in sWAT ↑pAMPk, CaMKKII activation in sWAT ↑Ca^{2+} influx in isolated WA (2 µM CAP) ➢ effects blunted in TRPV-/- vs wt mice
[85] C57BL/6	DIO+DI	male n=6 per group	0.01% w/w capsaicin in HFD DIO 10 weeks, 10 week DI	↓BW, ↓weight gain, ↑eWAT, ↓rWAT mass -food intake, ↓WAT adipocyte size ↑glucose tolerance, ↑adiponectin, ↓leptin ↑TRPV1 expression WAT
[86] Sprague-Dawley rats	intra-muscular	female n=9-18 per group	0.6, 0.7, 0.8 mg/kg BW capsaicin or DMSO, 80 to 120 min	↑BAT and rectal T with 0.8 mg/kg BW -BAT weight, -mito content ↑BAT respiration
[87] Std ddY mice	intragastric tube	male n=9-10	10 mg/kg BW capsiate or vehicle, 2 weeks	-BAT mass, ↓eWAT, ↓pWAT ↑VO_2, ↑FO, ↑CHO, ↑UCP1 protein (BAT) ↑UCP1 mRNA (eWAT, BAT),

(87) Std ddY mice	intragastric tube, acute	male n=4 per group	10 mg/kg BW capsiate or vehicle for 30 min	↑UCP1 mRNA in BAT
(88) healthy young men British	acute	male	breakfast with 3g chili sauce	↑post-meal EE
(89) long distance runners Japanese	acute crossover	male n=8	breakfast with or without 10 g red pepper	↑post-meal EE (30 min) ↑RER, ↑CHO, ↓FO ➢ effect blocked by propranolol
(90) healthy young men Caucasian	placebo crossover	male n=10	appetizer with or without 6 g of red pepper	↓energy intake at lunch and dinner ↑sympathetic: parasympathetic nerve activity
(91) healthy lean subjects Caucasian	placebo crossover	male n=11 female n=19	1030 mg red pepper in lunch	-EE post-meal -RER -CHO, -FO, ↑peak plasma GLP-1,-ghrelin
(92) overweight subjects (mean BMI=29.4 kg/m^2) Caucasian, AA, other	placebo parallel	male (ethnicity) Placebo (16,9,3) 3 mg (15, 9, 1) 9 mg (10, 4, 2)	0, 3, 9 mg dihydrocapsiate in gel capsule 4 weeks	-RMR (p=0.054 for 3 mg vs placebo) ↑RMR dihydrocapsiate vs placebo
(93) Meta-analysis effect of capsaicin or capsiate on EE, RER	capsiate on EE 13 RCTs capsiate on RER 9 RCTs capsaicin on EE 13 RCTs capsaicin on RER 10 RCTs female/male unknown		capsaicin doses: <7, 20-35 mg, 135-150 mg/d dihydrocapsiate doses: <1.5, 2-4 or 6-9 mg/d	↑EE at 2-9 mg/d for capsiate ↑EE at 135-150 mg/d for capsaicin ↑FO at 6-9 mg/d capsiate ↑FO at 20-150 mg/d for capsaicin ↑SNS activity (1 RCT)
(94) healthy adult participants (BMI 20-30) Caucasian	acute controlled	N=15 per group (m8, f7)	0 or 7.68 mg/d capsaicin with 100% or 75% of daily energy requirements 26 hours	-TEE 100% CAP vs 100% control (c) -DIT 75% CAP vs 100% c, ↓75 % c vs 100% -REE 75% CAP vs 100% c, ↓75 % c vs 100% ↑FAO 75% CAP vs 100% c, -75 % c vs 100% ↓CHO 75% CAP vs 100% c

[95] healthy adults BMI 25-30 kg/m^2 44% Hispanic, 41% white, non-Hispanic, 13% black, 2% others	placebo parallel	capsinoids (m21, f22) Placebo (m17, f20)	6 mg capsinoids or placebo capsule with MCTG, rapeseed oil 12 weeks	-BW, -fat mass, -abdominal fat -EE (only m): 54 kcal/d higher with CAP (p=019) -FO (only m): 21 mg/min higher with CAP (p=0.06)
[96] lean, healthy subjects Singapore	crossover cold vs capsinoids	Male n=8, female n=12 BAT+ m6/f6 BAT- m2/f6	12 mg capsinoids in capsule with rapeseed oil and MCTG	↑FDG-uptake in BAT ↑EE, higher in BAT+ subjects ↑FO, ↓RER plasma –GLC, -TAG, ↑C, ↑NEFA
[97] young healthy men Japanese	placebo crossover acute	male n=18 BAT+ n=10 BAT- n=8	9 mg capsinoids or placebo capsule with rapeseed oil, MCTG 2 hours	↑EE in BAT+ with capsinoids vs placebo -RER, -skin T
Berberine	barberry, supplements from bark, root, stems or leaves from plants of the *Berberis* genus (e.g. goldenseal, goldthread, Oregon grape, tree turmeric)[98]			
[99] db/db mice	i.p.	male BBR n=17 vehicle n=16	5 mg/kg BW on chow diet 26 days	↓BW, ↓eWAT mass, ↓sWAT adipocyte size ↓intra-abdominal fat, ↑IS, ↑BAT mRNA, PPARα, PGC1α ↓FAS ↓WAT mRNA FAS, PPARγ, SREBP1c, aP2
[99] 3T3-L1 adipocytes	acute	male	5 µg/mL BBR for 60 min	↑pAMPK, ↑pACC
[100] db/db mice	long-term i.p	male n=5 per group	5 mg/kg BW on chow diet 26 days at 22°C or 30°C	↓BW, ↓fat mass, ↓plasma NEFA ↑rectal T, ↑VCO_2, ↑VO_2, ↑EE ↑cold-resistance (core T) ↑BAT activity (PET/CT) ↑BAT mito content, ↑oxphos, ↓BAT mass ↑BAT UCP1, PGC1α, CPT1, pAMPK protein

				↑iWAT thermogenic genes (UCP1, NRF1) ↑UCP1+ cells, ↑mito content, ↑UCP1 protein ➢ effects blunted at 30°C
(101) C57BL/6	DI	male	5 mg/kg BW, i.p. on chow diet, 4 weeks	↑hepatic FGF21 expression, ↑plasma FGF21 ↑iBAT mRNA (UCP1, DIO2, PRMD16)
(102) C57BL/6	DIO	male n=7-8	1.5 mg/kg BW/d on HFD DIO 8 weeks, DI 6 weeks	↓BW gain, ↓pWAT, iWAT mass ↑rectal T, ↑EE, ↑VO_2, ↑BAT activity, volume (PET/CT), ↑UCP1+ cells in BAT ↓BAT PRDM16 promoter methylation ➢ effects blunted in adiponectinCre AMPKα1/2 mice
(102) BAT SVF cells	long-term	male	250 nM BBR during differentiation until d8	↑basal and uncoupled respiration ↑BA adipogenesis (↑UCP1+ cells) ↑fatty acid oxidative BAT-specific genes ↑UCP1, PGC1α, PRDM16 protein
(102) patients with NAFLD mean BMI=29 kg/m2 China	before-after	not defined	1.5 g BBR/d 1 month	↓BW, ↓WC, ↓BMI, -total fat mass, ↓vWAT mass, ↓sWAT mass ↓HOMA-IR ↑BAT volume, BAT activity
(103) subjects with NAFLD China	controlled parallel	LSI (m32/f30) LSI+P (m28/f32) LSI+BBR (m38/f24)	LSI+1.5g BBR/d, LSI+15 mg/d pioglitazone, LSI only 16 weeks	↓hepatic fat content vs LSI, ↓BW, ↓BMI vs LSI and vs LSI+pioglitazone -HbA1c, ↓HOMA-IR vs LSI,
(104) newly diagnosed diabetics no pharmacotherapy China	placebo parallel	placebo (m38, f28) BBR (m31, f21)	1.5 g BBR/d or placebo 12 weeks	-BW, ↓BMI, -WHR plasma –FBG, ↓PBG, ↓HbA1c, -HOMA-IR, ↓C, - insulin, -TAG

(105) type 2 diabetics with poor glycemic control China	before-after	n=48 sex not stated	1.5 g BBR/d plus prescribed diabetes medication 12 weeks	↓WC, ↓WHR, -BMI plasma ↓FBG, ↓PBG, -TAG, ↓C, ↓insulin ↓HOMA-IR
(106) obese adults Caucasian	before-after	male n=2 female n=5	1.5 g BBR/d 12 weeks	-BMI, -WHR, - fat percentage plasma –GLC,-TAG, ↓C, ↓ALT, ↓AST -plasma inflammatory markers

AA, African American, BAT, brown adipose tissue; BBR, berberine; BW, body weight; BMI, body mass index, C, cholesterol; CHO, carbohydrate oxidation; d, day; DI, dietary intervention; DIO, diet-induced obesity; DIT, diet-induced thermogenesis; EE, energy expenditure; EMCL, extramyocellular lipid; f, female; FBG, fasting blood glucose; FO, fat oxidation; HC, hip circumference; HFHS, high fat high sucrose; IS, insulin sensitivity, IGT, impaired glucose tolerance; i.p., intraperitoneal; LSI, life style intervention; m, male; MCTG, medium chain triglyceride; mito, mitochondria(l); NAFLD, non-alcoholic fatty liver disease, NEFA, non-esterified fatty acids; ovx, ovariectomized, PBG, postprandial blood glucose; RCT, randomized controlled trial; REE, resting energy expenditure; RER, resting energy expenditure; SEE, sleeping energy expenditure; SUV, standardized uptake value; T, temperature; TAG, triacylglycerol, TEE, total energy expenditure; WC, waist circumference; WHR, waist-hip-ratio; WAT, white adipose tissue, wt, wild-type; - unchanged, ↓decrease, ↑increase compared to placebo or baseline

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