ELETRONIC SUPLLEMENTARY INFORMATION (ESI)

Table S1. Desing with *in vitro* studies and the main results

Authors	Cell	Carotenoid and dose	Duration	Main results
9. Liu, et al., 2017	3T3-L1 cells	5–30μM of Zeaxanthin	8 days	25 and 30μM had toxicity; 5, 10, and 15 μM zeaxanthin ↓ total lipid contents; Downregulation of PPARγ gene and level protein of the peroxisome proliferator-activated receptor γ (PPARγ) decreased in a dose-dependent manner; ↓ Acetyl CoA carboxylase (ACC), FAS, fatty acid binding protein 4 (FABP4), and perilipin; 5, 10, and 15 μM induced AMPKα activation.
10. Liu et al., 2019	3T3-L1 cells	5, 10 and 15 μM of zeaxanthin and cells on day 0 were pre-incubated with 10 μM compound C (CC), an inhibitor of AMPK.	8 days	↓ lipid accumuation; 10 and 15 μM ↑ UCP1 and SIRT1; 15 μM stimulated AMPK activation; ↓ ACC, and FABP4, and induced the expression of proliferator-activated receptor gamma coactivator 1 alpha (PGC1α), uncoupling protein 1 (UCP1), and sirtuin 1(SIRT1); AMPK activation were blocked with CC and the expression of adipogenic genes were induced, and browning-related genes reduced.
70. Mukherjee, S., & Yun, J. W. (2022)	3T3-L1 cells	20 μM β-carotene	6-8 days	Upregulation of genes and protein expression of UCP1 and PGC1-α; ↓ protein expression of FAS and ACC; Activation of AMPK; ↑ CPT1a protein,

71. Yoshikawa, et al., 2020	3T3-L1 cells	2.5, 5 and 10 μM fucoxanthin	72 hours	Triacylglycerol content reduced with 5 and 10 μM; 5 and 10μM increased fatty acid and glycerol release and stimulated AMPK and ACC phosphorylation; 10 μM decreased FAS protein expression.
72. Lai et al., 2012	3T3-L1 cells	10 and 50 μg/mL PSO or fucoxanthin, or Xanthigen	48 hours	50 μg/mL activated AMPK.
74. Jo et al., 2017	3T3-L1 cells	10 μM capsanthin	2 days	Inhibited adipogenic gene expression of PPARγ and CCAAT/enhancer-binding protein alpha (C/EBPα); induction of UCP1 and activation of AMPK.
76.Kang et al., 2012	3T3-L1 cells	10 μM fucoxanthin	24 hours	Stimulated AMPK, ACC and liver kinase B1 (LKB1) phosphorylation; ↑ expression of carnitine palmitoyltransferase 1a (CPT-1a).

Table S2. Study desing with animal model and main results with the equivalent dose

Authors	Animal model	Design	Duration of supplementation	Main results	Human equivalent dose*
9. Liu et al., 2017	Male C57BL/6J mice	Group 1: normal diet; Group 2: high fat diet (HFD) for 4 weeks, and then HFD groups were received 20 and 40 mg/kg body weight zeaxanthin	4 weeks	20 mg/kg: ↓ body weight gain and fat accumulation in epididymal adipose tissue; ↓ gene expression of FAS, FABP4, and perilipin in epididymal adipose tissue; AMPK activation; Both doses: ↓ gene expression of PPARγ, C/EBPα, and SREBP1-c in epididymal adipose tissue.	1.62 or 3.24 mg/kg
67. Gu et al., 2018	C57BL/KsJ-Lepdb (db/db) mice and their lean littermates (wild-type)	Group 1: db/db; Group 2: 20 mg/kg of crocin/day Group 3: 20 mg/kg of crocin/day +BML-275, an inhibitor of AMPK	8 weeks	Induced AMPK activation in adipose tissue of db/db mice; ↓ epididymal and perirenal adipose tissue weight; ↓ adipocyte size; ↓ gene expression of C/EBPα, CCAAT/enhancer-binding protein beta (C/EBPβ), PPARγ in adipose tissue; ↑ gene expression of PPARα, LPL, and HSL in adipose tissue; Improvement in glucose tolerance; Crocin's effects on adipocyte differentiation and lipolysis was inhibited by BML-275.	1.62 mg/kg
69.Kang et al,	Male 4-week-old	Group 1: Normal diet;	70 days	↓ adipocyte size in epididymal adipose tissue; ↑ adiponectin expression in epididymal adipose tissue;	12.16 mg/kg

2012.	C57BL/6 mice	Group 2: HFD and Group 3: HFD+ 150 mg/kg body weight/day of *Petalonia binghamiae* extract (PBE) (rich in fucoxanthin)		Activated AMPK and ACC in edididymal adipose tissue.	
75. Algandaby M. M. (2020	Wistar rats	Group 1: normal diet; Group 2: high salt food pellets and high fructose drinking water; Group 3: high salt food pellets and high fructose drinking water + 5 mg crocin/kg body weight; Group 4: high	5 days per week during 12 weeks	10mg/kg crocin: ↓ body weight gain; Improved glucose tolerance; Activated AMPK; Both doses: ↓ visceral adipose tissue, HOMA-IR and serum levels of IL-6 and TNF-α.	0.81 mg/kg or 1.62 mg/kg

		salt food pellets and high fructose drinking water + 10 mg crocin/kg body weight			
76. Fang, K., & Gu, M. (2020)	Male mice with global knockout (KO) of AMPKα2 gene and Wild-type (WT) mice used as control	During 3 months HFD + a single dose of 100mg/kg streptozotocin, then seven days after, the rats with diabetes received 20 mg/kg of crocin	12 weeks	Crocin: ↓ Body weight and the perirenal and epididymal adipose mass in wild type diabetic mice; ↓ Fasting blood glucose in wild type diabetic mice.	1.62 mg/kg

*human equivalent dose calculated by body surface area (FDA, 2005).

Reference: U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research, Center for Biologics Evaluation and Research. (2005) Estimating the safe starting dose in clinical trials for therapeutics in adult healthy volunteers, U.S. Food and Drug Administration, Rockville, Maryland, USA, 2005.

Table S3. Studies with clinical trials

Authors	Type of clinical trial	Individuals	Design	Duration of supplementation	Main results
77. Behrouz et al., 2020	Randomized, double-blind, single center, parallel-group, controlled clinical trial.	Adults with BMI between 18.5 and 30 kg/m²	Placebo grupo or Treated group with 2 tablets of 15 mg crocin in main meals (breakfast and dinner)	12 weeks	Greater decrease in fasting blood glucose, insulin and HOMA-IR; AMPK phosphorylation did not change.
78. Abedimanesh et al., 2020	Randomized, double-blind placebo-controlled clinical trial	Adults patients with coronary artery disease (male and female age 40-65 years old without the experience of myocardial infarction)	Group 1: 30 mg/day crocin; Group 2: 30 mg/day saffron aqueous extract; Group 3: placebo	8 weeks	↓ serum MCP-1 and NF-kB expression; ↑ gene expression of AMPK and SIRT1.
81. Canas et	Randomized,	Children with a	Group 1	6 months	↑↓ total adiponectin and HMW-ADI form;

al., 2017	double-blinded	BMI at or above the 90th percentile	received two capsules of mixed carotenoids (2000 IU of β-carotene, 500 µg of α-carotene, 10 mg of lutein, 2 mg of zeaxanthin, 10 mg of lycopene, 500 µg of astaxanthin, and 10 mg of γ-tocopherol in each capsule) or placebo		subcutaneous adipose tissue; The percentage change in subcutaneous adipose tissue was correlated to the percentage change in serum β-carotene.
82. Mashhadi et al., 2018	Randomized, placebo-controlled trial	Adults with type 2 diabetes	Group 1: 8 mg astaxanthin; Group	8 weeks	↑ Serum adiponectin; ↓ Visceral body fat mass; serum trigylceride (TG), very low-density lipoprotein (VLDL) cholesterol, and fructosamine concentrations.

			2: placebo		
83. Yoshida et al., 2010	Randomized, double-blind, placebo controlled study	Healthy subjects with moderately hypertriglyceridemic	Group 1: placebo, Group 2: 6 mg/day of astaxanthin, Group 3: 12 mg/day of astaxanthin, Group 4: 18 mg/day of astaxanthin	12 weeks	Astaxanthin groups↓serum TG and increased HDL-cholesterol; 12 and 18 mg/day↑serum adiponectin levels.