Advances in Nutrition 14 (2023) 796–818

American Society for Nutrition
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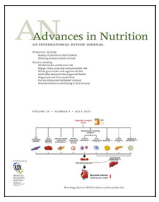
Advances in Nutrition
AN INTERNATIONAL REVIEW JOURNAL
journal homepage: https://advances.nutrition.org/



Review

The Metabolizable Energy and Lipid Bioaccessibility of Tree Nuts and Peanuts: A Systematic Review with Narrative Synthesis of Human and In Vitro Studies

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A B S T R A C T

Nuts are an energy-dense food, yet regular consumption is not associated with weight gain. A proportion of the fats found within nuts remains encapsulated within cell walls and cannot be digested. Metabolizable energy (ME) can be explored by measuring fecal fat excretion in human studies and fat release among in vitro studies. This systematic review with narrative synthesis aimed to examine the ME of tree nuts and peanuts (PROSPERO CRD42021252287). PubMed, MEDLINE, CINAHL, Cochrane, and Embase databases were searched to June 2021. Both in vitro and human studies (adults ≥18 y) were included. Data was synthesized via narrative synthesis with results reported in summary tables and compared between form, processing, and dose of nuts, where available. Twenty-one studies were included. The ME of nuts was consistently lower than that predicted by Atwater factors for investigated nut types (almonds, cashews, hazelnuts, pistachios, walnuts, and peanuts). The mechanisms may relate to a lower fat release from nuts, hence higher fecal fat excretion; however, this review did not consider the digestibility of carbohydrates and protein, which should be considered when interpreting the outcomes. ME was influenced by nut type (ME = 22.6 kJ/g for pistachios; ME = 18.5 kJ/g for raw almonds), physical form (flour > chopped > whole nuts), heat processing (butter > roasted > raw) and dose of consumption. The lower-than-expected ME may explain a lack of association between nut intake and body weight observed in the literature and has implications for the development of food composition databases, food labeling, and informing dietary guidelines. However, the strength of the evidence base was reduced by the variation in methods used between studies, suggesting that further clinical trials are needed to determine the impact of the findings of this review for clinical dietetics.

Keywords: calories, kilojoules, tree nuts, peanuts, metabolizable energy, lipid bioaccessibility, digestibility, weight

Statement of Significance

This study is the first to systematically review the metabolizable energy content and lipid bioaccessibility of tree nuts and peanuts. The results of this study suggest that the metabolizable energy of nuts is lower than expected, due to a lower lipid release during processing and digestion, and is impacted by nut type, physical processing, and heat treatment of nuts.

Introduction

Overweight and obesity are risk factors for developing chronic diseases, such as cardiovascular disease, type 2 diabetes, and some cancers [1]. Body weight is generally determined by energy balance, where energy intake exceeding energy expenditure can lead to weight gain. Therefore, it is important to regulate energy intake to maintain healthy body weight.

Abbreviations: ME, metabolizable energy; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCT, randomized controlled trial.

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https://doi.org/10.1016/j.advnut.2023.03.006
Received 11 April 2022; Received in revised form 31 October 2022; Accepted 14 March 2023; Available online 18 March 2023

Accurate information for the energy content of foods and beverages can facilitate the planning of optimal intakes required to achieve a healthy body weight.

Nutrition information, including the energy content, presented on packaged foods is strictly regulated by government agencies. For example, in Australia, the energy content of packaged food and beverage is mandated by the Food Standards Code [2]. Energy content is often estimated using Atwater factors that provide a value for each energy-yielding proximate (macronutrient)—namely carbohydrate, protein, fat, and alcohol—and multiplying this factor by the amount of macronutrient present in the food [3]. Bomb calorimetry is another method used to determine the energy content of foods. Bomb calorimetry calculates the energy content (in joules or calories) by placing a food sample into the chamber, which is surrounded by water, igniting the sample, and measuring the change in temperature of the water. These energy measurement methods—Atwater factors and bomb calorimetry—may not accurately reflect the energy from macronutrients that is digested, released, and absorbed by the body.

Weight-loss or weight-maintenance eating patterns often limit energy-dense foods to minimize positive energy balance. Tree nuts and peanuts (considered a groundnut) are energy-dense foods recommended in major dietary guidelines around the world [4,5], with a recommended intake of 1 serving (typically 30 g) on most days of the week. Regular nut consumption is associated with several health benefits, such as reduced risk of cardiovascular and coronary heart disease [6–8]. However, despite the well-established health benefits, nut consumption globally falls well below recommended intakes. Low nut intake has been reported to range from 3.3 to 5.2 g/d in Australia, New Zealand, and the USA [9–11]. A common barrier to regular nut consumption appears to be concern regarding body weight, with several studies reporting consumers believe that eating nuts will cause weight gain [12–16].

Contrary to these beliefs, regular tree nut and peanut consumption is associated with lower body weight [17–19]. From observational research, a meta-analysis of prospective cohort studies found nut consumption to be associated with a lower incidence of overweight or obesity [19]. From experimental research, a systematic review of randomized trials found that nut consumption did not result in changes in body weight compared to control diets, while studies that substituted nuts for other dietary components of similar energy content led to decreased body fat compared to the control diets [18].

A number of potential mechanisms have been proposed to explain the lack of an expected effect of tree nut and peanut consumption on body weight, one of which relates to the lower metabolizable energy (ME) of nuts. For the purpose of this research, among human studies, the term ME is defined as the amount of energy that is available to the body after nuts are ingested. In human studies, it is typically calculated as the gross energy of a food ingested minus the unabsorbed energy excreted in urine and feces [20]. Among in vitro studies, lipid release is typically measured, and there is the assumption that any unreleased nutrients are excreted from the body [21,22]. Understanding the ME of tree nuts and peanuts is essential to interpreting the lack of an effect on body weight gain and to help to dispel myths regarding nut consumption among consumers. Therefore, the aim of this systematic review was to synthesize the body of evidence for the ME and lipid bioaccessibility (and associated factors) of tree nuts and peanuts using a narrative synthesis.

Methods

Search strategy

This systematic review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 guidelines [23]. The protocol was registered with PROSPERO (https://www.crd.york.ac.uk/prospero/, CRD42021252287). The PubMed, MEDLINE (EBSCO), CINAHL (EBSCO), Cochrane CENTRAL, and Embase (Elsevier) scientific databases were searched from inception through to June 2, 2021 by CJN. Although MEDLINE is a subset of PubMed, in line with recommendations by Rosen and Suhami [24], both MEDLINE and PubMed were searched to ensure that recent studies were detected. Alternative spelling, phrases, and truncations were included in the search strings, with both controlled vocabulary and free-text search terms used. Search terms were piloted using sentinel articles. Following the search, backward and forward citation searching of eligible articles was conducted using citationchaser [25]. Search strings for all databases are provided in Supplementary Material 1. There was no restriction to the language or dates searched.

Selection criteria

Randomized controlled trials, feeding studies, and in vitro studies (research performed outside of a living organism) were eligible for inclusion in the review. Studies needed to: include adults aged 18 y and older (except for in vitro studies); explore the consumption of tree nuts that is typically included in nutrition research [26] (almonds, Brazil nuts, cashews, chestnuts, hazelnuts, macadamias, pecans, pine nuts, pistachios, walnuts), and/or peanuts, in the form of either whole nuts, chopped nuts, nut butters, or nut flours; and assess the ME as lipid release (in vitro studies) or fecal energy and/or fat excretion (human studies). Exclusion criteria were: studies conducted with children (under 18 y) or animals; studies investigating coconuts or cacao nuts (due to differences in the nutrient composition when compared with tree nuts and peanuts), nut oils, nut milks, and nut-containing foods (unless the results could be isolated to nuts); and systematic reviews and prospective cohort studies.

Screening and data extraction

The searches of each database and backward and forward citation searching were performed by one reviewer (CJN), and title/abstract and full text screening were performed independently by 2 reviewers (CJN, EPN) using Covidence (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia, Available at www.covidence.org). Conflicts at the title/abstract and full text stages were resolved through discussion to consensus between 2 reviewers (CJN, EPN) with an additional 2 reviewers (YCP, S-YT) consulted when required. Study details (country, study design, study population, mean BMI, mean age, control and intervention diets, nut type, nut form, nut dose, intervention duration, and outcomes) were extracted by 1 reviewer (CJN) and documented in summary tables, with separate tables for human and in vitro studies. Summary tables were checked for quality by a second reviewer (EPN). For studies that did not provide numerical values for the results but presented

results as a graph, WebPlotDigitizer online software was used to extract the numerical values [27].

Data synthesis

Data was synthesized via narrative synthesis. In the case of studies reporting ME or lipid bioaccessibility, values were extracted from each study and reported in summary tables, with descriptions of microscopy image results summarized in tables. In the cases of studies that compared ME or lipid bioaccessibility between consumption of nuts versus control, or doses, types, or forms of nuts, vote counting was used to synthesize results, based on whether there were significant increases, nonsignificant increases, significant decreases, or nonsignificant decreases in outcomes.

Quality assessment

Quality appraisal was conducted on the included studies independently by 2 reviewers (CJN, EPN), with disagreements resolved via consensus between reviewers. The quality of human studies was assessed using the Academy of Nutrition and Dietetics Quality Criteria Checklist – Primary Research [28]. The Office of Health Assessment and Translation risk-of-bias tool [29] was modified by CJN for assessment of in vitro study quality.

Results

Study characteristics and quality

A total of 12,530 articles were identified across the 5 databases. After the removal of duplicate articles and excluded studies, 20 records were identified as eligible. An additional 2 records were included after citation searching, bringing the total number of records to 22, describing a total of 21 studies. Figure shows the study selection process. There were 11 human records [30–40], 8 in vitro records [21,22,41–46], and 3 records with components of both in vivo and in vitro techniques [47–49]. Tables 1 and 2 summarize the characteristics of the in vitro and human studies, respectively.

Study quality among human studies (n=13) varied from 'neutral' to 'positive', and among the in vitro studies (n=11) varied from 'probably low risk' to 'definitely low risk.' The most common reasons for human studies being considered to be of 'neutral' quality were due to not reporting eligibility criteria and participant characteristics and not describing the method of randomization. The most common reasons for in vitro studies being considered to have 'probably low risk' were due to not discussing study limitations and not disclosing the funding source and/or conflicts of interest.

In vitro studies – lipid release

Among the in vitro studies (n=11), the nut types examined were almonds (n=9), walnuts (n=2), peanuts (n=1), pistachios (n=1), and hazelnuts (n=1), with 9 studies investigating only 1 nut type, while 2 studies investigated either 2 or 3 nut types (Table 1). Eight [21,22,41–43,47–49] of the 11 in vitro studies investigated the same dose of a single nut type but compared various forms or heat processing treatments (for example, Capuano et al., 2018 [21] compared raw and roasted hazelnuts). It should also be noted that some studies did not specify which nut forms were being investigated. Two [44,45] in vitro studies investigated several types of nuts (for example McArthur and

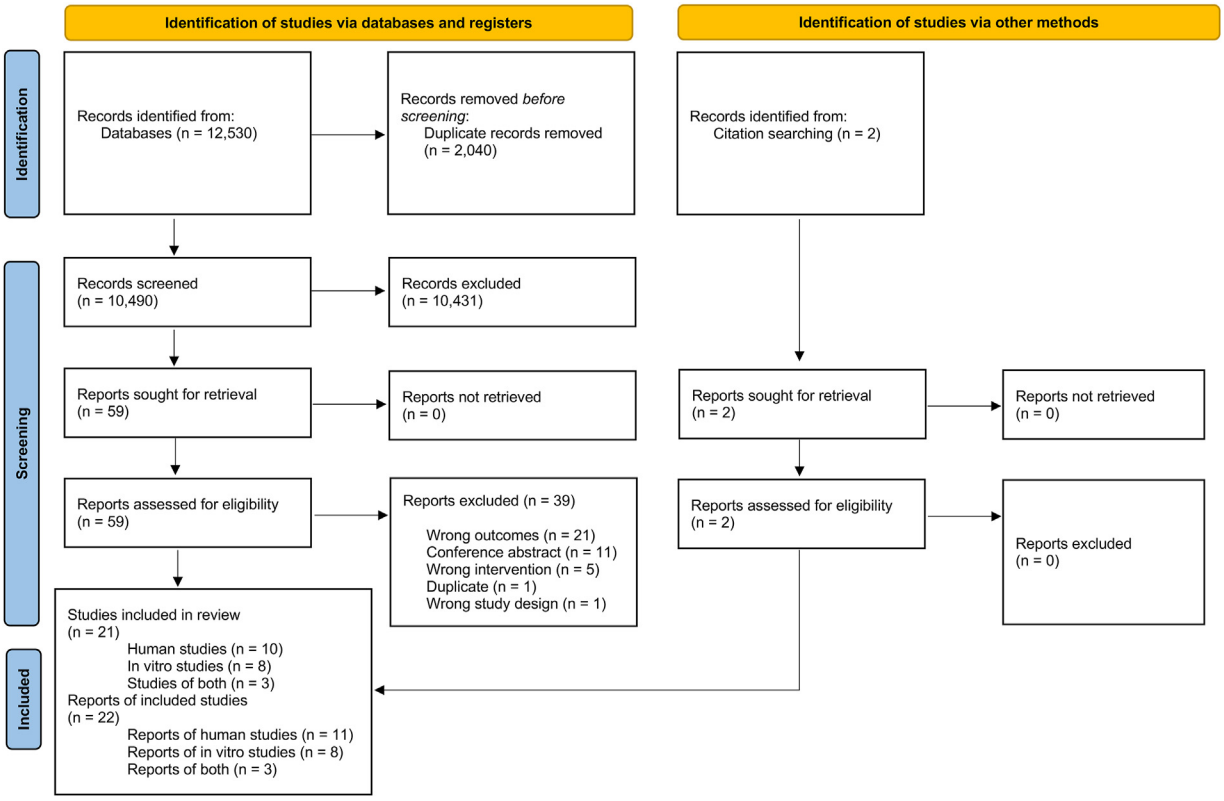

FIGURE. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of the study selection protocol.

TABLE 1
Characteristics of the 11 included in vitro studies examining the lipid release of tree nuts and peanuts

Reference	Preparation of samples	Nut type and form; nut dose	Particle size pre-digestion	Method/model of simulated digestion	Type and duration of simulated digestion	Lipid content determination	Quality appraisal
Capuano et al. (2018) [21]	Simulated mastication: hazelnuts were subjected to mechanical dry grinding; sieving determined particle size Extraction of oil bodies	Hazelnuts (whole) 1: raw particles 2: roasted particles 3: raw oil bodies 4: roasted oil bodies Dose was "standardized based on the initial lipid content in order to have always the same lipid/lipase activity ratio." 50 g hazelnut particles were used to extract oil bodies.	1-2 mm	INFOGEST protocol (modified) Oral phase: sample mixed with Simulated Salivary Fluid (final ratio 50:50 v/v), 2 min. Gastric phase: oral phase mixed with Simulated Gastric Fluid (final ratio 50:50 v/v), $CaCl_2$ added to achieve 0.075 mM in final mixture, pH adjusted to 3.0 with 1 M HCl, porcine pepsin added to achieve an activity of 2000 U/mL, digestion time 2 h at 37°C, sufficient mixing using a shaking water bath at 37°C. Intestinal phase: gastric phase mixed with Simulated Intestinal Fluid (final ratio 50:50 v/v), bile salts added to achieve 10 mM, $CaCl_2$ added to achieve 0.3 mM, lipase activity adjusted to 2000 U/mL by mixing pancreatin extract from porcine pancreas with pure lipase from porcine pancreas Type II in a ratio of 10:1 as lipase activity in pancreatin extract was found to be low. The mixture was titrated using 1 N NaOH over 120 min with an end point of pH 7.0.	Oral phase: 2 min Gastric phase: 2 h Intestinal phase: 120 min	Soxhlet solvent extraction using petroleum ether	Definitely low
Grassby et al. (2014) [22]	Cubes: carefully cutting almond cotyledons into 2-mm cubes. Flour: fine grinding of almond cotyledons (skin removed); mechanical sieving determined mean particle size	Almonds 1: raw whole 2: flour 1.5-g amounts	Raw cubes: 2 mm Flour: 200-250 μm	Two variants (Simple Theoretical Model STM; and Extended Theoretical Model ETM) of a theoretical model were constructed to predict lipid bioaccessibility. In vitro digestion of lipid in cubes and flour was performed as described by Mandalari et al. (2008) [48]. In vitro digestion under both gastric and duodenal conditions. Each digestion assay was performed 4 times, and the solid digested almond material was recovered for lipid analysis. Total lipid loss (as a percentage of original lipid content of almonds) was then determined.	Total of 3 h digestion (under both gastric and duodenal conditions)	The lipid value was calculated as the difference between the total surface area of the cell profile and the surface area of nonlipid components (e.g., protein) and expressed as a percentage of the total cell profile surface area. The lipid content of cells was then calculated as a percentage volume.	Probably low
Grassby et al. (2017) [47]	Human mastication by 1 volunteer for 8 d (4 d per muffin type).	Almonds 1: flour 2: particles 85 g almonds within muffin (220 g). Muffin served with 80 g custard.	AF: muffins made with almond flour (<450 μm) AP: muffins made with almonds particles (1700–2000 μm)	Gastric digestion: Masticated muffin samples (~180 g each) were fed into the dynamic gastric model (DGM) for 63 min in presence of 20 mL priming acid. Composition of simulated gastric acid solution as reported by Mandalari et al. (2014) [43]. Simulated gastric enzyme solution was prepared with porcine gastric mucosa pepsin and a gastric lipase analog. Single-shelled lecithin liposomes was added to the gastric enzyme	Human mastication (mean): 3:22 (AF) and 6:38 (AP) Simulated digestion: Gastric phase: 63 min Duodenal phase: 8 h	Lipid extraction using a Soxhlet extraction method with n-hexane	Probably low

(*continued on next page*)

TABLE 1 (*continued*)

Reference	Preparation of samples	Nut type and form; nut dose	Particle size pre-digestion	Method/model of simulated digestion	Type and duration of simulated digestion	Lipid content determination	Quality appraisal
				solution at final concentration 0.127 mM. A total of 7 samples (35 g) were removed from the DGM at 9-min intervals. Amounts of acid secretions added during gastric digestion were 28 mL (for AF) and 21 mL (for AP). Amounts of gastric enzymes added during gastric digestion were 28 mL (for AF) and 29 mL (for AP). Duodenal digestion: A pooled sample (42 g) obtained from an aliquot (6 g) of each gastric sample, was transferred to a tube with addition of simulated bile solution and pancreatic enzyme solution, incubated at 37°C at 170 rpm for 8 h. Aliquots (10 g at 1-6 h, then 15 g at 7 and 8 h) were taken every hour and replaced with fresh bile and pancreatic enzymes.			
Grundy et al. (2015) [41]	Human mastication by 15 volunteers	Almonds 1: whole raw 2: whole roasted 4-5 g per sample. 10 samples per mastication session	Range from: <500 μm 500-1,700 μm >1,700 μm	Participants were blinded to almond form and masticated 10 samples. Expectorated samples with water. Volunteers (n=4) provided masticated samples. Lipid extraction was performed with hexane as solvent according to the Soxhlet extraction method. Estimation of lipid release using mathematical model (n=15).	4 mastication sessions (20-25 s each)	1: Mathematical model (n=15) 2: Soxhlet extraction (n=4)	Definitely low
Grundy et al. (2015) [42]	Prepared as: 1: separated raw and roasted almond cells 2: raw and roasted almond particles (ground to different size ranges) 3: human masticated samples of raw and roasted almonds	Almonds: raw and roasted (compared to an almond oil emulsion as a reference sample) 19 mL of sample	Almond particles: 4 size ranges: 1000-2000 μm 500-1000 μm 250-500 μm <250 μm (flour)	In vitro duodenal digestion using pH-stat method (adapted from previous studies). Rates of lipolysis were continuously measured by titration of FFA with 0.15 M NaOH at 37°C and an endpoint of pH 7.0. Each assay was performed over 1 h in a mechanically stirred reaction vessel of a pH-stat instrument (Titrino 848 plus, Methrohm UK Ltd.). Reaction medium as follows: *1*) 19 mL of sample (oil emulsion, separated cells, or almond particles) containing 300 mg of lipid, dissolved in beta-Lg solution; *2*) 15 mL of bile salt solution (31.5 mM in 10 mM phosphate buffer, pH 7.0, 37°C); *3*) 1 mL of NaCl (5.63 M in deionized water), and 1 mL of $CaCl_2$ (0.375 M in deionized water). The system was adjusted to pH 7.0 with 0.15 M NaOH and then 1.5 mL of freshly prepared lipase solution were added (40 mg/mL in 10 mM phosphate buffer).	In vitro duodenal digestion: 60 min	Lipids present in the aqueous phase of the samples were extracted from the reaction vessel at different time points, using a 2:1 chloroform-methanol solution (v/v) containing C15 internal standards [50].	Definitely low
Mandalari et al. (2008) [48]	Whole almonds (NA and BA) were cut into 2-mm cubes	Almonds 1: whole natural (NA) 2: whole blanched (BA)	NA and BA: 2 mm cubes FG: 200 μm	Gastric digestion: 1.5 g of each almond meal was suspended in 12.4 mL of acidic saline and readjusted to pH	Gastric digestion: 2 h Duodenal digestion: 1 h	Lipid extraction performed with a Soxhlet automatic	Probably low

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	Finely ground (FG) almonds without skin Defatted finely ground almond plus almond oil (DG) was prepared by extracting 25 g of FG almonds (oil and dried defatted solid were recombined in the original ratio as the FG almonds)	3: finely ground flour (FG) 4: defatted finely ground flour (DG) 1.5 g samples fed into gastric digestion		2.5 as required. The PC vesicle suspension, pepsin, and gastric lipase analog were then added so that the final concentrations in the aqueous phase were 2.4 mmol/L, 146 units/mL, and 0.56 mg/mL, respectively. The almond/aqueous phase ratio was 0.12 g/mL. Samples were placed in an orbital shaking incubator (170 rpm, 37°C) for 2 h. "Control digestions" of the 4 almond meals were performed in saline solution with no enzyme additions. Duodenal digestion: In vitro gastric digesta were used as starting material. The pH was raised to 6.5 by addition of NaOH and solutions of bile salts, $CaCl_2$, BIS-TRIS, and enzymes in 150 mmol/L NaCl asses. The final PC concentration was 2.1 mmol/L and the almond/aqueous phase ratio was 0.11 g/mL. Digestion performed in a shaking incubator (170 rpm, 37°C) for 1 h.		Soxtec 2050 extraction using n-hexane as solvent. Expressed as a % of dry weight.	
Mandalari et al. (2014) [43]	Four healthy adults (50% M, 50% F) masticated 28 g of almonds	Almonds 1: raw 2: roasted 60-g samples of masticated almonds fed into digestion.	Raw masticated almonds: mean 500 (SEM: 29) μm (maximum size 1002 [SEM: 0.2] μm) Roasted masticated almonds: mean 365 (SEM: 12) μm (maximum size 893 [SEM: 0.1] μm)	Gastric digestion: Individual masticated almond samples (60 g) were fed into the dynamic gastric model (DGM) for 60 min with a representative drink of water (150 mL) in the presence of priming acid (20 mL). Simulated gastric secretion, bile and pancreatic juice were prepared as reported by Mandalari et al. (2008) [48]. The simulated gastric acid solution contained… The simulated gastric enzyme solution was prepared by… A suspension of single-shelled lecithin liposomes (Mandalari et al. 2008 [48]) was added to the gastric enzyme solution at a final concentration of 0.127 mM. A total of 6 samples (48 g for each raw and roasted sample) were removed from the DGM at 10-min intervals. Duodenal digestion: A pooled sample (42 g), obtained from an aliquot (7 g) of each gastric sample, was transferred to a Sterilin plastic tube for duodenal digestion with the addition of simulated bile solution (8.4 mL) and pancreatic enzyme solution (23.5 mL), and incubated at 37°C under shaking conditions (170 rpm) for 2 h. Porcine pancreatic lipase, porcine colipase, porcine trypsin, bovine alpha-chymotrypsin and porcine	Gastric digestion: 1 h Duodenal digestion: 2 h	Original almond materials (raw and roasted), post-mastication and digesta residues recovered were analyzed for total lipid. Lipid extraction was performed using a Soxhlet extraction method (Association of Official Analytical Chemists 1995 Official Methods of Analysis), with n-hexane as the solvent.	Definitely low

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TABLE 1 (*continued*)

Reference	Preparation of samples	Nut type and form; nut dose	Particle size pre-digestion	Method/model of simulated digestion	Type and duration of simulated digestion	Lipid content determination	Quality appraisal
				alpha-amylase were added to the pancreatic solution. Each gastric sample removed from the DGM every 10 min and the pooled duodenal sample after 2 h incubation were centrifuged at 3700 rpm for 15 min (7°C) to separate the soluble fraction from the residue; all samples were immediately snap-frozen (liquid nitrogen) and retained for analysis.			
Mandalari et al. (2018) [49]	Simulated oral digestion: samples were minced 3 times using a mincer	Almonds 1: natural whole (NA) 2: roasted whole (RA) 3: diced roasted (DA) 4: butter (AB) 25 g sample	Particle size after simulated mastication: NA, RA, and DA: 1000 μm and above. AB: <850 μm	Simulated oral digestion: Minced samples then added 12.5 mL of Simulated Salivary Fluid at pH 6.9 (0.15 M NaCl, 3 mM urea) and 900U Human Salivary Amylase dissolved in 1 mL SSF. Mixed the sample.	Simulated oral digestion	Lipid extraction was performed with a Soxhlet automatic Soxtec 2050 extraction (Foss Analytical, Hilleroed, Denmark) using n-hexane as a solvent.	Probably low
McArthur and Mattes (2020) [44]	Mastication by 7 healthy humans.	Walnuts (whole unsalted) Almonds (whole roasted salted) Pistachios (whole dry-roasted) Dose: Mastication: 4 portions of 5 g of nuts 30 mL (containing 5 g masticated nuts) samples were fed into digestion	Walnuts: 338 μm Almonds: 308 μm Pistachios: 316 μm	Gastric digestion: 30 mL samples were vortexed and acidified with HCl until it reached pH 3.5. 2 mL pepsin solution (2000 U/mL) was added, and pH was adjusted to 2.5 with HCl. The final volume was adjusted to 40 mL with saline, capped with N_2 to minimize contact with O_2, and then incubated at 37°C in a shaking water bath for 60 min. After, pH was adjusted to 5.0. Intestinal digestion: Addition of 2 mL of pancreatin-lipase (2000 U/mL) solution and 3 mL bile. pH adjusted to 6.5 with $NaHCO_3$, and the final volume brought to 50 mL with saline. After, the tube was flushed with N_2 and incubated in a shaking water bath at 37°C for 120 min. Following intestinal digestion, the digesta was subjected to 60 min of 10,000 *g* centrifugation to remove aqueous fraction and isolate the suspended particles.	Gastric digestion: 1 h Intestinal digestion: 2 h	Total lipid analysis using a Soxhlet extraction method, with petroleum ether as the solvent	Definitely low
Paz-Yépez et al. (2019) [45]	Simulated mastication using grinder	Walnuts (raw peeled) Peanuts (roasted) Amount of ground nuts used in each experiment was estimated to always have 0.35 g fat in the tube	Two particle sizes: large (>1.2 mm) and small (<1.2 mm)	Oral stage: Simulated salivary fluid (5 mL) with alpha-amylase from human saliva was added to the ground nuts. It was mixed and incubated for 3 min at 37°C in an incubator chamber Selecta. Gastric stage: Simulated gastric fluid (pH 3) was added to the oral bolus (1:1 v/w). Pepsin was added to the SGF to reach a concentration in the gastric mixture of 2000 U/mL. The pH of the mixture was adjusted with HCl (1 N) to pH 2.8 and samples were flipped at 55 rpm for 120 min at 37°C using an Intell-Mixer RM-2 and incubator chamber Selecta.	Oral: ~3 or more min Gastric: 2 h Intestinal: 2 h	FFA analysis: Two methods were used: *1*) a spectrophotometric method which allows estimating the overall FFA was used for all the digested samples, and *2*) a chromatographic method which allows the determination of the FFA profile was additionally used in a selection of samples	Definitely low

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				Intestinal stage: Simulated intestinal fluid (pH 7) containing bile salt (1 or 10 mM) and pancreatin (either 0, 1000, 2000, 3000 or 4000 LU/g of fat) was added in ratio 1:1 (v/w) to each tube containing the gastric chyme. The pH was adjusted with NaOH (1 N) to either 6 or 7. Samples were flipped at 55 rpm for 120 min at 37°C and pH was monitored and readjusted if necessary (pH. below 5.7 might inactivate lipase)			
Swackhamer et al. (2019) [46]	Simulated mastication by food processor	Almonds: whole raw Dose: Shaking water bath: ~15 g Human Gastric Simulator: ~60 g	Particles between 2 mm and 4 mm obtained by sieving	Compares a shaking water bath model and the human gastric simulator model. Shaking water bath model: Adding simulated gastric juice (37°C) to almond particles (ratio 5 mL to 1 g). Mixture placed in a shaking water bath (Thermo-Fisher 2872) at 37°C and 100 rpm. After 6 0min, pH was adjusted to 3, and after 120 min adjusted to 2. After 180 min, added simulated intestinal juice (37°C) in a 1:1 (v/v) ratio with the simulated gastric juice. pH adjusted to 7. After 60 min of intestinal digestion (240 min total time) pH readjusted to 7, and after 120 min intestinal digestion (300 min total) pH again adjusted to 7. Samples were collected at 8 timepoints (gastric: 1, 5, 15, 30, 180 min, intestinal: 185, 195, 360 min). Human Gastric Simulator: Adding simulated gastric juice to almond particles in same ratio as SWB. During gastric phase, contents were subjected to peristaltic contractions at frequency 3 contractions per min. At end of gastric phase, simulated intestinal fluid was added in a 1:1 (v/v) ratio with the simulated gastric juice. The bottle was transferred to the SWB at 37°C. pH adjusted in same way as described in SWB.	Shaking water bath model (with and without simulated gastric and intestinal juices): 6 h total (3 h per gastric and intestinal phase) Human Gastric Simulator using simulated digestive juices: 6 h total	FA extraction and preparation: FAs extracted from liquid digesta (using Folch method) and analyzed using gas chromatography	Probably low

Abbreviations: AB, almond butter; AF, almond flour; AP, almond particles; BA, blanched almonds; DA, diced almonds; DG, defatted finely ground; DGM, dynamic gastric model; FA, fatty acids; FFA, free fatty acids; FG, finely ground; NA, natural almonds; RA, roasted almonds; SWB, shaking water bath.

TABLE 2
Characteristics of the 13 included human studies examining the metabolizable energy or lipid bioaccessibility of tree nuts and peanuts in adults aged 18 y or older

Reference; country	Study design	Population; mean BMI in kg/m^2; mean age in years	Sample size (completers)	Nut type and form; nut dose	Intervention duration	Control diet	Intervention diet	Fecal energy and fat measurement	Quality appraisal
Baer, Gebauer & Novotny (2012); USA [30]	RCT (crossover)	Healthy; 27.9; 50	16 (50% M, 50% F)	Pistachios (whole) 1: 42 g/d 2: 84 g/d	18 d	Typical American foods (no pistachios) for weight maintenance (all foods provided), with fat:fiber ratio matched to nut diet. Mean energy 10,780 kJ/d.	As per control diet with a proportionate reduction (isocaloric). Mean energy: 11,010 kJ/d (42 g/d pistachios);11,230 kJ/d (84 g/d pistachios). Completeness of fecal collection was determined by blue dye: administered on Day 9, and again 7 d later.	Energy: Adiabatic bomb calorimetry (Parr Instrument Company) of diets, feces and urine. Fat: Petroleum extraction (Foss).	Positive
Baer, Gebauer & Novotny (2016); USA [31]	RCT (crossover)	Healthy; 28.8; 53.1	18 (56% M, 44% F)	Walnuts (halves and pieces) 42 g/d	3 wk	Typical American diet (no walnuts) for weight maintenance. All foods provided (17% protein, 29% fat, 54% CHO) and weekday breakfasts and dinners consumed at center; lunches and weekend meals consumed offsite.	As per control diet with proportionate reduction of foods for isocaloric inclusion of 42 g/d walnuts. Completeness of fecal collection (7-10 d) was determined by blue dye.	Energy: Adiabatic bomb calorimetry (Parr Instrument Company) on diet sample, feces, urine. Fat: Petroleum ether extraction (Foss).	Positive
Baer & Novotny (2018); USA [32]	RCT (crossover)	Healthy; 28.4; 56.9	18 (50% M, 50% F)	Cashews 42 g/d	4 wk	Controlled diet (no cashews) providing 33.3% fat, 16.8% protein, 49.9% CHO, for weight maintenance. Weekday breakfasts and dinners consumed at center; lunches and weekend meals consumed offsite.	As per control diet with proportionate reduction of foods for isocaloric inclusion of cashews. Completeness of fecal collection (one week) was determined by blue dye (administered at beginning and end of collection).	Energy: Adiabatic bomb calorimetry (Parr Instrument Company) for diets and feces. Fat: Petroleum ether extraction (Soxtec, Foss, Eden Prairie, USA) for diets and feces.	Positive
Cassady et al. (2009); USA [33]	RCT (crossover)	Healthy; 23.1; 24 (range 19-43)	13 (62% M, 38% F)	Almonds (raw whole) chewed: 1: 10 times 2: 25 times 3: 40 times 55 g/d	4 d	Typical Western foods (nil nuts). Mean energy 10,266 kJ/d (35% fat, 15% protein, 50% CHO). All foods provided and weekday breakfasts and dinners consumed at center; lunches and weekend meals consumed offsite.	As per control diet with proportionate reduction of foods for isocaloric inclusion of 55 g/d almonds. Completeness of fecal collection was determined by colored dye: on Day 1 of collection, 3 capsules containing green food coloring were ingested; on Day 4, capsules containing red coloring were consumed.	Energy: Bomb calorimetry with a Parr 1281 Bomb Calorimeter (Parr Instruments). Fat: Automated Soxhlet extraction (Ankom XT15 Extraction System).	Positive
Ellis et al. (2004); UK &	2 × pre-post experiments (Study A:	Chewing study: Healthy; 24.7; 37	Chewing study: 7 (71% M,	Almonds 1: whole raw 2: whole roasted	Chewing study: 1 d Digestibility	Chewing study: No control diet Digestibility study:	Chewing study: Following a 2-h fast, participants masticate 2-g	Energy: Not reported Fat:	Neutral

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Canada [34]	chewing study and Study B: digestibility study)	Digestibility study: Healthy; 24.3; 31	29% F) Digestibility study: 3 (100% M, 0% F)	Chewing study: 2 g Digestibility study: 100 g on Day 1, 150 g on Day 2, and 200 g on Day 3.	study: 4 d	3-d period of nil nut consumption (fecal control)	samples (30 chews over 30 s) and expectorated. Digestibility study: Almond consumption increased during intervention: Day 1 100 g/d; Day 2 150 g/d; Day 3 200 g/d. Limited intake of other plant foods. Fecal collection: one sample collected on Day 4 of intervention, another sample collected after 3 d of nil nut consumption.	Chewing study: Not reported Digestibility study: Analysis of total lipids using methods of the Association of Official Analytic Chemists (AOAC) "Official Methods of Analysis."	
Gebauer et al. (2016); USA [35] Mandalari et al. (2018); USA [49]	RCT (crossover)	Healthy; 30.6[1]; 56.7	18 (56% M, 44% F)	Almonds 1: natural (NA) 2: roasted (RA) 3: diced roasted (DA) 4: butter (AB) 42 g/d	3 wk	Typical American diet (no almonds) for weight maintenance. All foods provided; energy range 1,600-4,000 kJ/d. (31% fat, 16% protein, 53% CHO). Weekday breakfasts and dinners consumed at center; lunches and weekend meals consumed offsite.	As per control diet with proportionate reduction of foods for isocaloric inclusion of 42 g/d almonds. Completeness of fecal collection (9 d) was determined by blue dye (administered at start of collection period and 7 d later).	Energy: Adiabatic bomb calorimetry (Parr Instrument Company) on diet sample, feces, urine. Fat: Not reported Fecal samples were examined and photographed using an Olympus BX60 microscope and ProgRes Capture Pro 2.1 software	Positive
Grassby et al. (2017); UK [47]	RCT (crossover)	Ileostomy; BMI not reported; age not reported	1 (sex not reported)	Almonds (natural) AF: muffins made with almond flour AP: muffins made with almond particles 85 g/d	1 d	No control diet	Participants fasted from 20:00 on day prior. New stoma bag on study day. Breakfast (muffin served with custard) was consumed within 15 min. Lunch and dinner were controlled and provided 4 h and 10 h after breakfast, respectively. Contents of stoma collected every 2 h for 10 h, then at convenience for a further 16 h.	Energy: Not reported Fat: Soxhlet extraction in n-hexane	Positive
Hollis & Mattes (2007); USA [36]	RCT (crossover)	Healthy; 25.9; 24	20 (0% M, 100% F)	Almonds (raw unsalted) 1,440 kJ serving/d	10 wk Feeding study for ME: 4 consecutive days (during week 10 of each study arm).	Usual diet. Feeding study for ME: meals provided (10,500-12,000 kJ/d, 55% CHO, 35% fat, 15% protein).	Nil instructions on how to include 1,440 kJ serving into diet. Feeding study for ME: as per control diet with addition of 1,440 kJ serving of almonds. Completeness of fecal collection was determined by colored dye: on Day 1, blue food color marker was	Energy: Bomb calorimetry (Parr Instruments, Moline, IL, USA). Fat: Not reported	Positive

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TABLE 2 (*continued*)

Reference; country	Study design	Population; mean BMI in kg/m^2; mean age in years	Sample size (completers)	Nut type and form; nut dose	Intervention duration	Control diet	Intervention diet	Fecal energy and fat measurement	Quality appraisal
							ingested; on Day 4, a red marker was ingested. Fecal collection from Day 1 until appearance of red marker.		
Levine & Silvis (1980); USA [37]	Feeding study (crossover)	Healthy; BMI not reported; age not reported	10 (sex not reported)	Peanuts 1: whole 2: butter 3: oil Diet contained a total of 80g of fat; 76 g was in the form of whole peanuts, peanut butter, or peanut oil	6 d	No control diet	Participants consumed vegetarian diet containing one of the peanut forms. Each diet contained 80 g fat (76 g from peanut product) and 20g crude fiber (high-fiber diet) or 5g crude fiber (low-fiber diet). Fecal collection: samples collected on days 4 through 6.	Energy: Not reported Fat: Titration	Neutral
Mandalari et al. (2008); UK [48]	Feeding study (crossover)	Ileostomy; BMI not reported; age not reported	2 (0% M, 100% F)	Almonds 1: natural cubes (2 mm) 2: blanched cubes (2 mm) 20 g/d: 10 g with breakfast, another 10 g with lunch	24 h	Not reported	Overnight fast followed by 10 g almonds at breakfast (nut-free cereal and semi-skimmed milk) and 10 g almonds at lunch (sandwiches and drink). Total ileal effluent collection every 2 h for 12 h, then at convenience for a further 12 h.	Energy: Not reported Fat: Lipid extraction was performed with a Soxlet automatic Soxtec 2050 extraction using n-hexane as solvent	Neutral
Nishi et al. (2021); Canada [38]	RCT (crossover)	Individuals with hyperlipidaemia, but otherwise healthy; 25.7; 64.5	22 (55% M, 45% F)	Almonds 1: full-dose 73 g/d 2: half-dose 38 g/d (and half-dose muffins)	1 mo	Participants followed a self-selected, low-fat therapeutic diet, supplemented with muffins (22.2% daily energy).	As per control diet, supplemented with 73 g/d almonds, or 38 g/d almonds and half-dose muffins. All supplements isocaloric with each other. Fecal collection: 3-d fecal collection in final week of each phase.	Energy: Macronutrients and dietary fiber were measured in freeze-dried fecal samples by standard Association of Official Analytical Chemists methods for macronutrients and fiber. Fat: Methods of Folch and gas chromatography were used to determine the fatty acid profiles of fecal samples.	Positive
Novotny, Gebauer & Baer (2012); USA [39]	RCT (crossover)	Healthy; 27.4; 56.0	18 (56% M, 44% F)	Almonds (natural whole) 1: 42 g/d 2: 84 g/d	18 d	Typical American foods (no almonds) for weight maintenance. All foods provided. Weekday breakfasts and dinners consumed at center; lunches and weekend meals consumed offsite.	As per control diet with proportionate reduction of foods for isocaloric inclusion of almonds. Completeness of fecal collection was determined by blue dye: 9-d collection period marked by Brilliant Blue capsule (15 mg) administered at	Energy: Adiabatic bomb calorimetry (Parr Instrument Company). Fat: Petroleum ether extraction (Soxtec; Foss).	Positive

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							beginning of collection and again 7 d later.		
Traoret et al. (2008); USA, Ghana, Brazil [40]	RCT (parallel with crossover between control and intervention)	Healthy; 21.8; 24.3	63 (sex not reported)	Peanuts 1: whole 2: butter 3: oil 4: flour 70 g/d	7-9 d	Typical diet respective to culture (no peanut products). All foods provided. Mean energy 10,171 kJ/d (55% CHO, 30% fat, 15% protein).	As per control diet with proportionate reduction of foods for isocaloric inclusion of either whole peanuts (mean 10,598 kJ/d diet), peanut butter (mean 10,460 kJ/d diet), peanut oil (mean 9,909 kJ/d diet) or peanut flour (mean 10,694 kJ/d diet). Completeness of fecal collection was determined by colored dye: 4-d fecal collection. Beginning marked by Red Carmine and FD&C 13% blue aluminum lake, administered on Day 1 of intervention. Marker administered again 3 d later.	Energy: Bomb calorimetry (Bomb calorimeter 1280, Parr Instruments Moline, IL, USA). Fat: A modified method of Folch extraction [50].	Neutral

Abbreviations: AB, almond butter; AF, almond flour; AP, almond particles; CHO, carbohydrate; DA, diced almonds; F, female; M, male; ME, metabolizable energy; NA, natural almonds; RA, roasted almonds; RCT, randomized controlled trial.

[1] BMI calculated by review authors from provided mean height and mean weight values.

Mattes, 2020 [44] studied walnuts, almonds, and pistachios). One in vitro study [46] compared 2 methods of simulated digestion for the fatty acid bioaccessibility of almonds.

Among the in vitro studies, the main outcome was lipid release and was explored under a range of conditions (e.g., several phases of digestion) and included various nut types (almonds, walnuts, peanuts, pistachios, and hazelnuts), forms (such as chopped nuts and butter), and heat treatments (raw, roasted, or blanched). Lipid release was investigated at the oral, gastric, duodenal, and the broader intestinal phases of digestion. Mastication of nut samples was either simulated or performed by humans and followed by simulated digestion. One study [41] investigated lipid release after human mastication with no simulated digestion; although this study explored lipid release only after mastication, it estimated lipid release using a mathematical model and Soxhlet extraction and, therefore, was considered to be an in vitro study.

Table 3 presents the results of in vitro studies. Lipid release was measured in all in vitro studies and reported as a percentage of total lipid content prior to digestion in all studies except for one [45], which reported lipolysis as milligrams of free fatty acids per gram of fat. Lipid release was never complete (i.e., 100%) with values ranging from 1.9% to 97.1%. However, lipid release was measured at various stages of simulated digestion (e.g., mastication, gastric digestion, duodenal digestion) of nut forms such as masticated whole nuts (n=11 studies) and more processed forms such as flours (n=4 studies), which potentially explains the large range of values. Lipid release was lowest after the initial phase of oral digestion and increased with progression to gastric, duodenal, and intestinal phases of digestion. For example, after the oral phase (either simulated or human mastication), lipid release ranged from 1.9% to 12.4% among whole nuts, whereas after the intestinal phase, lipid release ranged from 5% to 78.8% among whole nuts.

The physical form of nut (e.g., whole, chopped) and the use of heat treatment (e.g., raw, roasted) appeared to affect lipid release. For instance, Grassby et al. [47] compared muffins made with almond flour and muffins made with almond particles. The muffins were masticated by humans and then subjected to simulated gastric and duodenal digestion. Throughout the different phases of digestion, the almond flour muffin consistently had higher lipid release than the almond particle muffin (oral: 4.4% versus 1.9%; gastric: 41.6% versus 5.8%; duodenal: 97.1% versus 57.6%). These results suggest that lipid release depends on the form of nut, where more processed forms are more easily digested (i.e., higher lipid release). Similar results were observed in Mandalari et al. [48] and Mandalari et al. [43]. In studies that compared several nut forms, the raw nuts had lower lipid release than more processed nuts (such as roasted, chopped, flours) [21,22,41–43,47–49], and in studies that measured lipid release at various stages of digestion, lipid release increased with later stages of digestion [43,46–48].

McArthur and Mattes [44] investigated lipid release among several nut types. Whole walnuts, almonds, and pistachios were masticated by humans and then subjected to simulated gastric and intestinal digestion, and results showed pistachios had the highest lipid release (78.8%) after the intestinal phase, followed by walnuts (77.4%) and almonds (76.9%) [44]. These results suggest that the type of nut has a small impact on lipid release during digestion, whereas the physical form of nuts and the level of processing (e.g., flour, butter) appeared to have a greater impact on lipid release.

Human studies

A total of 13 studies from 14 records were conducted with humans. Nine of the 13 human studies were randomized controlled trials with a crossover design, as shown in Table 2. Other study types included feeding studies and pre-post experiments. Eligible human studies were conducted in a range of countries, including the USA [30–33,35–37,39,40,49], the UK [34,47,48], Canada [34,38], Ghana [40], and Brazil [40].

In human studies, the sample size varied from 1 to 63 participants. Eight studies included both adult male and female participants, 2 studies [36,48] included female participants only, and 3 studies [37,40,47] did not report the sex of the participants. Investigated nut types in the human studies were almonds (n=8), peanuts (n=2), walnuts (n=1), pistachios (n=1), and cashews (n=1). All human studies investigated only 1 nut type. The forms of nuts investigated in the human studies included whole nuts (n=7), chopped nuts (n=4), nut butters (n=3), and nut flours (n=3), and heat processing types included raw nuts (n=7), roasted nuts (n=2), and blanched nuts (n=1). It should also be noted that 2 studies [32,38] did not specify which nut forms were investigated.

The main outcome that was measured in the human studies was the ME of nuts and was reported as energy content, fecal fat excretion, or digestibility of lipids and energy. Supplementary Material 2 provides the formulas used to calculate the ME of nuts in the studies. Microscopy images were also used in 4 human studies [34,35,48,49] to show cell wall structure and lipid release in fecal samples. These outcomes were explored under a range of conditions (e.g., almonds chewed 10 times versus 25 times and 40 times) and included various nut types and forms (such as raw, roasted, chopped, and butter).

Table 4 summarizes the results of the human studies. All human studies collected fecal samples to determine the lipid excretion during the nut intervention, except for 2 studies [47,48], which collected ileal effluent. In human studies that reported on ME of nuts (n=5), the ME was calculated using formulas that considered the energy of both the nuts alone and the background diet (estimated using Atwater factors) and energy excreted from the body, as shown in Supplementary Material 2.

ME

Five of the 13 human studies [30–32,35,39] reported ME values of the investigated nut types. The Atwater factors predict an energy content of between 22 and 30 kJ/g for peanuts and tree nuts, depending on the type of nut [51]. In this review, the ME of nuts ranged from 18.5 to 22.6 kJ/g. When the ME values are compared to the Atwater factors, the ME of almonds was found to be up to 26% lower [35,39] than what was predicted; cashews were 14% lower [32], walnuts 22% lower [31], and pistachios approximately 5% lower [30] than predicted.

Fecal fat excretion

Ten of the 13 human studies reported on fecal fat excretion [30–34,37–40,47]. In 3 out of 10 studies, the excretion of fat in feces was significantly higher following consumption of nut-containing diets compared with control diets [31,32,34]. Three of the 10 studies compared a higher dose of nuts with a

TABLE 3
Main findings of the 11 included in vitro studies examining the lipid release of tree nuts and peanuts

Reference	Type and duration of simulated digestion	Outcomes measured	Results
Capuano et al. (2018) [21]	Oral phase: 2 min Gastric phase: 2 h Intestinal phase: 120 min	FFA release (as % of total lipid content before digestion)	Raw particles: 5% Roasted particles: 11% ($P < 0.05$ vs raw particles) Raw oil bodies: 18% Roasted oil bodies: 26% ($P < 0.05$ vs. raw oil bodies)
Grassby et al. (2014) [22]	Total of 3 h digestion (under both gastric and duodenal conditions)	Lipid release of almond cubes and flour after simulated digestion (% of total lipid)	Cubes: 9.9 (SD: 0.71) % [1] Flour: 39.3 (SD: 0.18) % [1]
Grassby et al. (2017) [47]	Human mastication (mean): 3:22 (AF) and 6:38 (AP) Simulated digestion: Gastric phase: 63 min Duodenal phase: 8 h	Total lipid release (% of original lipid present in muffin) during mastication and simulated digestion	AF muffins: After mastication: 4.4 (SE: 0.4) % After gastric digestion: 41.6 (SE: 1.6) % After gastric and duodenal digestion: 97.1 (SE: 1.7) % AP muffins: After mastication: 1.9 (SE: 0.2) % After gastric digestion: 5.8 (SE: 0.1) % After gastric and duodenal digestion: 57.6 (SE: 1.1) % ($P < 0.005$ AP vs. AF muffin)
Grundy et al. (2015) [41]	4 mastication sessions (20-25 s each)	Percentage of lipid release after mastication estimated by: 1: Mathematical model (n=15) 2: Soxhlet (n=4)	Mathematical model (n=15): Natural: 8.5 (SE: 0.67) % Roasted: 11.3 (SE: 0.17) % ($P < 0.05$ vs. natural) Soxhlet (n=4): Natural: 7.9 (SE: 0.70) % Roasted 11.1 (SE: 1.09) % ($P < 0.05$ vs. natural) No significant difference found between mathematical and theoretical methods
Grundy et al. (2015) [42]	In vitro duodenal digestion: 60 min	FFA release (%) after 1 h simulated duodenal digestion	Raw almond oil: 19.3 (SE: 0.9) % Raw almond oil emulsion: 67.8 (SE: 2.7) % Roasted almond oil: 20.2 (SE: 0.6) % Roasted almond oil emulsion: 70.4 (SE: 3.1) % Raw cells: 31.2 (SE: 2.3) % ($P < 0.05$ vs. masticated sample) Roasted cells: 31.4 (SE: 2.9) % ($P < 0.05$ vs. masticated sample) Raw particles: 1000-2000 μm: 44.2 (SE: 5.3) % ($P < 0.05$ vs. masticated sample) 500-1000 μm: 55.7 (SE: 1.6) % ($P < 0.05$ vs. masticated sample) 250-500 μm: 60.9 (SE: 1.2) % ($P > 0.05$ vs. masticated sample) <250 μm (flour): 63.9 (SE: 1.6) % ($P > 0.05$ vs. masticated sample) Roasted particles: 1000-2000 μm: 39.3 (SE: 1.1) % ($P < 0.05$ vs. masticated sample) 500-1000 μm: 48.2 (SE: 2.2) % ($P < 0.05$ vs. masticated sample) 250-500 μm: 55.4 (SE: 1.4) % ($P > 0.05$ vs. masticated sample) <250 μm (flour): 59.7 (SE: 0.8) % ($P > 0.05$ vs. masticated sample) Masticated raw almonds: 56.0 (SE: 5.2) % Masticated roasted almonds: 58.2 (SE: 1.2) %
Mandalari et al. (2008) [48]	Gastric digestion: 2 h Duodenal digestion: 1 h	Total lipid losses (% of original amount present)	Gastric digestion (means ± range): NA: 7.6 ± 0.18% ($P < 0.005$ vs. FG and DG, NS vs. BA) BA: 9.7 ± 0.38% ($P < 0.005$ vs. FG and DG, NS vs. NA) FG (flour): 31.1 ± 0.25% ($P < 0.005$ vs. NA

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TABLE 3 (*continued*)

Reference	Type and duration of simulated digestion	Outcomes measured	Results
			and BA, NS vs. DG) DG (flour): 32.1 ± 0.51% ($P < 0.005$ vs. NA and BA, NS vs. FG) Gastric + duodenal digestion (means ± range): NA: 9.9 ± 0.71% ($P < 0.005$ vs. FG and DG, NS vs. BA) BA: 13.0 ± 0.21% ($P < 0.005$ vs. FG and DG, NS vs. NA) FG: 39.3 ± 0.12% ($P < 0.005$ vs. NA and BA, NS vs. DG) DG: 34.0 ± 0.24% ($P < 0.005$ vs. NA and BA, NS vs. FG)
Mandalari et al. (2014) [43]	Gastric digestion: 1 h Duodenal digestion: 2 h	Total lipid loss (as % of the original amount present) due to mastication and digestion.	Lipid release as a result of mastication: Raw: 7.9% Roasted: 9.6% (both $P < 0.005$ vs. post-gastric) Lipid release after gastric phase: Raw: 16.3% Roasted: 15.9% Lipid release after duodenal phase: Raw: 32.2% Roasted: 32.8% (both $P < 0.005$ vs. post-gastric; both $P < 0.0005$ vs. mastication)
Mandalari et al. (2018) [49]	Simulated oral digestion	Lipid release after mastication (%)	NA: 8.9 (SD: 0.7) % RA: 11.8 (SD: 1.1) % DA: 12.4 (SD: 0.8) % AB: 6.2 (SD: 0.4) % ($P < 0.001$ vs. RA and DA)
McArthur and Mattes (2020) [44]	Gastric digestion: 1 h Intestinal digestion: 2 h	Lipid release (as % of the original lipid present in undigested nuts)	Lipid bioaccessibility (after intestinal phase): Walnuts: 77.4% Almonds: 76.9% Pistachios: 78.8% No significant difference between nut types ($P > 0.05$)
Paz-Yépez et al. (2019) [45]	Oral: ~3 or more min Gastric: 2 h Intestinal: 2 h	Lipolysis (expressed as mg FFA/g fat)	Under healthy intestinal digestion conditions (pH 7 and 10 mM bile salts) and 2000 LU/g pancreatin: Large walnut particles: 689 ± 65 mg FFA/g fat Small walnut particles: 708 ± 68 mg FFA/g fat Large peanut particles: 205 ± 1 mg FFA/g fat ($P < 0.05$ vs. large walnut, small walnut, and small peanut particles) Small peanut particles: 780 ± 35 mg FFA/g fat
Swackhamer et al. (2019) [46]	SWB model (with and without simulated gastric and intestinal juices): 6 h total (3 h per gastric and intestinal phase) HGS using simulated digestive juices: 6 h total	Total bioaccessible fatty acid (%) after each phase of digestion Bioaccessibility of individual FAs (C16:0, C18:1, and C18:2) Particle breakdown	180 min (end of gastric phase): HGS: 6.55 (SD: 0.85) % SWB: 4.54 (SD: 0.36) % ($P < 0.05$ between methods) End of intestinal phase: HGS: 8.88 (SD: 0.36) % SWB: 7.87 (SD: 0.49) % ($P > 0.05$ between methods)

Abbreviations: AB, almond butter; AF, almond flour; AP, almond particles; BA, blanched almonds; DA, diced almonds; DG, defatted finely ground; FFA, free fatty acids; FG, finely ground; HGS, human gastric simulator; NA, natural almonds; RA, roasted almonds; SWB, shaking water bath.
[1] significance not reported

lower dose of nuts and a nut-free control diet and found significantly increased fat in the feces of both of the nut-containing diets compared with the control diet [30,38,39]. Of these 3 studies that compared 2 doses of nuts, 2 studies [38,39] found significant differences in fecal fat excretion among the 2 nut-containing diets, indicating a dose-response relationship. One of 10 ten studies reported nonsignificant decreases in fecal fat excretion after consumption of peanut butter and peanut flour, compared to a nut-free control diet, and the authors considered these decreases were also not clinically significant [40].

Three of the 10 studies did not have a control group [33,37,47]. Cassady et al. [33] investigated the impact of mastication on a 55-gram dose of whole, raw almonds. The almonds were

TABLE 4
Main findings of the 13 included human studies examining the metabolizable energy or lipid bioaccessibility of tree nuts and peanuts in adults aged 18 y or older

Reference; country	Fecal excretion	Mean fat and/or energy digestibility (%) or microscopy images	Metabolizable energy (ME) content (mean)
Baer, Gebauer, and Novotny (2012); USA [30]	**CONTROL** Fat: 2.0 (SE: 0.8) g/d Energy: 546.8 (SE: 55.6) kJ/d **INTERVENTION** 42 g/d dose: Fat: 6.7 (SE: 0.8) g/d ($P < 0.05$ vs. control) Energy: 759.4 (SE: 55.6) kJ/d ($P < 0.05$ vs. control) 84 g/d dose: Fat: 8.7 (SE: 0.8) g/d ($P < 0.05$ vs. control) Energy: 923.4 (SE: 55.6) kJ/d ($P < 0.05$ vs. control and 42 g/d dose)	**CONTROL** Fat: 97.3 (SE: 0.7) % Energy: 89.5(SE: 0.4) % **INTERVENTION** 42 g/d dose: Fat: 92.4 (SE: 0.7) % Energy: 87.4 (SE: 0.4) % (both $P < 0.05$ vs. control) 84 g/d dose: Fat: 91.5 (SE: 0.7) % Energy: 86.8 (SE: 0.4) % (both $P < 0.05$ vs. control)	22.6 kJ/g
Baer, Gebauer, and Novotny (2016); USA [31]	**CONTROL** Fat: 2.2 (SE: 0.6) g/d Energy: 140 (SE: 8.9) kcal/d (= 586 kJ/d) **INTERVENTION** Fat: 10.2 (SE: 0.6) g/d Energy: 217 (SE: 8.9) kcal/d (= 908 kJ/d) (both $P < 0.05$ vs. control)	**CONTROL** Fat: 97.0 (SE: 0.6) % Energy: 90.4 (SE: 0.3) % **INTERVENTION** Fat: 89.0 (SE: 0.6) % Energy: 87.8 (SE: 0.3) % (both $P < 0.05$ vs. control)	5.22 (SE: 0.16) kcal/g (= 21.84 kJ/g)
Baer and Novotny (2018); USA [32]	**CONTROL** Fat: 1.7 (SE: 0.3) g/d Energy: 129.6 (SE: 8.1) kcal/d (= 542 kJ/d) **INTERVENTION** Fat: 3.6 (SE: 0.3) g/d Energy: 186.3 (SE: 8.1) kcal/d (= 779 kJ/d) (both $P < 0.05$ vs. control)	**CONTROL** Fat: 97.8 (SE: 0.3) % Energy: 94.9 (SE: 0.2) % **INTERVENTION** Fat: 96.1 (SE: 0.3) % Energy: 92.9 (SE: 0.2) % (both $P < 0.05$ vs. control)	137 (SE: 3.4) kcal per 28 g serving (= 573 kJ/28 g) 4.89 kcal/g [2] (= 20.46 kJ/g)
Cassady et al. (2009); USA [33]	**INTERVENTION** Fat: 10 chews: 4 1g 25 chews: 3 1g ($P < 0.05$ vs. 10 chews) 40 chews: 29 g ($P < 0.05$ vs. 10 chews) Energy: 10 chews: 3,901 kJ 25 chews: 3,295 kJ ($P > 0.05$ vs. 10 chews) 40 chews: 3,103 kJ ($P > 0.05$ vs. 10 chews)	Not reported	Not reported
Ellis et al. (2004); UK & Canada [34]	Chewing study: Not reported Digestibility study: **CONTROL** 2.8 (SE: 1.5) g lipid **INTERVENTION** 21.4 (SE: 14.4) g lipid ($P < 0.05$ vs. control)	Chewing study: Microscopy images show ruptured cells at the at the fractured surface and the free lipid released from cells. Cell walls and oil bodies are still intact in cellular layers underlying the fractured surface (no lipid release). Visible oil droplets on the fractured surface of almond particles. Visible intracellular lipid droplets released from the fractured cell layer. Digestibility study: Microscopy images show intact almond tissue containing intracellular lipids, with some cell walls ruptured, releasing lipid and bacteria located inside cells. Bacterial fermentation eroding cell walls of fractured cells. Bacteria growing on cell wall surface. Fecal bacteria have digested the cell walls and gained access to inside cell.	Not reported

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TABLE 4 (*continued*)

Reference; country	Fecal excretion	Mean fat and/or energy digestibility (%) or microscopy images	Metabolizable energy (ME) content (mean)
Gebauer et al. (2016); USA [35] Mandalari et al. (2018); USA [49]	Not reported	**CONTROL** Fecal matter contained recognizable remains of plant tissue (comprising food remains, micro-organisms, mucin). No free lipid drops were observed. **INTERVENTION** Natural: recognizable multicellular particles of almond tissue; few free lipid drops, lipids are confined within cell walls Roasted: recognizable multicellular particles; numerous free lipid drops as well as coalesced lipid present within cells Chopped: appearance of chopped roasted almond tissue; multicellular particles containing coalesced lipid and an abundance of free lipid Butter: smaller multicellular particles of almond tissue; very few lipid drops	Natural: 4.42 (SE: 0.24) kcal/g ($P < 0.05$ vs. all other forms) (= 18.49 kJ/g) Roasted: 4.86 (SE: 0.24) kcal/g ($P < 0.05$ vs. whole natural, almond butter, $P > 0.05$ vs. chopped) (= 20.33 kJ/g) Chopped: 5.04 (SE: 0.20) kcal/g ($P < 0.05$ vs. whole natural, almond butter, $P > 0.05$ vs. roasted) (= 21.09 kJ/g) Butter: 6.53 (SE: 0.19) kcal/g ($P < 0.05$ vs. all other forms) (= 27.32 kJ/g) Measured ME for natural, whole roasted, and chopped roasted $P < 0.05$ vs Atwater factors; almond butter $P > 0.05$ vs. Atwater factors
Grassby et al. (2017); UK [47]	**INTERVENTION** AF muffins 0-10 h: 1.7 g fat [1] 0-24 h: 2.7 g fat [1] AP muffins 0-10 h: 20.9 g fat [1] 0-24 h: 29.6 g fat [1]	**INTERVENTION** Lipid digested: AF muffins 0-10 h: 96.5% [1] 0-24 h: 94.4% [1] AP muffins 0-10 h: 56.5% [1] 0-24 h: 38.3% [1]	Not reported
Hollis and Mattes (2007); USA [36]	Not reported	Digestibility coefficient of the diet: **CONTROL** 96% **INTERVENTION** 95% ($P < 0.05$ vs. control) (accounts for ~84 kJ/d of almond)	Not reported
Levine & Silvis (1980); USA [37]	% Dietary fat excreted per day: **INTERVENTION** High-fiber diet: Peanuts: 17.8 (SE: 5.3) % Peanut butter: 7.0 (SE: 1.4) % ($P < 0.05$ vs. peanuts) Peanut oil: 4.5 (SE: 1.4) % ($P < 0.05$ vs. peanuts and peanut butter) Low-fiber diet: Peanuts: 16.8 (SE: 11.7) % Peanut butter: 4.2 (SE: 1.7) % ($P < 0.05$ vs. low-fiber peanuts and high-fiber peanut butter) Peanut oil: 1.8 (SE: 0.4) % ($P < 0.05$ vs. low-fiber peanuts and peanut butter, and high-fiber peanut oil)	Not reported	Not reported
Mandalari et al. (2008); UK [48]	Not reported	After 3.5 h: the nutrients of the cells in the first cellular layer (fractured cells) have been digested. The cell walls and intracellular nutrients are still intact in the underlying cells. After 12 h: release of nutrients underneath the fractured surface (~3-5 layers), and losses of intracellular contents from intact cells underneath the fractured surface.	Not reported
Nishi et al. (2021); Canada [38]	**CONTROL** Fat: 5.9 (SE: 0.9) g/d Energy: 155.4 (SE: 16.1) kcal/d (= 650 kJ/d) **INTERVENTION** Half-dose: Fat: 10.2 (SE: 0.7) g/d ($P < 0.05$ vs. control) Energy: 177.7 (SE: 9.6) kcal/d ($P > 0.05$ vs. control) (= 743 kJ/d)	**CONTROL** Fat: 89.5 (SE: 2.0) % Energy: 92.3 (SE: 0.8) % **INTERVENTION** Half-dose: Fat: 84.0 (SE: 1.3) % ($P < 0.05$ vs. control) Energy: 91.0 (SE: 0.5) % ($P < 0.05$ vs. control) Full-dose: Fat: 83.2 (SE: 1.2) % ($P < 0.05$ vs. control) Energy: 90.1 (SE: 0.6) % ($P < 0.05$ vs. control)	Not reported

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TABLE 4 (*continued*)

Reference; country	Fecal excretion	Mean fat and/or energy digestibility (%) or microscopy images	Metabolizable energy (ME) content (mean)
	Full-dose: Fat: 12.9 (SE: 1.0) g/d ($p<0.05$ vs control) Energy: 207.5 (SE: 14.5) kcal/d ($P < 0.05$ vs. control) (= 868 kJ/d)		
Novotny, Gebauer, and Baer (2012); USA [39]	**CONTROL** Fat: 1.7 (SE: 0.8) g/d Energy: 132.2 (SE: 13.4) kcal/d (= 553 kJ/d) **INTERVENTION** 42 g/d: Fat: 6.3 (SE: 0.8) g/d ($P < 0.05$ vs. control) Energy: 217.7 (SE: 13.4) kcal/d ($P < 0.05$ vs. control) (= 911 kJ/d) 84 g/d: Fat: 10.8 (SE: 0.8) g/d ($P < 0.05$ vs. control) Energy: 282.3 (SE: 13.4) kcal/d ($P < 0.05$ vs. control) (= 1,181 kJ/d)	**CONTROL** Fat: 97.8 (SE: 0.8) % Energy: 90.5 (SE: 0.5) % **INTERVENTION** 42g/d: Fat: 93.1 (SE: 0.8) % ($P < 0.05$ vs. control) Energy: 87.5 (SE: 0.5) % ($P < 0.05$ vs. control) 84g/d: Fat: 89.9 (SE: 0.8) % ($P < 0.05$ vs. control) Energy: 85.5 (SE: 0.5) % ($P < 0.05$ vs. control)	4.6 (SE: 0.8) kcal/g (= 19.25 kJ/g)
Traoret et al. (2008); USA, Ghana, Brazil [40]	**CONTROL** Fat: WP: 187.3 (SE: 21.8) kJ/d PB: 220.1 (SE: 35.6) kJ/d PO: 166.3 (SE: 14.4) kJ/d PF: 214.9 (SE: 31.1) kJ/d Energy: WP: 646.5 (SE: 55.2) kJ/d PB: 623.4 (SE: 58.4) kJ/d PO: 626.6 (SE: 36.0) kJ/d PF: 663.6 (63.6) kJ/d **INTERVENTION** Fat: WP: 271.2 (SE: 22.7) kJ/d PB: 213.8 (SE: 31.3) kJ/d PO: 191.4 (SE: 24.1) kJ/d PF: 189.9 (SE: 25.1) kJ/d Energy: WP: 800.2 (SE: 63.5) kJ/d PB: 703.0 (SE: 74.6) kJ/d PO: 704.7 (SE: 78.0) kJ/d PF: 668.9 (SE: 60.3) kJ/d NS between groups	Not reported	Not reported

Abbreviations: AF, almond flour; AP, almond particles; ME, metabolizable energy; NS, PB, peanut butter; PF, peanut flour; PO, peanut oil; not significant; SE, standard error.

[1] significance not reported

[2] calculated by CJN

masticated either 10 times, 25 times, or 40 times. The results showed a significantly higher fecal fat excretion in the 10-chews sample, indicating that mastication affected how much fat can be absorbed [33]. Grassby et al. [47] compared the amount of fat excreted after consumption of muffins made with almond flour and muffins made with almond particles. The muffins made with almond particles had a higher amount of fat excreted post-consumption, suggesting that particle size (either due to nut form or the degree of mastication) influenced the amount of energy available to the body [47]. The impact of fiber intake on fat absorption was explored by Levine and Silvis [37]. A high-fiber diet showed more dietary fat in the feces after consumption of whole peanuts (17.8%) and peanut butter (7.0%) than a low-fiber diet (whole peanuts: 16.8%; peanut butter: 4.2%) [37].

Energy and lipid digestibility

Seven [30–32,36,38,39,47] out of the 13 human studies reported fat and/or energy digestibility results. In 3 studies, the digestibility of fat and energy was significantly lower in nut-containing diets compared with nut-free diets [31,32,36]. Additionally, 3 of the 7 studies compared higher and lower doses of nuts with a nut-free diet and found lower digestibility of fat/energy in higher doses of nuts compared with lower doses and nut-free diets [30,38,39]. For example, Baer, Gebauer, and Novotny [30] reported lower digestibility of fat and energy after consuming 84 g/d of pistachios (fat: 91.5%; energy: 86.8%) compared with consumption of half-dose 42 g/d (fat: 92.4%; energy: 87.4%) and a nut-free control diet (fat: 97.3%; energy 89.5%) [30]. The effect of nut form (e.g., whole, chopped) and level of processing (e.g., roasting, nut butter) on fat/energy

digestibility were explored in 1 out of the 8 studies [47]. Grassby et al. [47] compared muffins made with almond particles and muffins made with almond flour (smaller particle size). Particle size appeared to influence the digestibility of fat, with the almond flour muffins being more digestible than almond particle muffins [47].

Microscopy images

Four of the 13 human studies used microscopy imaging of fecal samples to explore the cell structure and lipids [34,35,48,49]. Ellis et al. [34] used microscopy imaging to explore the cell structure of *1*) masticated samples of almonds and *2*) fecal samples after 3 d of almond consumption. Ruptured cells and released lipids were observed in both masticated and fecal samples, with some cell walls remaining intact, trapping lipids within [34]. One study [48] observed ileal effluent (fecal sample) from an ileostomy participant at 3.5 h and 12 h of digestion. At 3.5 h, the first layer of cells had been broken and the energy within had been digested, with underlying cells still intact, while at 12 h, approximately 3 to 5 layers of cells had been ruptured and the lipids released [48]. Another study by Mandalari et al. [49], a secondary analysis of Gebauer et al. [35], compared microscopy images of fecal samples after consuming raw almonds, roasted almonds, chopped almonds, and almond butter. The images showed that after consumption of raw almonds, the lipids were confined within cell walls, whereas free lipids were released, and some lipids remained within cells after consumption of the roasted almonds. In comparison, there was an abundance of released lipids following the consumption of chopped almonds, and very few lipid drops were visualized following consumption of almond butter [35,49].

Discussion

The findings of this systematic review indicate that the ME of tree nuts and peanuts is lower than what would be expected following application of Atwater factors. In vitro studies demonstrated potential mechanisms for these effects, which appeared to be due to lower lipid release following nut consumption. Human studies indicated greater fecal fat excretion following nut consumption, though effects varied according to the nut processing method. Taken together, regardless of nut type, the ME was found to be lower than that predicted by Atwater factors, potentially influenced by a lower lipid release during digestion, increased fat in feces, the processing form of the nut (e.g., roasted, flour), and/or the digestibility of the overall pattern of eating. These results may, in part, explain the lack of an effect of nut consumption on body weight reported in the literature [17–19].

The recommended intake of nuts is approximately 30 g on most days of the week. Using Atwater factors, the energy content of a 30 g serving ranges from 765–800 kJ for almonds, 760–775 kJ for cashews and 750–765 for pistachios [52]. Based on the findings of this review, the ME values for a 30 g serving of these nut types could be as low as 555–635 kJ for almonds (range provided due to the various studies on almonds), 615 kJ for cashews, and 680 kJ for pistachios. The mechanisms responsible for a lower ME of nuts are discussed in further detail below.

Mechanisms responsible for lower ME in tree nuts and peanuts

The lower-than-expected ME of nuts observed in this systematic review appear to be due to the increased fat excretion associated with nuts. Although this review did not consider carbohydrate or protein digestibility, it should be noted that a large proportion (between 70% and 90%) of their energy content is derived from lipids [52]. While nuts have a high-energy and high-fat content, the lipids are found within the cell walls [34]. These lipids are trapped in the cell walls during digestion, unless the cell walls are physically ruptured, which may occur during mastication or during the processing of nuts [21,33–35,41–43,48,49]. If the cell walls are physically ruptured prior to or during digestion, then the lipids are released and made available to the body for absorption. However, cell walls that remain intact are unable to release the lipids for absorption.

In the current review, in vitro studies largely explored the impact of the cell wall structure on lipid release by performing lipid extraction at various stages of simulated digestion, supported by human studies that conducted microscopic imaging of fecal fat excretion. By performing lipid extraction at different stages of digestion, the in vitro studies concluded that not all of the lipids present in nuts are released after consumption, and hence are excreted in feces.

Within human studies, the ME and fecal fat excretion were explored. ME contents were calculated using formulas (Supplementary Material 2), and each study used slightly varied formulas and measured different outcomes, thus resulting in potentially conflicting values. Fecal fat excretion was higher in nut-containing diets compared with nut-free diets and was influenced by the dose of nuts, degree of mastication, and fiber content of the diet. Consumption of a higher dose of nuts led to increased fat in the feces, indicating that the fat within nuts is only partially absorbed [30,38,39]. It should be noted that, within the human studies in this review, nut consumption was explored as part of a habitual diet, which is an important consideration. This review found that the fiber content of the overall diet impacts on the ME of nuts [37], and these results are supported by the literature [53]. These findings highlight the importance of considering the overall diet in which nuts are consumed when estimating their ME.

Nut type and dose

Variation in the ME and the mechanisms that influence it was observed among the investigated nut types. Fecal fat excretion after consumption of 42 g/d of pistachios and cashews was, on average, 759 kJ/d and 779 kJ/d, respectively [30,32], but was higher for the same amount of walnuts at 908 kJ/d [31], suggesting that the digestibility varies based on nut type. In contrast, in studies that compared lipid release among several types of nuts within the same study [44,45], there were consistent results. McArthur and Mattes [44] reported a range of 76.9% to 78.8% for lipid release among walnuts, almonds, and pistachios [44]. Paz-Yépez et al. [45] explored the effect of particle size on lipolysis in walnuts and peanuts. Small particles resulted in similar amounts of free fatty acids being released from walnuts and peanuts (708 mg and 780 mg, respectively, $P > 0.05$). However, there was a significant difference in free fatty acid release from large walnut particles (689 mg) and large peanut

particles (205 mg) [45]. Although lipid release differs based on nut type, it appears to have a small impact.

Variation in the ME content of nuts also differed within nut types based on dose. The results of included studies in this review consistently showed that a higher dose of nut consumption had a nonsignificantly lower ME energy when compared with a lower dose of the same nut type [30,38,39]. These findings suggest that the digestibility of energy in nuts decreases with a higher nut intake. This may be due to the higher volume of fiber consumed with a larger dose of nuts.

Taken together, it appears that while higher nut dose resulted in lower ME, there is a lack of consistency in the impact of nut type on lipid release, fecal fat excretion, or digestibility within and between studies. Differences between studies examining a single nut type were observed, whereas results were comparable within studies that compared multiple types of nuts. This lack of consistency may therefore be the result of differences in study population and methodology between studies, rather than true differences between nut types. Future in vitro and human studies should investigate lipid release among several nut types and doses using consistent methods to explore the effect of nut type and dose on ME.

Nut processing

Understanding other reasons for the variation in ME among nuts, for instance, the physical form of the nuts (such as whole versus chopped nuts) and the heat treatment (such as raw versus roasted nuts), may be helpful in predicting the effect of nut consumption on body weight. The ME content of tree nuts and peanuts appeared to vary depending on the physical form and heat treatment of the nut, with more highly processed nuts (such as roasted nuts and nut butters) found to have higher lipid release compared to less processed nuts (whole raw nuts). Table 5 compares ME and/or lipid release of nut types versus heat processing and physical form.

In this review, the roasted form of nuts was examined among almonds, hazelnuts, pistachios, and peanuts across 8 studies [21,34,35,41–45,49]. It is thought that the roasting process likely increases the lipid release from the cell walls by partially rupturing the cell walls prior to digestion [44]. Additionally, since roasted nuts are more brittle than their raw counterparts, they are physically harder and, therefore, require more mastication before swallowing, which leads to smaller-sized particles and further cell wall rupture [35]. Particle size is indicative of lipid release because smaller particles reflect a larger amount of

TABLE 5
The metabolizable energy or lipid release findings of nut type vs. heat treatment and physical form of nut, from in vitro studies and human studies (in adults aged 18 y or older)

	References	Heat treatment		Skin removal	Physical form				Consistency
		Raw (reference form)	Roasted	Blanched	Whole (reference form)	Chopped	Particles	Flour	Butter (grinding)
Almond	[22, 35, 39, 41–44, 47–49]	↓ v. roasted ↓ v. blanched 18.5 kJ/g (26% lower than expected) [1]	↑ v. raw 20.3 kJ/g (19% lower than expected) [1]	↑ v. raw	↓ v. flour ↓ v. chopped ↓ v. butter ↓ v. walnut ↓ v. pistachio 19.2 kJ/g (23% lower than expected) [1]	↑ v. whole ↓ v. butter 21.1 kJ/g (17% lower than expected) [1]	↓ v. flour	↑ v. whole ↑ v. particles	↑ v. chopped ↑ v. whole 27.3 kJ/g (1.4% lower than expected) [1]
Cashew	[32]	NR	NR	NR	20.5 kJ/g (14% lower than expected) [1]	NR	NR	NR	NR
Hazelnut	[21]	↓ v. roasted	↑ v. raw	NR	NR	NR	NR	NR	NR
Peanut	[37, 40, 45]	NR	NR	NR	↓ v. butter ↓ v. flour	NR	↓ v. walnut	↑ v. whole ↑ v. butter	↑ v. whole ↓ v. flour
Pistachio	[30, 44]	NR	NR	NR	↑ v. almond ↑ v. walnut 22.6 kJ/g (5% lower than expected) [1]	NR	NR	NR	NR
Walnut	[31, 44, 45]	NR	NR	NR	↑ v. almond ↓ v. pistachio 21.8 kJ/g (22% lower than expected) [1]	NR	↑ v. peanut	NR	NR

NR, not reported.
↑: higher metabolizable energy or lipid release, including significant and nonsignificant differences
↓: lower metabolizable energy or lipid release, including significant and nonsignificant differences
[1] from all energy sources in nuts

ruptured cell walls and, in turn, a greater lipid release. One study included in this review explored the effect of blanching on the ME of almonds and found that the blanching process affects cell wall structure and lipid release, thus natural almonds have a lower ME than blanched almonds [48].

The particle size of nuts during digestion also determines the lipid release and, in turn, ME available for absorption. Chopped nuts and nut flours have a higher ME compared with whole nuts, as observed in this review. Whole nuts rely only on mastication to rupture cell walls, and so have a lower ME than nuts that have been chopped or processed prior to consumption. Chopping or grinding nuts can impact cell structure by physically rupturing the cell walls. The particle size of nuts, either due to mastication or due to processing, has an impact on energy absorption.

Finally, nut butters are one of the most processed forms of nuts. They are typically prepared by roasting nuts and then grinding into a paste consistency, containing very small nut particles. The roasting process combined with the physical breakdown of nuts implies that nut butters have a higher ME content compared to other, less processed forms. Due to this higher degree of processing that nut butters undergo, the lipids have been released prior to consumption and are easily absorbed during digestion, increasing the energy available to the body. It appears that the ME of nut butters is higher than whole and chopped nuts but lower than flours and oils and is not significantly different to what Atwater factors predict for nut butters [35,37,40,49]. Taken together, the findings of this review suggest that the physical form and heat treatment of nuts has a substantial influence on ME, which should be considered when interpreting the effect of nut consumption on body weight.

Strengths and limitations

The strength of this review is the inclusion of both human and in vitro studies to provide a complete understanding of the ME of nuts. The inclusion of human studies considers the consumption of nuts as part of a diet compared to in vitro studies, which investigate nuts alone but provide further insight into the underlying mechanisms of nuts. However, this review has some limitations. First, studies were restricted to published records, which may have resulted in publication bias. Second, there was variation in the methods used in each of the included studies. For instance, in the in vitro studies, several phases of simulated digestion were examined, and the human studies varied in the methodology of intervention diets and fecal collection duration, as well as nut type, dose, and form. This variation may have resulted in inconsistency in study results, reducing the strength of the overall evidence base. However, it should be noted that the control and intervention diets in human studies were tightly controlled for energy and macronutrient intake, and so it is unlikely that results would be influenced by differences in the diet. Furthermore, several human studies included a small number of participants; however, it should be noted that the human studies were labor-intensive and utilized a crossover design, allowing for a smaller sample size to be used. Human studies were heterogeneous in design, and the inclusion of in vitro studies in this review may impact the generalizability of findings. The primary focus of in vitro studies was lipid bioaccessibility; however, it is important to note that human studies that reported on ME considered energy from all macronutrients. Due to the nature of the review question, a meta-analysis was not appropriate for this systematic review, with narrative synthesis conducted instead. Finally, this review focused only on one energy regulation mechanism of nuts. Although the lower ME may partly explain the lack of an effect of nut consumption on body weight, increases in energy expenditure and dietary compensation following nut consumption also require further exploration [36,54–56].

Conclusion

This systematic review has indicated that the ME of tree nuts and peanuts is consistently lower than what is calculated using Atwater factors. The underlying mechanisms for these findings appear to be higher fecal fat excretion in human studies and lower-than-expected lipid release in the in vitro studies. Nut type, physical form, level of heat processing, and dose influence fat release, and hence ME should be considered when examining the effects of nut consumption on body weight. This lower-than-predicted ME may in part explain the lack of associations between nut intake and body weight observed in the literature and should be considered when creating nutrition messages for nut consumption. The lower ME of nuts observed in this review has potential implications for the development of food composition databases, food labeling, and informing dietary guidelines. However, given the variation in methods used between studies, further clinical trials are needed to determine the impact of the findings to clinical dietetics. As such, the findings of this review should be interpreted with caution. This systematic review has identified gaps in the research, which future studies should address. In particular, future studies should investigate the ME of understudied nuts, such as chestnuts, macadamias, pecans, and pine nuts, to further understand the mechanisms across all nut types.

Author disclosures

CJN receives a matching PhD scholarship, which is equally funded the University of Wollongong and Nuts for Life. YCP has been previously involved in clinical trials funded by and received funding from the California Walnut Commission, received funding and research support from the Almond Board of Australia, and received funding from Nuts for Life. S-YT was previously involved in clinical studies that were funded by the Almond Board of California, International Nut and Dried Fruit Council, and the California Walnut Commission. EPN has previously received research funding from Nuts for Life, the California Walnut Commission, and the International Nut and Dried Fruit Council.

Acknowledgments

The authors' responsibilities were as follows—CJN, YCP, S-YT, EPN: conceived and designed the study, analyzed the data, and wrote the manuscript; CJN: collected the data; and all authors: read and approved the final manuscript.

Funding

This work was supported by Nuts for Life via a matching PhD scholarship which CJN receives (matching scholarship is equally

funded by the University of Wollongong and Nuts for Life). Nuts for Life were not involved in the study design, data collection, analysis or interpretation, or writing of the report. There were no restrictions regarding publication.

Data availability

Additional data on quality appraisal is available from the author upon request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.advnut.2023.03.006.

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