DOI: 10.7860/JCDR/2022/51949.15852

Review Article

Nutrition Section

Influence of Protein Diet on Weight Change in Obesity: A Systematic Review

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ABSTRACT

Introduction: High protein in the diet has been shown to have a beneficial effect in promoting weight loss through its effect on satiety. This effect is mediated in part by the release of anorexigenic hormones which decrease subsequent food intake, leading to weight loss. A high protein content enhances muscle mass, has a higher thermogenic effect. The effect of a high protein meal on weight loss and satiety has been the subject of concern as only few studies are available. Therefore, the rationale of this review was to investigate the evidence supporting a relationship between protein content on weight loss and satiety in obese subjects.

Aim: The aim of this systematic review was to compare the effect of high dietary protein versus normal protein content or non protein diet on both weight loss and satiety in obesity.

Materials and Methods: In this systematic review, the studies were identified by searching Ovid Medline, Scopus, PubMed, and Evidence Based Medicine (EBM)-review Cochrane database and was restricted to English language only, from the inception until 10th June 2019. Studies which were included fulfilled the following criteria: Randomised Controlled Trial (RCT) duration of atleast 3 weeks; subject age ≥18-year-old; obese or overweight subject whose Body Mass Index (BMI) ≥25; composition of protein diet of 20-30%; satiety assessment by the Visual Analogue Scale (VAS) and Satiety Quotient (SQ); report on the mean difference of weight loss.

Results: Total 727 studies were screened, eleven studies were selected as they fulfilled the inclusion criteria. In the overall analysis, five studies revealed a significant difference in satiety measurement while only three studies had observed significant difference in weight loss. The remaining studies showed a similar mean weight loss and satiety outcome achieved in both the control and intervention groups.

Conclusion: The present systematic review demonstrated that the high protein content in the diet shows no significant effect on weight loss and satiety. However, it is important to note that though weight loss is mainly due to energy restriction, high protein in diet could influence satiety and thus both can complement each other.

Keywords: Dietary intervention, Energy balance, Energy restriction, Obesity, Satiety quotient

INTRODUCTION

High dietary protein has been well known and recognised to produce higher satiating effects than carbohydrate and fat by stimulating the released of satiety hormones [1-3]. Upon ingesting any protein meal, the hypothalamus will detect the entry of amino acids, thereby stimulating the endocrine cells in colon and ileum to increase the production of Glucagon-Like Peptide-1 (GLP-1) and Peptide YY (PYY) hormones [4-6]. These orexigenic hormones play a role in decreased subsequent food intake, leading to weight loss. Furthermore, not only protein meal assist in the development of lean body mass, but it also increases the body thermogenesis mediated via multiple metabolic processes (e.g., gluconeogenesis, deamination, and urea formation) involved in breaking down of protein meal [7-10].

Failure in adhering to energy-restricted diets due to the feeling of hunger has always been one of the major concerns in compliance with weight-loss diet interventions in obesity since inducing weight loss requires achieving negative energy balance [11,12]. Hence, by achieving satiety, obese participants may consume less subsequent food which will facilitate weight loss [13-16]. Besides, this strategy will also heavily influence eating behaviour as it influences the self-regulation of food intake [17-20].

Interestingly, many studies have been done to determine the influence of dietary protein on body weight loss [21-23], but not many studies were done to relate both weight loss and satiety outcome in obesity [12,24]. This is because many short-term studies had been done to link satiety and food intake instead and fewer studies were conducted to determine the relationship between satiety, reduced energy intake and weight loss in the longer term [25-35]. These studies have yet to be systematically reviewed to evaluate the role of dietary protein on both weight loss and satiety in obesity.

Therefore, this research aims to investigate the evidence supporting the effect of protein content on weight loss and satiety in obese subjects. To the best of our knowledge, this is the first systematic review, done to investigate the effect of high dietary protein on weight loss and satiety in obesity.

MATERIALS AND METHODS

A systematic review was conducted on four different databases which were Ovid Medline, Scopus, PubMed and EBM-review Cochrane.

Inclusion and Exclusion criteria: The inclusion and exclusion criteria were determined according to the Population, Intervention, Control and Outcomes (PICO) framework [Table/Fig-1] and a list of keywords was established and used to conduct the literature search [Table/Fig-2].

	Inclusion	Exclusion
Population	Subjects with obesity or overweight (BMI >25) and age 18 years and above of any sex and race.	1. Review article, case report, editorials, letters and comments. 2. Duplicate studies. 3. Less than three weeks duration. 4. Subjects aged below 18 years. 5. Subjects with genetic disease such as Cushing syndrome, and hyperinsulinemia. 6. Subjects who have undergone surgical procedures such as bariatric surgery. 7. Pregnant subjects.
Intervention	A high content of protein diet intervention (20-30%).	
Comparator	Low protein diet or non protein diet or subjects with normal BMI value.	
Study	- Randomised Controlled Trials (RCT). - Duration of study atleast 3 weeks. - Limited to publication using the English language only. - Able to report on the content of protein mean weight loss and satiety results among study participants. - Able to report primary outcome measures: weight changes, and satiety measured by validated method e.g., visual analogue scale and Satiety Quotient (SQ).	

[Table/Fig-1]: PICO framework with inclusion and exclusion criteria.

	Keywords
1	Dietary protein or high protein diet or protein diet
2	Weight change or weight loss or weight reduction or changes in body composition
3	Obese or overweight or fat distribution or fat composition or body fat mass or fat free mass or body mass index or BMI
4	Satiety or Sated or Fullness or desired to eat or frequency of eating or hunger suppression
5	#1 and #2 and #3 and #4

[Table/Fig-2]: List of keywords.

Search Strategy

A comprehensive search was performed using electronic databases including Ovid Medline, Scopus, PubMed, and EBM-review Cochrane from inception until 10th June 2019. The last search was performed on 10th June 2019. The search terms used were as follows: "protein diet" AND ("weight change" OR "weight loss" OR "weight reduction" OR "changes in body composition") AND {"obesity" OR "overweight" OR "fat distribution" OR "body fat mass" OR "fat free mass" OR "Body Mass Index (BMI) "} AND ("satiety" OR "fullness" OR "frequency of eating" OR "hunger suppression." The full search strategy is detailed in [Table/Fig-2]. References of the eligible studies and relevant systematic review were also manually screened for other eligible studies. The search for eligible studies was not restricted in terms of publication period or geographical setting.

Study Criteria and Selection

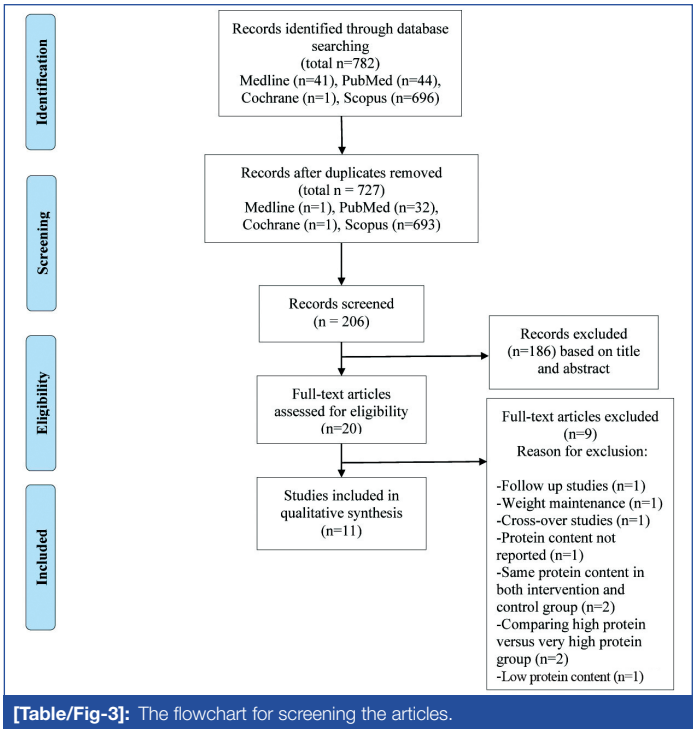
Studies that met the following criteria were included: (i) Population: adult, overweight or obese regardless of sex and race; (ii) Intervention: high protein diet consisting of meat, dairy products, nuts, or certain grains and beans given as a main meal, snack, or supplement for atleast 3 weeks. The protein composition must be atleast 20-30% of the total dietary composition. In studies comparing two type of protein diet, a dietary protein with a higher composition was considered as the study intervention; (iii) Comparator: Low or normal protein intake prescribed similarly to the intervention as defined above. Comparison to a non protein diet was also considered in this review; (iv) Study design: RCTs with atleast two parallel arms comparing high protein versus low or non protein diet; (v) Able to report primary outcome measures: weight changes, and satiety measured by validated method e.g., visual analogue scale and Satiety Quotient (SQ). Additional outcome considered included BMI changes and energy expenditure.

The exclusion criteria were as follows: (i) Population: subjects with underlying genetic disorder, Cushing syndrome, hyperinsulinemia, or subjects who have undergone a surgical procedure such as bariatric surgery. Pregnant subjects were also excluded; (ii) Other intervention and comparator protocol used; (iii) Study duration less than three weeks and study design other than RCTs (e.g., prospective or retrospective observational studies, reviews, experimental studies, and editorial) including abstract and conference proceeding; (iv) Studies with insufficient data or information and failed to report the outcome of interest.

To ensure no potential paper was overlooked, the references in any reviews were also screened. Duplicates were then removed from the study. The titles and abstract were independently reviewed for eligibility by two researchers (SY and BC). The full texts of eligible articles were assessed, and any disagreement were discussed with a third reviewer (JG) until a consensus was reached. The screening and selection process of the included studies is summarised in [Table/Fig-3]. The systematic review was conducted according to the Preferred Reporting Items for Systematic Review and Meta-analyses (PRISMA) guidelines [36].

Data Extraction and Management

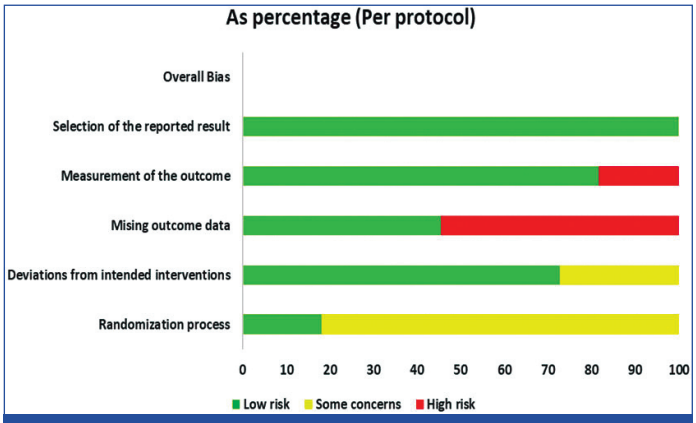
Data extraction into a pre-piloted and standardised form was performed independently by two reviewers (SY and BC). Study characteristics, including first author, geographical setting, participant's demographic information (e.g., mean age, underlying co-morbidity, proportion of gender), study duration, intervention and comparator used, were extracted. Primary outcomes (mean or percentage of weight changes, and satiety measured by validated method) were also extracted. Additionally, changes in BMI and energy expenditure were extracted. In case of missing or incomplete information, the respective author was contacted by email to request for the missing data if necessary.



[Table/Fig-3]: The flowchart for screening the articles.

Quality Assessment

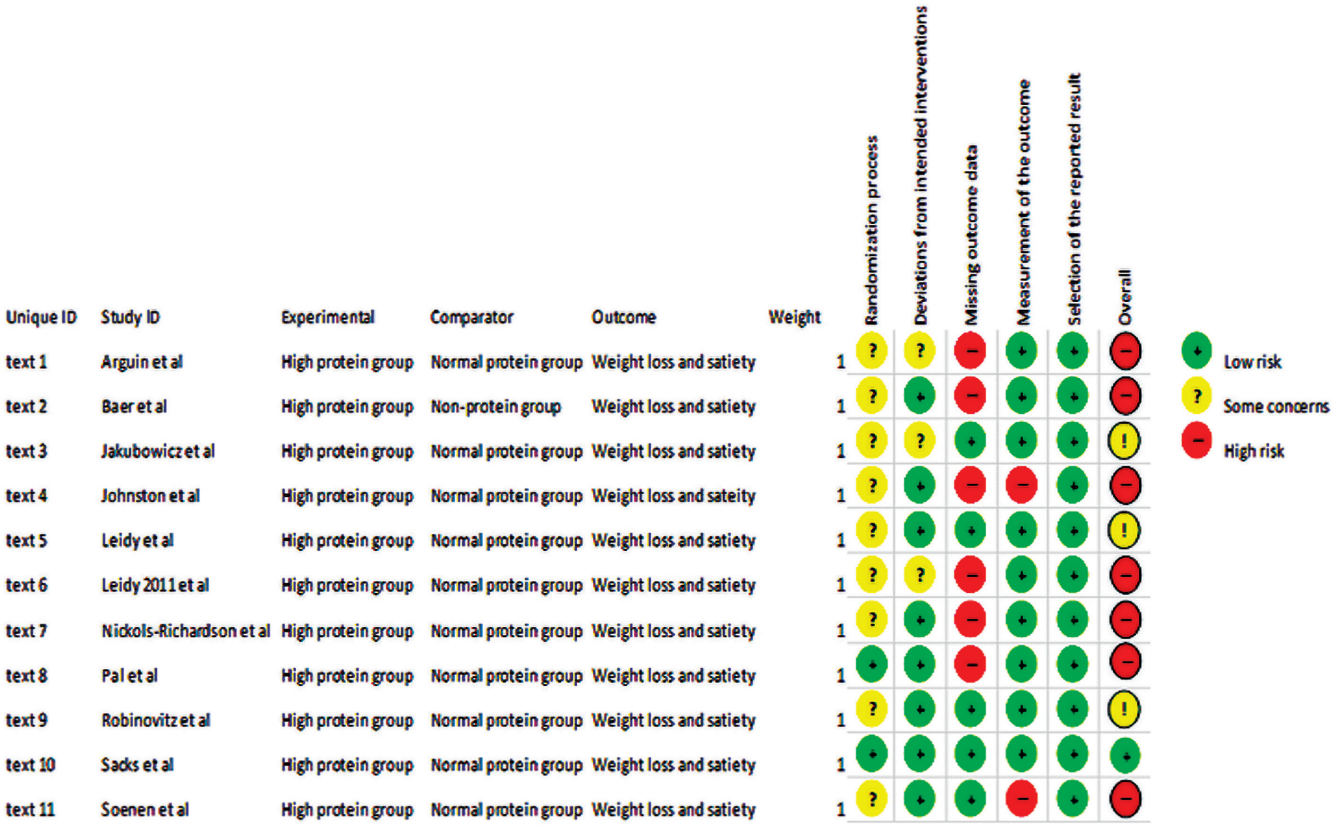
The methodological quality of the included studies was evaluated using the Cochrane Risk of Bias tool for RCT (RoB 2) [37]. The tool consisted of five domains which recommend the reporting of the randomisation process, blinding of participants/personnel/outcome assessor, completeness and selectiveness of outcome reporting. Each domain was judged as at being a "high", "low" or "unclear" RoB. If all the domains were judged to be "low", the overall RoB for a particular study was deemed as low. If any of the domain was judged as "high", the overall RoB for a particular study was deemed as high or unclear RoB [Table/Fig-4,5] [34,35,38-46]. Two reviewers (SY and NA) independently assessed the quality of each included study. Any conflict was discussed with a third reviewer (BC) until a consensus was reached.



[Table/Fig-4]: The graph of overall bias for all the included studies [34,35,38-46].

Data Synthesis

The study characteristics and methodological quality were summarised and tabulated. A meta-analysis was not performed because the intervention and comparator used were highly heterogeneous.



[Table/Fig-5]: The Risk of Bias (RoB) assessment for all the included studies [34,35,38-46].

RESULTS

After the screening process, which is detailed in [Table/Fig-3] only 11 articles were included in this review. The selected studies varied among one another in terms of intervention features which include dietary protein content, source of protein, intervention duration, and level of energy restriction. Three studies restricted their participants to consume 1500-1700 kcal/day [34,38,39], while four studies reduced the participants' energy intake by 200-750 kcal [35,40-42]. There were three studies that did not have energy restriction diet [43-45] while one study [46] prescribed ad libitum diet.

Furthermore, across the selected studies, the protein content consumed in control group ranged from 10-18% or 0.8 g/kg/day while high protein group consumed 20-30% or 1.2-1.4g/kg/day of protein. The end of study measurement was obtained after the end of study intervention ranging from six weeks to two years in nine studies while two studies measured after the end of the energy restriction period. The summary of the study characteristics of the selected studies are tabulated in [Table/Fig-6].

DISCUSSION

In this study, authors systematically reviewed studies that investigated the effect of high dietary protein on satiety and weight loss. Contrary to our expectations, most of the studies did not show a significant difference in both weight loss and satiety outcome. Among these eleven studies, five studies showed significant differences in satiety [35,40,41,43,45]. This can be explained by the decrease in concentration of ghrelin upon consuming high protein meal compared

Study and year, country of origin and duration	Study population, no of participants, number and percentage of dropout rate, Gender % Male BMI	Type of meal intervention	Groups	High protein group	Low protein or non protein group	Body weight measurement	Body weight		Weight change p-value	Satiety assessment; p-value of satiety measurement
				Source of protein (Dosage of protein in g or %)	Source of protein (Dosage of protein in g or %)		Pre in kg	Post or % change or change in kg		
Jakubowicz D et al., (2017) [34] **Country:** Venezuela **Duration:** 12 weeks	Obese, T2DM, N=56 D=14.3% Gender (male): 46.4% Age: 58.9±4.5 BMI average: 32.11±0.1	Breakfast, restricted to 1500 kcal/ day	Whey	a) Whey (42 g, 25%), b) Various source such as egg, tuna and soy (42 g, 25%)	Soy (17g 11%)	NR	Whey: 90.5±1.3	Whey: Post: 8.4±0.2	p<0.001	Visual analog scale; No significant differences
			Various				Various Source: 90.2±1.4	Various Source: 6.8±0.3		
			Soy				Soy: 91.3±1.9	Soy: 3.8±0.3		
Leidy HJ et al., (2007) [35] **Country:** USA **Duration:** 12 weeks	Overweight and obese women, N=54 D=14.8% Age: 50±2 Gender (male): 0% BMI range: 26-37	3-course meal, restricted to 750 kcal/day	Pork meat	Pork meat (1.4 g/kg/ day, 30%)	Milk (0.8 g/kg or 18%)	Fasted-state body weight was measured using an electronic platform scale (ES200L; Mettler, Toledo, OH)	Pork Meat: 82.6±3.4	Pork meat: -8.1±0.4	Not significant	Visual analog scale (Postprandial feeling of fullness was reduced by 27% in the NP group, whereas the HP group only had a reduction of 10%); Visual analog scale p<0.005
			Milk				Milk: 83.4±2.2	Milk: -9.5±1.0		

Johnston CS et al., (2003) [38] **Country:** USA **Duration:** 6 weeks	Overweight N=20 D=20% Age: 19-54 Gender (male): 10% BMI range: (≥5 kg over their target body weight and height	3-course meal, restricted to 1700 kcal/ day	Animal source Other	Animal source (low fat and dairy meals) (134 d/day, 32%)	NR (64 g, 15%)	Tanita body composition analyser TBF-300 A (subjects were weighed in light clothes without shoes)	Animal source; 82.1±8.9 Other: 78.2±7.4	Animal source: -5.7±0.6 Other: -5.9±0.5	p=0.826	7 point-Likert scale; No significant difference
Nickols-Richardson SM et al., (2005) [39] **Country:** USA **Duration:** 12 weeks	Overweight premenopausal women N=28 D=17.9% Age: 32-45 Gender (male): 0% BMI range: ≥25-40	3-course meal, HP=no energy restriction, HC=1500-1700 kcal/ day	High protein Low protein	NR (94±29 g, 27%)	NR (63±16, 18%)	After an overnight 12-hour fast, women were weighed to the nearest 0.1 kg (ScaleTronix, Wheaton, IL)	HP: 84.6±12.7 HC: 79.8±12.1	HP: -6.4 kg* HC:-4.2 kg*	p<0.05	Cognitive eating restraint score; No significant difference
Leidy HJ et al., (2011) [40] **Country:** USA **Duration:** 12 weeks (Week 7th onwards is eating frequency sub-study)	Overweight and obese men, N=27 D= 22.4% (week 1-6) Age: 47±3 Gender (male): 100% BMI range: 25.0-34.9	3-course meal, restricted by 750 kcal/day	Pork meat, eggs Milk	Pork meat, egg (1.4 g/ kg/day, 25%)	Milk (0.8 g/kg or 14%)	NR	Pork meat and eggs 105.2±3.8 Milk: 99.2±3.9	Pork meat and eggs -6.2±0.6 Milk -6.0±0.5	Not significant	Hourly (15 hr) and AUC appetite and fullness response (hourly and AUC fullness responses, 511±56 mm VS 243±54 mm); AUC appetite and fullness response p<0.005
Rabinovitz HR et al., (2014) [41] **Country:** Israel **Duration:** 12 weeks	Overweight, obese and T2DM, N=59 D=22% Age: 45-70 Gender (male): 35.6% BMI range: ≥25-40	Breakfast, restricted by 500 kcal/day	High protein Low protein	NR (23-30%)	NR (12-18%)	Detecto Physician Beam Scale (HOSPEQ, Inc Miami, Florida), before breakfast, wearing light clothes but no shoes.	Breakfast, Restricted: Pre: 87.05±12.2 Other: 89.23±14.7	Breakfast, Restricted: -2.43±0.46 kg Other: -1.86±0.4 kg	p=0.35	Hunger-satiety questionnaire (Preoccupied with food and urge to eat before meal); Hunger-satiety questionnaire p<0.001
Sacks FM et al., (2009) [42] **Country:** USA **Duration:** 2 years	Overweight and obese, N=811 D=20.5% Age: 51±9 Gender (male): 36.5% BMI average: 33±4	3-course meal, Restricted by 750 kcal/day	High protein Low protein	NR (25%)	NR (15%)	Measured in the morning before breakfast	93±16	3-course meal -4.5 kg Other: -3.6 kg	p=0.22	Visual analog scale; No significant differences
Arguin H et al., (2017) [43] **Country:** Canada **Duration:** 16 weeks	Obese men, low satiety phenotype (LSP) and high satiety phenotype (HSP) N=69 D=15.9% Age: 41.5±5.7 Gender (male): 100% BMI range: 30-40	Ad libitum diet and ad libitum control diet, No energy restriction	High protein Low protein	Meat, poultry, fish, eggs, milk and dairy products, nuts and seeds, tofu and soya (20-25%)	Dairy products, lean meat, poultry and fish, Legume (10-15%)	dual-energy X-ray absorptiometry (DXA; GE Medical Systems Lunar)	101±11.3	LSP- 3.2±2.9 HSP- 5.6±4.0 LSP- 4.5±3.1 HSP- 6.4±5.8	p=0.53	Satiety Quotient (SQ) (SQ hunger, fullness, perceived food consumption and mean SQ); SQ p<0.05
Baer DJ et al., (2011) [44] **Country:** Canada **Duration:** 23 weeks	Overweight and obese N=73 D=18.9% Age range: 40-62 Gender (male): 46.6% BMI range: 28-33	Protein supplement, No energy restriction	Whey Soy Maltodextrin	a) Whey b) Soy (1.4 g/kg/ day)	Maltodextrin, non protein (0.8 g/kg/ day)	Participants fasted for atleast 12 hour before the measurements and refrained from exercise. Weight is measured by air displacement plethysmography (BodPod 2000A, BodPod 2.0 Software, Life Measurement)	90.8±10.4	Whey: -1.8 kg (2%) compared to CHO Soy: Reduce by 0.9 kg compare to CHO Maltodextrin: Comparator group	p<0.006 (significant weight loss in WP compared to CHO)	Visual analog scale; No significant differences
Pal S et al., (2014) [45] **Country:** Australia **Duration:** 12 weeks	Overweight and obese, N=89 D=21.3% Age: 48±2 Gender (male): 14.3% BMI range: 25-40	Protein supplement, No energy restriction	Whey Casein Non protein	a) Whey (54 g) b) Casein (54 g)	Glucose (Non protein) (54 g)	Measured in a fasted state and wearing light clothing without shoes using UM-018 Digital Scales, Tanita, Tokyo, Japan)	Whey: 90.5±3.4 Casein 82.9±3.1 Non protein: 84.1±1.8	Whey: -0.8 kg* Casein: -0.8 kg* Non protein -0.3 kg*	Not significant	Visual analog scale p<0.05 (Significant increase rating of satiety in whey group compared to casein (p=0.025) and control (p=0.032))

Soenen S et al., (2013) [46] **Country:** USA **Duration:** 6 months (Phase 2: 6 weeks)	Obese N=72 D=10% Age: 44±4 Gender (male): 33.3% BMI average: 32±0.5	3-course meal, 67% energy restriction	High protein	NR (1.2 g/kg)	NR (0.8 g/kg/day)	Participants wearing underwear after an overnight fast by using a Bod Pod (Life Measurement)	3-course meal 90.0±14	3-course meal: -5 kg*	Not significant	visual analog scale of hunger and satiety, GLP-1 and PYY profile; No significant differences
			Low protein				Other: 90.0±14	Other: -6 kg*		

[Table/Fig-6]: Influence of protein diet on body weight and satiety in overweight and obese individuals [34,35,38-46].
LSP: Low satiety phenotype; HSP: High satiety phenotype; WP and WB: Whey protein group; SP: Soy protein group; CHO: Carbohydrate group; PB: Various protein source group; CB: High carbohydrate group; HPLF: High protein, low fat group; HCLF: High carbohydrate, low fat group; HP: High protein group; NP: Normal protein group; LC/HP: Low carbohydrate/high protein group; HC/LF: High carbohydrate/low fat group; BB: Big breakfast group; SB: Small breakfast group; HPD: High-protein diet; NPD: Normal-protein diet; SQ: Satiety quotient; VAS: Visual analog scale
[1]Values is stated as mean±standard deviation unless otherwise stated; *The average weight loss value was calculated based on the values provided in the respective study table. The formula used to calculate the value is stated below

$$\text{Formula} = \frac{(\text{Baseline} \times N) - (\text{End of study measurement} \times N)}{\text{Total number of participants involved (N)}}$$

to a normal protein meal. However, despite achieving satiety in the intervention group, there was no significant difference in weight loss. One possibility for no effect on weight loss could be due to non adherence (e.g., consuming higher calories intake than recommended) among the participants as reported in Rabinovitz HR et al., Baer DJ et al., and Pal S et al., conducted a protein supplement trial, with no energy restriction on the subjects and found a similar finding where the subjects in high protein group had significant decrease consumption of carbohydrate (p-value <0.05) compared to control group [41,44,45]. This result has supported the protein leverage hypothesis and may provide a significant finding in consuming protein supplements for achieving weight maintenance in long term.

Additionally, the two studies done by Leidy HJ et al., in (2007) and (2011) used a different source of protein in both the control and intervention groups [35,40]. The high protein group consumed animal protein while the normal protein group consumed milk and showed that higher protein (animal protein) had a better satiating effect than (normal protein) milk. However, the study design in these studies did not conclusively prove the effect of the source of protein as an important factor in inducing satiety [35,40]. Furthermore, a high adherence rate in high protein group was observed compared to normal protein group which may conclude that high dietary protein is more satiating and may be useful in weight management programs in the long term.

In our review, authors also found a statistically significant weight loss as an effect of protein in the diet in three studies [34,39,44]. However, in contrast to the previous studies, despite having significant weight loss, there was no significant change in satiety between control and intervention group in Nicols-Richardson SM et al., (2005) [39]. The study suggested that the participants in the control group may have the capability to restraint hunger when there is a strong motivation to lose weight. We also observed that the high dietary protein group in these studies achieved significant weight loss due to the satiety effect of the high protein content. Thus, the subjects with high protein in diet managed to lose weight through subsequently reduced food intake, thus supporting our hypothesis on the effect of high dietary protein on weight loss and satiety. Although significant weight loss was not achieved, there was a significant change in body composition such as the percentage of fat mass and lean body mass in Leidy HJ et al., (2011) and Arguin H et al., (2017) studies, respectively [40,43].

The remaining three of our included studies failed to achieve statistically significant changes in either satiety or weight loss [38,42,46]. Although, there was a reasonably significant difference in perceived satiety among the subjects in Johnston CS et al., (2004), the satiety measurement used was qualitative (e.g., 7-point Likert scale), thus making it difficult to evaluate the satiety effect [38]. Besides, consuming normal protein content may be sufficient to induce satiety as well. Furthermore, it is also possible that the weight loss achieved by both intervention and control group was due to energy restriction condition rather than the effect of macronutrient composition [38,46]. Also, having intensive behavioural counselling may be a key factor in motivating the participants to stay adhered to diet prescription and might result in successful weight loss, regardless of the type of diet [42].

Limitation(s)

There were several limitations to this review. First and most notable was the variety of different characteristics of the study protocols (i.e., source of protein, duration of intervention, level of energy restriction). Secondly, it was difficult to assess the quality of the experiment in most of the studies as clear details regarding methodology were not available. Thirdly, one of the studies did not comprehensively address the relationship between weight loss and satiety outcome since the priority of that study was to address the primary outcome which was the resting energy expenditure [46]. Lastly, the evidence presented in this review is only as good as the quality of the studies included. In this systematic review the effects of the types of protein provided have not been taken into account. Since, the effect of the type of proteins consumed has been shown to have some effect on muscle adaptation and metabolic process, which in may have an effect on body composition, muscle mass and energy expenditure [47]. In addition to this, an area which needs further exploration is the effect of age on satiety, hunger and energy balance [48]. In children as well, satiety and appetite can be affected by the composition of diet and protein content [49]. Hence, to take this work forwards, to areas which require systematic analysis of research done include the effect of the type of protein in the diet, and a consideration of age of the subjects and their interactions.

CONCLUSION(S)

In conclusion, our systematic review demonstrated that high protein content of the diet shows no significant effect on weight loss and satiety. However, it is important to note that weight loss is mainly due to energy restriction, while a high protein in the diet could influence satiety and thus both can complement each other.

Acknowledgement

This study was supported by International Medical University Internal Grant (Project ID No: BP I-01-2019(03)).

BC was the principal investigator and was responsible for the original ideas of the project. SY and NA conducted the systematic review along with JG and BC. Data analysis was conducted by NA, SY and BC. The manuscript was edited and drafted by BC and JG.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Aug 18, 2021
- Manual Googling: Oct 05, 2021
- iThenticate Software: Oct 12, 2021 (7%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? NA
- Was informed consent obtained from the subjects involved in the study? NA
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Aug 17, 2021**
Date of Peer Review: **Sep 15, 2021**
Date of Acceptance: **Oct 13, 2021**
Date of Publishing: **Jan 01, 2022**