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Systematic Review

Rose Hip as a Possible Herbal Remedy for Weight Loss: A Systematic Review

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Abstract

Background and objectives: Several studies have suggested that rose hip extracts have anti-obesity potential. Conventional medicines treating obesity are followed by multiple adverse side effects and is very cost full to society. This makes the investigation of herbal remedies with anti-obesity effects potential highly relevant. This systematic review aims to shed light on the results of existing literature reports on the correlation between the intake of rose hip extracts and anti-obesity effects.

Methods: A systematic literature search of PubMed and Web of Science was made to localize relevant experimental literature. Nine articles met the inclusion criteria, including one *in vitro* study, seven *in vivo* animal studies, and one human trial with pre-obese subjects. All nine articles are objectively reviewed in this systematic review.

Results: Eight out of nine articles, including the article on humans, presented significant anti-obesity effects. Though some limitations of the studies were found, including the human trial, seven possible metabolic mechanisms are suggested as the underlying cause of the significant effects.

Conclusions: Based on the findings of this review, rose hip extracts containing tiliroside found in the seeds have the potential to become a new herbal remedy with anti-obesity effects. Nevertheless, more research is needed to assess the effectiveness and optimal dosage of the rose hip treatment and to elucidate the underlying mechanisms of the effects.

Introduction

Obesity is associated with a higher risk of type 2 diabetes mellitus, cardiovascular diseases, stroke, fatty liver disease, and osteoarthritis among other diseases.[1] Despite attempts to change dietary patterns and increase the rate of exercise, many people struggle to lose weight and maintain weight loss; therefore, they need medication to promote sustained weight loss.[1] The available prescription medications for obesity help many people sustain their weight loss, thereby minimizing the incidence of obesity-related diseases.[1] This explains why the side effects of the medications are often tolerated. For example, the common side effects of the obesity medication Wegovy are nausea, gastrointestinal issues, vomiting, and constipation; whereas more adverse side effects include a higher risk of kidney failure, pancreatitis, and thyroid cancer.[2] To avoid these side effects of synthetically produced medications, the nutraceutical industry has investigated whether nature holds useful species or active compounds that have weight-lowering properties.[3]

During the past 20 years, the anti-obesity effects of plant flavonoids have been investigated.[4] Naturally, plants with a high content of flavonoids have been especially interesting. One example of such plant is the fruits of the plant family Rosaceae, called rose hip. This genus includes more than 100 subspecies that are found in most parts of the world. Thus, the appearance, including the color and size, as well as the nutritional content vary a lot from species to species.[5] Despite these differences, the botanical characteristics of rose hips are similar. Historically, the rose hips of different *Rosa* species have been used in traditional folk medicine as an herbal remedy to treat multiple diseases and disease-like conditions. For example, rose hips from *Rosa pratincola* were used to fight eye and stomach problems by the native North American people.[5] The hips consist of the hypanthium, also called the pericarp, and the seeds (Fig. 1).[6] The seeds are the actual fruits of the *Rosa* species, which is the reason for the name "pseudo fruit".[6] Rose hips

Keywords: Rose hips; *Rosa Canina* L.; Rosa davurica Pall.; Tiliroside; Herbal remedy; Weight loss; Visceral fat.

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Fig. 1. The pseudo fruits of *Rosa canina* as a whole and cut in halves. The seeds are visible, and the red fleshy part surrounding the seeds is called the hypanthium, pericarp, or shell.[6]

have some of the highest contents of ascorbic acid, also known as vitamin C, found in the plant kingdom. This water-soluble vitamin is a vital compound in many regards, protecting us against scurvy, being an important cofactor in the production of neurotransmitters, and playing a crucial role for a well-functioning immune system.[5] Rose hips also contain other vitamins like vitamin E as well as the precursors for vitamin A, carotenoids. Besides vitamins, rose hips have a high content of antioxidants, flavonoids, and fatty acids, including essential fatty acids. The fatty acid content, including the polyunsaturated fatty acid linoleic acid, is approximately four times as high in the seeds compared to the pericarp; whereas the levels of triterpenoids, galactolipids, vitamin E, and lycopene are higher in the pericarp.[5] Due to the variation of nutritional compounds in the pericarp and seeds, products containing only the pericarp, only the seeds, or both can have different effects on the body.[6]

Today, one of the most investigated rose hip species is the pseudo fruits of Rosa canina L. (RC). The sub-species RC is particularly rich in flavonoids, carotenoids, fatty acids, anti-inflammatory agents, and vitamin C.[6]

One particular glycosidic flavonoid, tiliroside, is found in the seeds of RC and has been investigated for its anti-obesity properties.[4,7] The aim of this study is to investigate how the intake of rose hips and possible anti-obesity effects are associated, through a systematic review of the existing literature on this topic. This review also aims to elucidate the underlying physiological mechanisms that might lead to weight loss during treatment with rose hip and discuss the findings of the review.

Methods

This review was conducted through a systematic literature search, used to locate relevant studies. Furthermore, a regular literature search was used to provide an adequate level of information to write the introduction section.

The systematic search was made by making two main blocks (1 and 2) with keywords and synonyms for rose hip and weight loss, respectively. A third block was made to further identify studies with a focus on tiliroside and included synonyms thereof (3). Both medical subject heading terms and free text words were used within each block (Table 1). All the words belonging to each of the blocks were combined with "OR" in the database (OR …OR). To gather the search blocks, they were combined with the "AND" command (AND …AND). The search protocol was conducted as shown in (Table 2). This search was made using the Web of Science and PubMed databases. One author ISBP conducted the search, and it was checked by the author KW. The systematic review was registered locally at the University of Copenhagen, but no international registration was made. The initial aim was a thesis on health perspectives of rose hip. During this process, the idea for this article occurred. Given the nature of the article, no protocol was published in an international register, it was only registered locally.

Eligibility criteria and screening method

After the systematic literature search, there were 33 available studies after removing replicates manually. To locate useful articles, the titles and abstracts were screened independently by to reviewers, ISBP and KW. Eligibility criteria were: (1) The study had to be an experimental study, and both *in vitro* and *in vivo* (animal or human) studies were included. (2) The primary or secondary outcome of the study had to be weight loss or loss of visceral fat mass. (3) The intervention of the study had to be treatment with any product made from rose hips of any species, including pure tiliroside extract made from rose hips.

Any study that did not meet all three abovementioned inclusion criteria was excluded. The screening method used was reading the abstracts and skimming the articles. This systematic method resulted in nine useful articles for this review.

Sought data items

The primary outcomes were the change in weight and fat mass before and after intervention, counting for both *in vitro* and *in vivo* studies. Both significant and non-significant results on this matter

Table 1. The blocks used for the block search as a part of the systematic literature search. These include Mesh terms and free-test keywords

Block #1
Mesh terms
Rosa [Mesh]
Free-text keywords
rosehip*
"rose hip"
"rose hips"
"rosa canina*"
"hyben vital"
hyben-vital
hyben

Block #2
Mesh terms
Weight loss [Mesh]
Intra-Abdominal Fat [Mesh]
Free-text keywords
visceral fat
"adipose tissue"
"abdominal fat*"
"fat percent"
"adipose cell*"
"adipose fat cell*"
obese*
Obesity

Block #3
Mesh terms
Flavonoids [Mesh]
Kaempferols [Mesh]
"tiliroside" [Supplementary Concept]
Free-text Keywords
tiliroside*
kaempferol*

Mesh, medical subject heading.

were included in the results (Table 3).[4,7–14]

Other data sought: Study design, duration of treatment and intervention, type of cell culture, animal sub-species, number of subjects, group size, inclusion criteria for the subjects, gender and age.

Quality assessment

All included articles were independently screened by both authors, assessing any potential risk of bias in the included articles. This included bias due to selection of participants, confounders, and measurement of outcomes, as well as the authors' own statement of conflict of interest. While our review did not identify a profound risk of bias in the included articles, it should be noted that no established risk of bias assessment tool was utilized in this analysis.

Results

Overview of included articles

The systematic research led to the inclusion of nine articles in this study. A flow diagram of the study selection process is found in Figure 2.[4,7–13] One article is a recent *in vitro* study,[8] while another article includes both an *in vitro* part and an *in vivo* part using mice as study subjects.[9] Six of the articles are *in vivo* model studies, where the study subjects are either mice or rats.[4,7,10–13] The ninth article included in this study, is a human randomized controlled trial (RCT) study with pre-obese humans as the study subjects.[14]

Methods and study design of included articles

In vitro findings

The study by Guillemet *et al*.,[8] aimed to investigate how 25 different botanical extracts affected the lipid accumulation, uncoupling protein 1 (UCP1) expression, and adenosine triphosphate production in human subcutaneous pre-adipose cells. This was done through a biphasic culture system, where the extracts first passed through a Caco-2-cell line, mimicking intestinal absorption. The extracts then were added to the pre-adipocytes to observe the effects. Green coffee extract was a positive control. Nagatomo *et al*.[9] performed similar research and used 3T3-L1 pre-adipocytes in their study. Rose hip and tiliroside extracts were added to the cells at three different doses, and berberine chloride was a positive control.

In vivo – animal study findings

Aim of the study

For six studies, either the main or secondary outcome was to measure the change of body weight and body fat content within the study subjects after an intervention of different rose hip treatments. Most of the studies also measured outcomes that did not relate to body weight or fat mass. These results are not included in this review.

Study subjects

The study subjects used were different species of mice, while Taherzadeh *et al*.[12] was the only *in vivo* study to use Wistar rats. Nagatomo *et al*.,[9] Ninomiya *et al*.,[7] Shen *et al*.,[10] Taherzadeh *et al*.,[12] and Cavalera *et al*.[11] used male study subjects; while Goto *et al*.[4] and Andersson *et al*.[13] used female test subjects.

Diets

In the reports by Nagatomo *et al*.,[9] Cavalera *et al*.,[11] Goto *et al*.,[4] and Taherzadeh *et al*.,[12] the study subjects were fed with a high-fat diet (HFD) either in combination with treatment or an inactive substitute. This investigates the treatments' ability to prevent the accumulation of fat. Shen *et al*.[10] and Andersson *et al*.[13] both used mice fed a low-fat diet as control groups, while the test groups were fed an HFD. The study by Ninomiya *et al*.[7] is the only one giving normal chow diet to both the control and test groups. All seven studies provided food *ad libitum* to the test subjects. The individual study protocols of each of the nine studies are listed in Table 3.

Table 2. The protocol for searching the Web of Science and PubMed, that led to a total of 33 articles to further filter through reading titles and abstracts, to assess for eligibility

Search date	Database	Inclusion and exclusion criteria	Search strategy	Number of results	Notes
3/12/23	PubMed	Year: 1995–2023	1: ("Rosa" [Mesh]) OR (rosehip* OR "rose hip" OR "rose hips" OR "rosa canina*" OR "hyben vital" OR "hyben" OR "hyben-vital")	1,744	The search of "#1 AND #3" made it possible to find articles that involve rosehip intake and weight loss, where potential effects were not attributed directly to the content of tiliroside.
			2: ("Flavonoids"[Mesh]) OR "Kaempferols"[Mesh] OR tiliroside* OR kaempferol*) OR ("tiliroside" [Supplementary Concept])	116,080	
			3: ("Weight Loss"[Mesh]) OR "Intra-Abdominal Fat"[Mesh] OR "adipose tissue*" OR "visceral fat" OR "abdominal fat" OR "fat percent*" OR "weight loss" OR "adipose cell*"	241,141	
			4: #1 AND #3	19	
			5: #1 AND #2 AND #3	5	
3/12/23	Web of Science	Year: 1995–2023	1: ("Rosa"[Mesh]) OR (rosehip* OR "rose hip" OR "rose hips" OR "rosa canina*" OR "hyben vital" OR "hyben" OR "hyben-vital")	1,367	The search of "#1 AND #3" made it possible to find articles that involves rosehip intake and weight loss, where potential effects were not attributed directly to the content of tiliroside.
			2: (("Flavonoids"[Mesh]) OR "Kaempferols"[Mesh] OR tiliroside* OR kaempferol*) OR ("tiliroside" [Supplementary Concept])	11,944	
			3: ("Weight Loss"[Mesh]) OR "Intra-Abdominal Fat"[Mesh] OR "adipose tissue*" OR "visceral fat" OR "abdominal fat" OR "fat percent*" OR "weight loss" OR "adipose cell*"	332,594	
			4: #1 AND #3	23	
			5: #1 AND #2 AND #3	3	

Length of intervention

The length of the interventions varied between 15 days and 20 weeks, as shown in the second column of Table 3.

***In vivo* – human study findings**

The study made by Nagatomo *et al*.[14] used pre-obese subjects in a single-center, double-blinded, randomized, placebo-controlled design, lasting for 12 weeks. The participants' food intake was measured by a meal survey, and their energy expenditure was measured by a pedometer and basal metabolism calculations. The participants were randomly assigned to two groups who were either assigned to be given a rose hip treatment for 12 weeks or a placebo.

Number of participants

***In vivo* – animal study findings**

The number of animals used in the different trials varied between 5 and 12 mice or rats. Ninomiya *et al*.[7] and Goto *et al*.[4] stated a range of animals per group to be between 5–7 mice and 6–7 mice, respectively, while all of the other studies stated the exact number of study subjects (Table 3).

***In vivo* – human study findings**

In the RCT study by Nagatomo *et al*.,[14] 152 subjects agreed to participate, while 32 participants met the inclusion criteria and were allocated randomly into two groups of 16 participants each. All 32 participants completed the 12-week trial.

Type of rose hip treatment – dosage, concentration, and variety of products

***In vitro* findings**

Guillemet *et al*.[8] made an RC hip water extract, making the concentration 0.72 g/L, which was added to the biphasic culture system. Nagatomo *et al*.[9] conducted an *in vitro* study using two extracts. The first was a commercial product called rosehip polyphenol EX (tiliroside content > 0.1%) was added to 3T3-L1 cells at doses of 62.5, 125, and 250 μg/mL. The second study was performed with

Table 3. An overview of the included studies including specification of study subjects, study design and test system, treatment, dosage, duration, and relevant significant results

Study	Subjects	Study design and test system	Treatment, duration	Relevant significant results
Guillemet *et al.*[a8]	-	IN VITRO Introduced to a Caco-2 cell line, and afterwards to human adipose cells. Lipid accumulation was measured. Positive control sample: green coffee extract	25 botanical extracts, including extract from *R. canina.*	Rose hip extract individually was the most efficient botanical extract Lipid accumulation (–33%) UCP1 expression (+40%) compared to green coffee extract. Rose hip and carrot seeds combined: Best overall effects on parameters.
Nagatomo *et al.*[b9]	C57BL/6J mice *n*=10 Age: 9 weeks Sex: male	IN VITRO (I) 3T3-L1 cells given treatment. Positive control: Berberine chloride. IN VIVO (II) A (*n*=5): HFD + RHE-t B (n=5): HFD.	IN VITRO (I) Rose hip extract (RHE): 125, 250, and 500 µg/mL Tiliroside: 31.3, 62.5, and 125 µg/mL Duration: 6 days. IN VIVO (II) Rose hip extract: 1% Rosehip Polyphenol Ex (<% tiliroside) (RHE-t) Duration: 8 weeks	IN VITRO (I) Tiliroside and RHE extracts significantly inhibited lipid accumulation above conc. above 31.3 and 125 µg/mL, respectively IN VIVO (II) A showed significantly lower body- and visceral fat content. A lower PPARγ protein expression in WAT was found (–38.8%).
Ninomiya *et al.*[b7]	ddY normal weight mice *n*=5–7 pr. group Age: 11 weeks Sex: male	A (*n*=5–7): Chow diet + RHE - a B (*n*=5–7): Chow diet, RHE - b 50 mg/kg/d C (*n*=5–7): Chow diet + RS - c D (*n*=5–7): Chow diet + RS - d E (*n*=5–7): Chow diet + TE - e F (*n*=5–7): Chow diet + TE - f G (*n*=5–7): Chow diet + TE - g H (*n*=5–7): Chow diet, control.	80% aqueous acetone R. canina extract (RHE) a) 25 mg/kg/d b) 50 mg/kg/d *R. canina* seed extract (RS): c) 12.5 mg/kg/d d) 25 mg/kg/d Tiliroside extract (TE): e) 0.1 mg/kg/d f) 1 mg/kg/d g) 10 mg/kg/d Duration:, days .	Significantly decreased body mass in B, C, D, E, F, and G. Significantly decreased visceral fat mass after treatment D, F, and G. Significantly increased expression of PPARα mRNA levels after single dose tiliroside 10 mg/kg. Extracts from the pericarps of *R. canina* showed no change in measured parameters.
Goto *et al.* [b4]	Obese, diabetic mice *n*=6–7 per group, total amount not specified. Age: 7 weeks Sex: female	A (*n*=6–7): HFD + TM B (*n*=6–7): HFD, control.	Tiliroside in methylcellulose (TM): 100 mg/kg/d Duration: 21 days	A nonsignificant decrease in body weight was seen for A. No significant decrease in body weight or visceral fat. Significantly decreased respiratory exchange ratio for A. Significantly increased activated AMPK in the liver and muscles. Significantly higher expression of PPARα and some FAO-related genes. Increased levels of adiponectin in plasma.

(continued)

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Table 3. *(continued)*

Study	Subjects	Study design and test system	Treatment, duration	Relevant significant results
Shen *et al*. [b10]	C57BL/6J mice *n*=32 Age: 4 weeks Sex: male	A (*n*=8): Chow diet + saline (*control*) B (*n*=8): HFD + saline C (*n*=8): HFD + Simvastin (*positive control*). D (*n*=8): HFD + *R. davurica* pall. extract	Saline: salt water, physiologic conc. Simvastin: 10 mg/kg/d *R. davurica* pall. extract: 200 mg/kg/d Duration: 12 weeks (5 weeks of HFD, 7 weeks of HFD + treatment)	Both C and D significantly inhibited the increase in body weight compared with B. Significantly increased mRNA expression of PPARα and other FAO-related genes. B altered gut microbiota, and D reversed this effect significantly.
Cavalera *et al*. [b11]	C57BL/6J mice *n*=24 Age: 8 weeks Sex: male	A (*n*=12): HFD+RHE B (*n*=12): HFD (control)	Rose hip powder* (RHE): 1/3 of total food intake Duration: 12 weeks *Powder from Orkla ASA, unknown species.	used in WAT and BAT in RH-mice significantly higher. Higher energy expenditure in group A mice during exercise. No significant changes in selected genes in BAT linked to consumption. In WAT, UCP1, bone morphogenetic protein 7, and other genes are upregulated in A. Some connected genes did not change. Cell death-inducing DNA fragmentation factor alpha-like effector A and phosphorylation of AMPK upregulated in A. Higher energy content of feces in A.
Taherzadeh *et al*. [b12]	Wistar rats *n*=24 Age: 6 weeks Sex: male	Pre-fed rats with HFD, 12 weeks. A (*n*=6): HFD (control) B (*n*=6): HFD + aerobic exercise (AE*). C (*n*=6): HFD + RHE D (*n*=6): HFD + AE + RHE. *AE: treadmill 5 times a week.	*R. canina* extract (RHE): 1E% of diet Duration: 12 weeks HFD *ad libitum*, 6-week treatment intervention.	Significantly decreased body weight and scWAT for B, C, and D. Significantly lower scWAT for B and D compared to C. Significantly higher levels of adipolin and irisin in D and not the other groups compared to A.
Andersson *et al*. [b13]	C57BL/6J mice *n*=41 Age: 6–8 weeks Sex: female	Prevention study (I) A (*n*=10): HFD B (*n*=10): HFD + RHE Intervention study (II) C (*n*=7): low-fat diet (control, all 24 w) D (*n*=7): HFD +RHE E (*n*=7): HFD	*R. canina* extract (RHE): 330.4 g/kg HFD (I) Duration: 20 w (II) Duration: 24 weeks (14 weeks of HFD, followed by 10 w of HFD + treatment)	(I) Significantly suppressed body weight in RH group during (I), already after 2 weeks. Body fat content significantly decreased after 5 weeks. (II) Less energy intake in RH group during (II). Significantly lower body weight for E than D after 3 weeks. Downregulation of genes in lipogenesis, while genes involved in FAO are not altered. Threefold higher levels of mRNA Peroxisome proliferator-activated receptor-gamma coactivator 1 alphain E. AMPK expression is not altered by RH supplement.
Nagatomo *et al*.[c14]	Human subjects with inclusion criteria: 25 > body mass index <30 *n*=32 Sex: 16 females, 16 males	Single-center, double-blinded, placebo RCT. A (*n*=16): Normal diet + Rose hip tablet B (*n*=16): Placebo.	Rose hip tablet: Rose hip polyphenol EX, <0.1% tiliroside. Placebo: Same appearance as Rose hip tablet. Duration: 12 weeks.	A and B were comparable throughout the whole study. Body weight significantly decreased after A and not B. Body fat mass was not significantly decreased in any of the groups or was different between groups. At week 8 and week 12, the visceral fat area was significantly decreased for group A. No significant change from week 0 in subcutaneous fat area for either A or B, but significantly lower in A compared to B. No difference in adverse events during trial for A and B. All occurring events were transient.

"Relevant significant results" displays whether the intervention of the study showed significant or non-significant changes in relevant outcomes. [a]*in vitro*; [b]*in-vivo* animal study; [c]*in-vivo* human study. AMPK, AMP-activated protein kinase; BAT, brown adipose tissue; FAO, fatty acid oxidation; HFD, high-fat diet; mRNA, messenger RNA; PPAR, peroxisome proliferator-activated receptor; RH, rose hip; RHE, rose hip extract; UCP1, uncoupling protein 1; WAT, white adipose tissue.

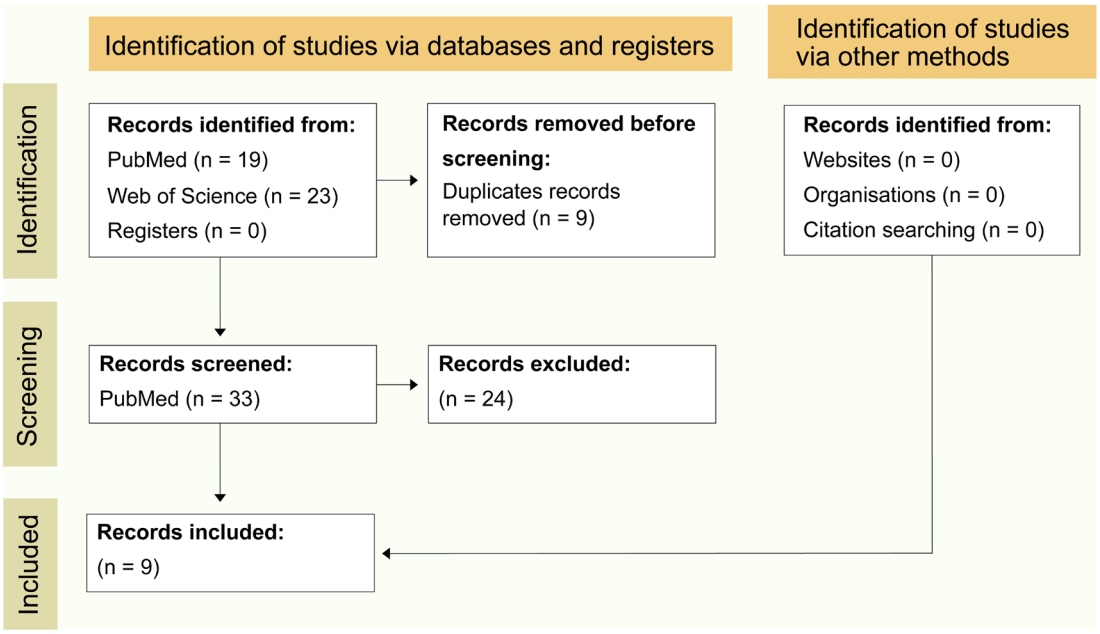

Fig. 2. Flow diagram elaborating the selection process of the studies included in this review.

tiliroside extract at doses of 15.6, 31.3, and 62.5 μg/mL.

In vivo – animal study findings

Some studies tested different types of rose hip extracts. Andersson *et al*.[13] used a pasteurized, freeze-dried, and puréed commercial RC product. The dosage used was 330.4 g/kg HFD. Shen *et al*.[10] was the only study not using RC. They used fruits from *Rosa davurica* Pall. The fruits were dried, crushed, and then extracted at 100°C with a 70% ethanol solution; afterwards, the *R. davurica* Pall content was dissolved in ethyl acetate, resulting in an extract with 63.58% flavonoid content, and the dosage was 200 mg/kg/d. Taherzadeh *et al*.[12] made an RC powder based on a 70% ethanol extract of RC seeds made at ambient temperature. The dose was estimated to be 1% of the given diet. Cavalera *et al*.[11] used a rose hip powder from Orkla ASA (Norway), where approximately 33% of the HFD mass consisted of rose hip powder.

Other studies tested both rose hip extracts and tiliroside extracts. The first study chronologically, Ninomiya *et al*.,[7] used three extracts: one RC-fruit extract in 80% aqueous acetone at doses of 25 mg/kg/d and 50 mg/kg/d, an extract from the seeds of RC at 12.5 mg/kg/d and 25 mg/kg/d, and a trans-tiliroside extract at 0.1–10 mg/kg/d.

Nagatomo *et al*.[9] also used Rosehip Polyphenol for their *in vivo* animal trial at a dosage of 1% of the diet. Another study, Goto *et al*.[4] aimed to test the effects of the glycoside tiliroside extracted from the seeds of RC at a dose of 100 mg/kg/d.

In vivo – human study findings

Nagatomo *et al*.[14] used the same Rosehip Polyphenol extract as Nagatomo *et al*.[9] to produce a tablet consisting of 100 mg of rose hip extract. The tablet was made indistinguishable from the placebo tablet, and one tablet was taken per day.

Effects of intervention on body weight and fat mass

In vitro findings

The rose hip treatment of the Caco-2 cell line and human adipose cells showed a significant reduction in lipid accumulation (–33%) and an increase in the expression of UCP1 proteins. The combination of carrot and rose hip extracts gave the most significant results.[8]

In vivo – animal study findings

Results regarding loss of weight and fat mass

Andersson *et al*.,[13] Nagatomo *et al*.,[9] Ninomiya *et al*.,[7] Shen *et al*.,[10] and Taherzadeh *et al*.[12] all demonstrated results showing a significantly decreased body weight after intervention. All of these studies also found a significantly decreased amount of visceral fat content, except Shen *et al*.,[10] who did not measure this parameter. Table 3 details the dosage, duration, and treatment leading to significant results. Goto *et al*.,[4] who treated the mice with a high dosage of tiliroside, 100 mg/kg/d, did not find any significant decrease in either body weight or visceral fat.

Relevant results of changed metabolism connected to adipose tissue and energy production. Several studies found changes in genes and proteins closely related to the regulation of adipogenesis and lipid metabolism. Nagatomo *et al*.[9] found decreased expression of peroxisome proliferator-activated receptor gamma (PPARγ) proteins in white adipose tissue (WAT). Meanwhile, Ninomiya *et al*.[7] found significantly increased expression levels of PPARα messenger RNA (mRNA) after a single dose of tiliroside (10 mg/kg), and Shen *et al*.[10] came to the same conclusion. Shen *et al*.[10] also found that the rose hip treatment could partly counteract microbial dysbiosis in animals fed an HFD. Cavalera *et al*.[11] and Goto *et al*.[4] both found an increase in phosphorylated AMP-activated protein kinase (AMPK) in subcutaneous fat and muscle tissue, respectively, while Cavalera *et al*.[11] also found an increase of UCP1, bone morphogenetic protein 7, and cell death-inducing DNA fragmentation factor alpha-like effector A expression in WAT as well as increased consumption in WAT and brown adipose tissue (BAT). Andersson *et al*.[13] found threefold higher levels of peroxisome proliferator-activated receptor-gamma coactivator 1 alpha mRNA in the treatment group, while other genes involved in fatty

acid oxidation (FAO) were not changed.

In vivo – human study findings

Nagatomo *et al*.[14] found significantly decreased body weight and visceral fat in the treatment group after the intervention, while the body fat percentage and subcutaneous fat mass were unchanged. The two groups were found to be equal at baseline. However, a non-significant lower fat area and visceral body weight were seen in the treatment group.

Potential adverse effects

In vitro findings

The cytotoxic effects of the 25 extracts used in the study by Guillemet *et al*.[8] were tested, and none of the extracts showed cytotoxic behavior.

In vivo – animal study findings

None of the studies by Andersson *et al*.,[13] Cavalera *et al*.,[11] Goto *et al*.,[4] Nagatomo *et al*.,[9] Ninomiya *et al*.,[7] Shen *et al*.,[10] and Taherzadeh *et al*.[12] include any information on adverse effects, but Taherzadeh *et al*.[12] did state that the safety of potential weight loss herbs must be further investigated.

In vivo – human study findings

Some adverse effects were observed in the study by Nagatomo *et al*.[14] in both the treatment and placebo groups. Adverse effects included headache, coughing, and abdominal pain; meanwhile, one case of loss of appetite and one case of sore throat were observed in the treatment group. All adverse effects showed no aggravation, and they were all transient.

Suggested physiological mechanisms leading to the outcomes: weight loss or loss of fat mass

All nine studies made qualified suggestions on what physiological mechanisms might be responsible for the significant results regarding intake of rose hip and loss of body weight or fat mass. These suggestions can be divided into four groups, which all give the same outcome:

1. Mechanisms leading to increased lipolysis and increased energy expenditure: Cavalera *et al*.[11] found the upregulation of phosphorylated AMPK (a) as well as the upregulation of BAT markers like UCP1, cell death-inducing DNA fragmentation factor alpha-like effector A, and bone morphogenetic protein 7, among others. Guillemet *et al*.[8] also found higher levels of UCP1. Taherzadeh *et al*.[12] found an increased production of irisin by adipose tissue, which is also a BAT marker (b). Goto *et al*.[4] presented higher plasma levels of adiponectin (c), leading to increased gene expression of PPARα (d), which is involved in FAO. Ninomiya *et al*.[7] also showed a higher production of PPARα. All these findings point toward higher energy expenditure through a higher degree of lipolysis or heat generation of the browning of WAT. Andersson *et al*.[13] did not find that higher levels of lipolysis can be the cause of significant weight loss.
2. Mechanisms resulting in decreased activity of lipogenesis and thereby lower degree of fat storage: Nagatomo *et al*.[9] and Andersson *et al*.[13] both showed the downregulation of lipogenic genes, including PPARγ, which is a key nuclear receptor protein responsible for adipogenesis and lipogenesis (e). Therefore, less fat is stored in the adipocytes and less pre-adipocytes differentiate into adipocytes. The polyphenols, especially kaempferol, of rose hips is suggested to act as antagonists of PPARγ.[9]
3. Mechanisms involving the intestines locally, resulting in less calorie uptake or production of beneficial substances: Cavalera *et al*.[11] also suggest another mechanism, which is that RC modifies the uptake of certain macronutrients, possibly leading to weight loss or loss of fat mass (f). The cellular and molecular interactions leading to this phenomenon are not commented on in their study. Shen *et al*.[10] found that the rose hip treatment reversed gut dysbiosis in obese mice and led to a higher microbiota diversity, which can result in higher production of health-promoting substances and possibly weight-loss-promoting substances (g).
4. Increased motility of the intestines: The human study by Nagatomo *et al*.[14] suggests that the results are caused by an enhanced activity of the autonomic nervous system (h). This will lead to increased motility of the intestines, which can result in the significant loss of visceral fat found in their study.

These four directions included different cooperating mechanisms, which all lead to the same goal: weight loss or loss of visceral fat. See Figure 3 for a visual representation of the mechanisms and their correlations.

Discussion

This review creates an overall impression that rose hip in doses which are realistic to achieve in your daily diet, can improve weight loss in animal models and also in humans. The same tendency was found two *in vitro* studies using human fat cell lines, indicating less fat accumulation in cells in the presence of rose hip extract.[8,9] Furthermore, six out of seven animal studies documented a statistically significant decrease in body weight loss as the result of treatment. Interestingly, the amount of visceral fat was also significantly reduced in studies, where this parameter was included. One study was not able to document a significant body weight loss although a clear trend was shown over time.[4] However, in the same study the estimation of several biological parameters involved in fat accumulation was statistically significant in favor of less fat accumulation. It is also of great interest that rose hip can demonstrate a body weight loss and a loss of visceral fat, also when testing humans in a blinded set up.[14]

It is encouraging to note, that fruits from a plant which can be found in the wild on sandy soil near beaches and in mountains and remote areas in many places of the world, as well as it is also found cultivated, can have such impact on fat accumulation. Rose hips have for a long time been known for its anti-inflammatory and antioxidant properties and it is available worldwide as a dry powder or as an extraction to cure pain in osteoarthritis,[15] and has been reported to lover total cholesterol also in humans.[16] In five out of six RCTs, patients with rheumatoid arthritis experienced pain relief and reduced stiffness when taking a dried powder of rose hips including pericarps and seeds. In one of these studies, the patients even reduced their intake of paracetamol by 50%, on average.[5] Arthritis is a common comorbidity of being overweight,[6] which in the context of this study is a very interesting connection. Thus, there is a possibility that rose hips might reduce symptoms of both conditions.[6] It is, however, an addition to our knowledge to see rose hip also as a possible modifier of fat accumulation. If so, it is worth speculating on possible biochemical mechanisms which can be responsible for the present findings and also what is the most interesting part of the fruit: the pericarp, the seeds or if tiliroside is possibly the only bioactive component of rose hip to perform the found results.

Intact rose hips

Treatment with whole rose hips, including pericarps and seeds, was used in three of the spoken studies.[8,10,14] The outcome was

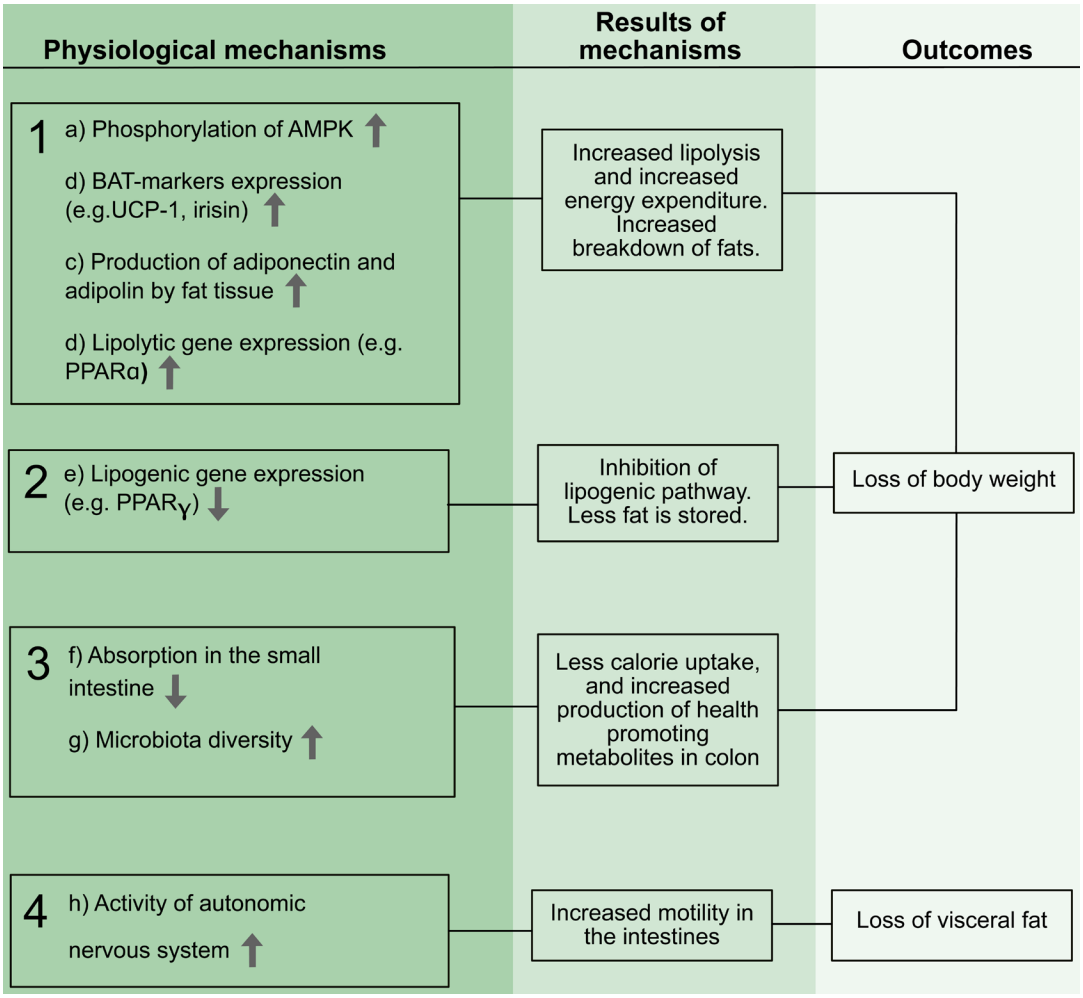

Fig. 3. Diagram showing the suggested physiological mechanisms by the nine articles, on how rose hip might exert its possible anti-obesity effect (a–g), and how they co-relate (1–4). The results of mechanisms further elaborate how these co-relating mechanisms lead to the outcomes of focus in this article, namely loss of body weight and loss of visceral fat. The arrows indicate whether the given mechanism is upregulated or downregulated. AMPK, AMP-activated protein kinase; BAT, brown adipose tissue; PPARα,peroxisome proliferator-activated receptor alpha; PPARγ, peroxisome proliferator-activated receptor gamma; UCP-1, uncoupling protein 1.

a decline in the accumulation of fat *in vitro*, a decrease in body weight in animal models (visceral fat was not measured) and a decrease of both body weight and visceral fat in humans. The suggested underlying mechanisms are found in Figure 3.

Rose hip flesh also called pericarps alone

A prevention of body weight gain was found, only using the pericarps from RC.[11] The suggested mechanisms were a transformation of white adipose cells into the thermogenically active beige adipose cells and a phosphorylation of AMPK inhibits lipogenesis and increases lipolysis.

However, when Ninomiya *et al*.[7] tested the effect of pericarps in mice in the same setup as fruits and seeds were tested, there were no impact on the weight at all. These contradictory observations make the impact on pericarps on weight reduction somewhat doubtful. More research on this subject is needed.

Rose hip seeds alone

Three of the papers referred to in this review use only the seeds for extraction.[7,9,12] Invariably these studies reported body weight loss and also loss of visceral fat in studies where this parameter was included. A decline in free fatty acids and triglyceride was also demonstrated. Suggested mechanisms were an upregulation of the genes for irisin and adipolin, an increase in adiponectin, activation of AMPK and an upregulation of PPAR.

Tiliroside isolated from rose hip as a monotherapy

Goto *et al*.[4] were not able to document any statistically significant decline in body weight only using tiliroside as a monotherapy although there was a trend over time. Plasma adiponectin increased and so did AMP-activated kinase. The authors concluded that there was an amelioration of obesity metabolic disorders. On the contrary a highly significant decline in body weight as well as in visceral fat was observed by Ninomiya *et al.,*[7] who also used tiliroside as monotherapy (Table 3).

The conclusion so far is that extractions from seeds and from whole fruits containing the seeds can lover bodyweight and improve lipid metabolism whereas extractions from the pericarp only

Table 4. The seven approved anti-obesity medicaments by the Federal Drug Administration of the USA

Medication	Effect	Possible side effects	Comments
Qsymia (Phentermine/ topiramate)	After 56 weeks, 70% had decreased their body weight by 5%.	Sedation, kidney stones, fatigue, anxiety, lack of focus.	Not approved by the European Medicines Agency
Orlistat	52.8% lose 5% of body weight.	Loss of vitamins, gas, hard-to-control stools, oily stools.	
Contrave	Body weight drop of 6.1% after 56 weeks at a high dose.	Nausea, headache, anxiety, and activation.	
Saxenda	Treatment and exercise resulted in long-term weight loss.	Gastro-intestinal side effects, pancreatic cancer, rarely thyroid cancer.	
Wegovy	Weight loss of 10–20%	Nausea, headache, gastrointestinal issues, diarrhea, constipation.	Long-term impact trials are needed.
Imcivree	80% and 45.5% reported more than 10% weight loss after 1 year.	Injection site response, increased pigmentation of the skin, nausea, vomiting.	
Mounjaro	Loss of 10.9 kg after 40 weeks combined with treatment with glargine (antidiabetic medicine)	Nausea, diarrhea, vomiting.	

The table includes the anti-obesity effects achieved by the individual medications as well as adverse side effects when receiving the product. All data are based on reports by Abdi Beshir *et al*.[1] and Siddiqui *et al*.[17]

seems less active possibly because of the lack of important constituents from the seeds, including tiliroside. Furthermore, tiliroside may not be able to stand alone, or will improve by not standing alone, according to the results from tiliroside monotherapy in comparison with the results when using extracts from the seeds.

When speculating on new treatments it is important to focus also on possible side effects. As rose hip especially rosa canina L, subspecies Lito, containing seeds and shells, has been tested in several placebo-controlled clinical trials and used in many countries for more than 20 years to alleviate pain from osteoarthritis and rheumatoid arthritis, there is strong evidence that rose hip is well tolerated.[15,16] This is in contrast to the reported side effects when using the traditional FDA approved weight lowering agent listed in Table 4.[1,17]

Reducing body weight from prescription medicine is cost full to the society.[18] So if any low-cost herbal remedy, which is easy to grow and harvest can modify weight gain or weight loss, even to a smaller extend, it is of interest. The rose hips presented in this review is not cost full and they are easy to grow.

Tiliroside is an important molecule, although it can possibly not stand alone, it is still worth speculating on other sources of tiliroside. Most spoken other sources which is easy to get and to grow is raspberry and seeds from strawberry.[19,20] Although we were able to find claims in the literature that these two fruits can lower body fat, we were not able to find well designed placebo-controlled, clinical studies in humans to suggest it. This can possibly be because a plant, which can lower bodyweight, needs more than tiliroside to be successful.

Limitations

Naturally, this review also has limitations. Eight of out nine studies used the hips of Rosa Canina L, while one study used *Rosa davurica* Pall. This means that the abovementioned significant results can only be attributed these two species, and no other versions of rose hips so far. In addition, no other parts of the plants besides the fruits have been assessed.

Furthermore, this review only included results regarding reduced body weight, loss of fat mass and metabolic parameters closely related to the regulation of fat metabolism and energy production. There are several other outcome measures in the nine papers among them symptoms of the metabolic syndrome, glucose tolerance and liver health. It would be interesting to assess these outcomes in another review paper.

Further perspectives

These preliminary studies on rose hip warrant a full scale randomized, double-blinded, placebo-controlled clinical trial on humans designed with a certain power to assure we dare to trust in what we find. Such study should aim, in a dose dependent manner, to compare fruits, seeds and tiliroside as monotherapy to placebo. We would suggest the duration of such study should be at least 6 months as eliminating fat from the body using herbal fractions can be a more time-consuming process than using prescription medicine.

Conclusions

This review has investigated the correlation between rose hip extracts and anti-obesity effects. Herbal remedies with anti-obesity effects are highly wanted due to the cost and multiple adverse effects of conventional anti-obesity medications. Eight out of nine included articles presented significant anti-obesity results, bearing in mind that some of the studies have some limitations. Nevertheless, this review suggests that there is potential for extracts of rose hips (*R. canina* L and *R. davurica* Pall.) to have anti-obesity effects. It is also suggested that the seeds of the rose hips are necessary to attain the bodyweight-lowering effects, possibly due to the glycosidic flavonoid tiliroside found in the seeds. Further studies are highly needed to expand the knowledge on what dosage leads to the most significant results, along with the effectiveness of rose hip treatment in general. Seven underlying mechanisms responsible for the anti-obesity effects are suggested in this review. To further elucidate the underlying physiological mechanisms, more research is necessary.

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Conflict of interest

The authors have no conflicts of interest to declare.

Author contributions

ISBP was the main author of this paper. KW wrote the parts concerning the physical mechanisms and was deeply involved in writing of the discussion.

Data sharing statement

All data extracted from the included studies can be found in within this article.

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