Int. J. Plant Bas. Pharm. (2022) 2(1), 64-81

INTERNATIONAL JOURNAL OF PLANT BASED PHARMACEUTICALS
https://ijpbp.com

REVIEW

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Edible seeds with potential anti-obesity impact: A Review

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ARTICLE INFO

Article History:

Received: 17 December 2021
Revised: 16 January 2022
Accepted: 16 January 2022
Available online: 21 January 2022

Edited by: B. Tepe

Keywords:
Alternative medicine
Dietary supplements
Functional food
Seeds
Obesity
Weight loss

ABSTRACT

Obesity and related metabolic diseases prevalence rates have risen dramatically in the recent decades, leading to severe health issues and increased mortality rates. A pressing need is evolved for a potential solution addressing obesity undermining. Bariatric dietary supplements and alternative medicine are recently gaining growing attention as a panacea for obesity owing to their rich nutritional profile and bioactive compounds. This systematic review was conducted to evaluate the current knowledge of some purported dietary seeds commonly used as functional food; quinoa (*Chenopodium quinoa*, L.), chia (*Salvia hispanica* L.), Hab El-Rashad (*Lepidium sativum*, L.), pumpkin (*Cucurbita pepo* L.) and fenugreek (*Trigonella foenum-graecum*). Due to the limited scientific evidence for their efficacy, future studies should empirically investigate dietary intervention structure to evaluate the impact on body mass status.

1. Introduction

Obesity is a major worldwide health problem that has increased widely in the past years. Recently, obesity rates or overweight people have continued to rise. The World Health Organization (WHO) defined obesity as an excessive accumulation of fats that lead to high health risk (Chooi et al., 2019). Obesity is illustrated by body mass index (BMI), which is the individual's weight in kilogram divided by the square of height in meters. WHO and CDC's Division of Nutrition, Physical Activity, and Obesity (DNPAO) defined the normal range of BMI as18.5 to 24.9 kg/m^2, overweight range as 25 to 29 kg/m^2, obese range as 30 to 39 kg/m^2, while severe obesity range is considered to be ≥ 40 kg/m^2 (Chooi et al., 2019; Petersen et al. 2019).

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e-ISSN: 2791-7509
doi: https://doi.org/10.62313/ijpbp.2022.17

Nearly one-third of the global population suffers from obesity and its cardiometabolic complications, leading to premature mortality (Chooi et al., 2019). Obesity incidence is a multifactorial problem (Figure 1) that plays a significant role in the pathogenesis of different diseases. Obesity increases the implications of many chronic diseases, including type 2 diabetes, hypertension, cardiovascular diseases, heart attacks, strokes, fatty liver, and several types of cancer (Blüher, 2019).

Consequently, the Food and Drug Administration (FDA) has been approving several dietary supplements as a potential means to control obesity and its related risk factors. Nowadays, edible fruits seeds use is very common and trendy as food supplements with anti-obesity effects. The use of these seeds could be due to the interplay between the secondary metabolites content and their potential effect to modulate the oxidative stress and inflammation that accompany the obesity besides their hypoglycemic effect, decreasing lipogenesis and enhancing lipolysis (Rodríguez-Pérez et al., 2019).

Please cite this article as: Hosny, H., Omran, N., Handoussa, H., 2022. Edible seeds with potential anti-obesity impact: A Review. International Journal of Plant Based Pharmaceuticals, 2(1), 64-81, https://doi.org/10.62313/ijpbp.2022.17.

In 1985, WHO estimated that about 65% of the world population predominately depended on plant-based traditional medicines for their primary health care. According to a survey done by WHO, 80% of 122 compounds identified from 94 plant species were used for the similar ethnomedical purpose. About 80% of the world's population currently relies on traditional medicines for their primary health needs, mainly by using plant extracts (Cragg and Newman, 2013).

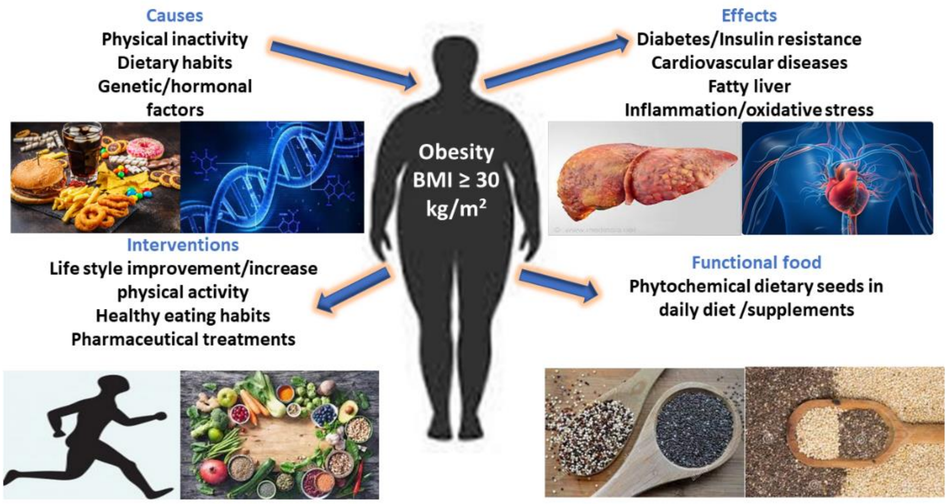


Figure 1. Schematic overview of the vicious cycle of obesity showing possible effects, cause, medical and functional food interventions

In the past years, seeds have been used widely against the battle of many chronic diseases, including obesity and related diseases. Every day, there is growing evidence about the use of dietary seeds and natural products either in food industries or in drugs and supplementary products (Moreno-Valdespino et al., 2020). Ancient people used medicinal plants to treat many illnesses, including obesity, and recently the use of medicinal plants has been widely increasing for their benefits and fewer side effects compared to allopathic medicines (Hussain et al., 2019). The nutritional supplements industry worldwide is now moving towards more beneficial attractive options by choosing particular types of food with known mechanisms to help decrease the worldwide tragedy of obesity (Monteiro and Cannon, 2019).

This review differs from previous societal ones by focusing specifically on seeds recommended by many health care professionals who provide treatments for obesity. The purpose of this review is to provide background information on their role in food intake and body weight in humans and their mechanism of action. These seeds are quinoa, chia, Hab El-Rashad, pumpkin, and fenugreek seeds.

2. Materials and methods

In the present review, several scientific databases, including PubMed, Web of Science, Wiley, Science Direct, Google Scholar, ACS Publications, Taylor & Francis, Springer, and Europe PMC, were searched for relevant literature using the keywords: obesity, natural products, dietary seeds, phenolic compounds, quinoa, chia, Hab El-Rashad, pumpkin and fenugreek seeds. All citations were combined using EndNote X8 (Thomson Reuters, Toronto, Canada). A total of 10.404 citations were recognized, and duplicates were removed (n = 2.176).

3. Inclusion/exclusion criteria

Data included in this review was based on the information derived from studies demonstrating the nutritional content of the seeds' nutritional content and their anti-obesity, antioxidant, anti-inflammatory effects in vivo and in vitro reports describing seeds' pharmacological and biological effects.

In the past years, edible seeds commonly used in the food industry have gained lots of importance due to many pharmacological activities that increased their application in the field of nutrition and as potential food supplements, as shown in Table 1.

4. Edible dietary seeds

4.1. Quinoa seeds

Quinoa (*Chenopodium quinoa*) seeds, as shown in Figure 2A, are widely cultivated in South America. They have a rich nutritional profile, as shown in Table 2, and a climate-resistant ability, making them an important seed that will be used widely in the future food industry (Bakhtavar and Afzal, 2020). Quinoa belongs to the family Amaranthaceae, order Caryophyllales which belongs to the core eudicots. It was known as 'suba' by the Bogota culture and 'jupha' or 'quinia' by the Bolivia culture. The species were domesticated within the South American range region, around the Titicaca Lake, approximately 5000 years ago. Presently it extends to the north and the south of the continent on the range of mountains, from Colombia to the south of Chile, where it is often found growing wild or cultivated (Burrieza et al., 2019). Quinoa is an herbaceous plant that grows annually, and its seeds are used as an alternative to cereals with high nutritional content.

For many years, it has been an indigenous grain in the Andes and has recently gained growing attention due to its higher protein, fat, and fiber content. Generally, fermented products have a strong antioxidant activity and are regarded as excellent antioxidant foods (Hirich et al., 2020).

Quinoa is an essential crop of food that can meet the demands of basic human nutrition stated by the United Nations of Food and Agriculture Organization. It is helpful for human health because of its nutrient abundance, including amino acids, minerals, dietary, and active polysaccharides, as demonstrated in Table 3 (Teng et al., 2020). Previous research has shown that quinoa has a strong anti-obesity effect. Yao et al. (2015) stated that quinoa seed consumption that lasted for 30 days resulted in an extensive decrease in body weight, levels of triglycerides (TGs), and low-density of lipoprotein (LDL) among 22 students aged 18-45 years (Yao, et al., 2015).

Table 1. Phyto-therapeutic seeds pharmacological activity

Seed	Pharmacological activity	Type of study	Dose/extract form	Result	Reference
Quinoa (*C. quinoa*)	Anti-obesity	3T3-L1 cell culture	12.5 and 25 mg/ml total extract	Renders triglycerides accumulation, down regulation of PPAR- γ and C/EBPα, controlling adipogenesis	(Yao et al., 2015)
		Human (22 patients age range 188-45 years)	Seeds incorporated in cereal bar for 30 days	Improved lipid profile (decreased serum cholesterol and triglycerides)	(Graf et al., 2015)
		Human (age range 18-45 years)	2.05 g/kg/day methanolic extract	Decreased serum triglycerides, total cholesterol, and LDL	(Ng and Wang, 2021)
	Antioxidant	Randomized clinical trial	Seed powder	Prevents lipid peroxidation, radical scavenging	(Fernández-López et al., 2020)
		Animal model (rats)	0.88 gm/kg/day methanolic extract	Increased liver glutathione and superoxide dismutase expression	(Ng and Wang, 2021)
		Animal model (mice)	20 mg/kg seed powder	Decreased lipid peroxidation, increased levels of glutathione and superoxide dismutase	(Saxena et al., 2017)
	Anti-diabetic	Animal model (rats)	310 gm/kg total extract	Decreased serum lipid profile, serum glucose	(Paśko et al., 2010)
		Human (age range 18-45)	20 gm/kg/day alcoholic extract	Improved glycemic profile, decreased serum glucose levels	(Ng and Wang, 2021)
	Anti-inflammatory	Animal model (rats)	100 gm/kg seeds	Decreased levels of protein carbonyls and interleukin (IL)-6	(Noratto et al., 2019)
		Human (age range 18-45)	25 gm/kg/day methanolic extract	Decreased levels of IL-6, no significant effect on TNF-α level	(Ng and Wang, 2021)
	Antiviral Antimicrobial	*Pomacea canaliculata*	100 and 500 μg/ml total extract	The predominance of saponins resulted in decreased permeability into bacterial/viral membranes leading to the lysis effect	(El Hazzam et al., 2020)
	Analgesic Immunostimulant	Animal model (mice)	70-90 mg/kg seeds	Increased anti-body responses (IgG/IgA)	(El Hazzam et al., 2020)
	Cosmetic agent (Emulsifying agent)	The cell-free broth at room temperature	Ethanolic extract	Emulsification potential in a different range of pH and temperature, to be incorporated in skin and hair products	(Bezerraa et al., 2020)
	Hepatoprotective	Human (age range 18-45)	4.8 gm/kg/day ethanolic extract	Improved liver functions, including ALT and AST levels, improved liver histopathological analysis	(Ng and Wang, 2021)
		Animal model (mice)	20 mg/kg seed powder	Improvement in histopathology of the liver after administration of quinoa seed powder	(Saxena et al., 2017)
Chia (*S. hispanica*)	Anti-obesity	Animal model (rats)	50 mg/kg seeds	Decreased serum lipid profile and rat's body weight	(Panchal, 2012)
		Human (77 participants)	Chia seed powder	Increased adiponectin levels, decreased C-reactive protein, and induced weight loss	(Felemban et al., 2020)
		Animal model (rats)	Chia seed oil	Improved lipid and glycemic profiles, decreased body weight	(Melo et al., 2019)
	Antioxidant	Dynamic gastrointestinal model simgi®	0.75 and 0.95% w/w seeds	Decreased serum glucose level and improved glycemic profile	(Tamargo et al., 2020)
		A gastrointestinal tract simulation	Ethanolic extract	Induced antioxidant activity through radical scavenging and *in vitro* ferrous ion chelation	(Melo et al., 2019)
	Anti-diabetic	Animal model (rats)	20% seeds	Normalizing fasting blood sugar levels, accompanied by decreased body weight	(Alamri, 2019)
		Randomized clinical trial (15 human participants)	25 gm/day chia seeds	Decreased serum glucose levels approaching normal levels	(Felemban et al., 2020)
		Randomized clinical trial	-	Decreased insulin resistance, improved glycemic profile, and decreased BMI	(Felemban et al., 2020)
	Anti-inflammatory	Animal model (rats)	133 gm/kg seeds	Decreased lipid peroxidation and oxidative stress	(Marcinek and Krejpcio, 2017)
		Animal model (rats)	Seed powder	Improvement in inflammation status through decreasing inflammatory cytokines	(Melo et al., 2019)
		Animal model (Wistar rats)	Seed powder	Decrease levels of thiobarbituric acid reactive substances (TBARS)	(Melo et al., 2019)
	Anti-hyperlipidemic Anti-cancer	-	-	Enrichment of α-linolenic acid induces apoptosis in tumor cells, normalizing lipid profile to normal levels	(Gazem and Chandrashekariah, 2016)

Seed	Pharmacological activity	Type of study	Dose/extract form	Result	Reference
		Animal model (mice)	Chia seed oil	Remarkable decreases in the tumor weight, activating caspase activity and promoting apoptosis	(Melo et al., 2019)
	Antimicrobial and antifungal	Human (20 patients with the duodenal ulcer)	1.4 gm total extract	Decreasing the symptoms and inhibition of *Helicobacter pylori* growth	(Pachi et al., 2020)
	Anti-hypertensive	Human (males and females suffering from hypertension)	Seed powder	Significant decrease in blood pressure with no renal or hepatic alteration	(Felemban et al., 2020)
		Randomized single-blind trial (11 men and 9 women, age range 18-75)	Chia seed oil	Control and decrease blood pressure and induce vasodilatation	(Melo et al., 2019)
Hab El-Rashad (*L. sativum*)	Anti-obesity	Animal model (rats)	100 mg/kg methanolic extract	Improvement of lipid and glycemic profiles along with decreased insulin resistance	(L'hadj et al., 2019)
		Animal (rats)	Seed powder	Improved lipid profile, decreased total cholesterol, and triglycerides, decreased body weight	(Shah et al., 2021)
	Antioxidant	*In vitro* analysis on human blood	40 µg/ml oil extract	Free radical scavenging	(Alqahtani et al., 2019)
		In vitro DPPH assay	Ethanolic extract	Significant antioxidant activity was determined	(Baregama and Goyal, 2019)
		Animal model (rats)	Ethanolic extract	The radical scavenging effect, decreased lipid peroxidation	(Shah et al., 2021)
	Anti-diabetic	Animal model (mice)	200 mg/kg ethanolic extract	Decreased fasting blood glucose levels along with decreased body weight	(Desai et al., 2017)
		Animal model (mouse)	Crude extract	Decreased serum glucose level and improved lipogenesis in diabetic mouse	(Shah et al., 2021)
		Animal model (rats)	Ethanolic extract	Improve insulin resistance and pancreatic beta cells integrity	(Shah et al., 2021)
	Anti-inflammatory	*In vitro* analysis on human blood	100, 200, 300 µg/ml oil extract	The anti-inflammatory effect was manifested by the protection of cell membrane	(Alqahtani et al., 2019)
		Animal model (rats)	Seed oil	Modulating inflammatory mediator leukotriene B4	(Shah et al., 2021)
		Animal model (rats)	Methanolic extract (50, 100, 200 mg/kg/day)	Decreased circulating inflammatory cytokines, decreased liver inflammation	(Shah et al., 2021)
	Antimicrobial	*Salmonella typhi* and *Streptococcus pneumonia*	Methanolic extract	Inhibition of bacterial growth	(Al-Snafi, 2019)
		Staphylococcus aureus, *Bacillus cereus* and *Escherichia coli*	Methanolic extract	Inhibition of bacterial growth manifested in zone inhibition	(Baregama and Goyal, 2019)
		Streptococcus equine and *Corynebacterium pseudotuberculosis*	Ethanolic extract (200 mg/ml)	Inhibition of growth	(Shah et al., 2021)
	Anti-fungal	*Aspergillus flavus*	Methanolic extract (30 mg/ml)	Complete growth inhibition	(Baregama and Goyal, 2019)
	Cytotoxic activity	Hep2 cells	Ethyl acetate extract	A potent cytotoxic effect was detected owing to the rich flavonoid content in the seed extract	(Baregama and Goyal, 2019)
	Diuretic activity	Animal model (rats)	Alcoholic extract (100 mg/kg)	Increased water excretion along with sodium and potassium excretion	(Patel et al., 2009)
	Anti-hypertensive	Animal model (rats)	Aqueous extract	Decreased blood pressure without affecting the heart rate	(Shah et al., 2021)
		Animal model (mice)	Aqueous extract (1000 mg/kg)	Decreased blood pressure	(Shah et al., 2021)
Pumpkin (*C. pepo*)	Anti-obesity	Animal model (rats)	100 mg/kg total extract	Decreased body weight and enhanced lipid profile	(Kalaivani et al., 2018)
		Animal model (rats)	Hydro-alcoholic extract (400 mg/kg/day)	Improved weight loss and modulates lipid profile	(Ghahremanloo et al., 2018)
	Antioxidant	*In vitro* analysis	50 mg/kg seeds	Radical scavenging activity, decreased lipid peroxidation	(Sharma et al., 2020)
		Animal model (rats)	Alcoholic extract	Decreased lipid peroxidation due to abundant polyphenols	(Adnan et al., 2017)
	Anti-diabetic	Animal model (rats)	200 mg/kg total extract	Decreased blood glucose levels and fasting blood glucose approaching normal levels	(Kushawaha et al., 2017)
		Animal model (diabetic rats)	Seed powder	Inhibit bile acid absorption, modulate glycemic profile	(Adnan et al., 2017)
		Animal model (rats)	Aqueous extract	Control diabetes through inhibition of α-amylase	(Sharma et al., 2020)
	Anti-inflammatory	Animal model (mice)	40-50 mg/kg seeds	Decreased the expression of inflammatory cytokines including IL-12, IL-1β, and TNF-α	(Dong et al., 2021)
	Hypotensive	Animal model (rats)	2 gm/day seed oil	Decreased blood pressure due to relaxation of vessels	(Kaur et al., 2019)
	Hepato-protective	Animal model (rats)	Seed powder	Decreased liver damage through histopathological examination	(Sharma et al., 2020)
	Anti-cancer activity	Animal model (rats)	Methanolic extract	Inhibit tumor growth	(Sharma et al., 2020)
		In vitro cell lines: breast carcinoma (MCF7) and liver carcinoma (HEPG2)	Seed oil	Significant cytotoxic effect on (MCF7) and (HEPG2) cell lines	(Adnan et al., 2017)

Seed	Pharmacological activity	Type of study	Dose/extract form	Result	Reference
	Antimicrobial activity	*Staphylococcus aureus* and *Escherichia coli*	Seed oil	Inhibition zone of growth of 60%	(Adnan et al., 2017)
Fenugreek (*T. foenum-graecum*)	Anti-obesity	Animal model (rats)	300 and 500 mg/kg alcoholic extract	Decreased lipid profile and body weight	(Gurunath, 2019)
		Animal model (rats)	Aqueous extract	Decreased fat accumulation and improved lipid profile through improving lipid metabolism and decreasing lipase enzyme	(Yao et al., 2020)
		Randomized clinical trial (39 overweigh males)	Aqueous extract	Decreased the fat absorption and prevented lipid accumulation	(Yao et al., 2020)
	Antioxidant	Animal (rats)	Daily intake of seeds	Decreases oxidative stress and decreased LDL oxidation	(Srinivasan, 2019)
		Animal (rats)	Aqueous extract	Decreased lipid peroxidation and increased glutathione and beta-carotene	(Almatroodi et al., 2021)
		In vitro analysis (DPPH assay)	Seed oil	Hight antioxidant percent showing radical scavenging activity	(Almatroodi et al., 2021)
	Anti-diabetic	Animal model (rats)	200 mg/kg aqueous extract	Decreases serum glucose levels	(Alsieni et al. 2021)
		Human (diabetic patients)	Fenugreek gum	Decreased serum glucose and improved insulin resistance	(Yao et al., 2020)
	Anti-inflammatory	Animal model (mice)	0.2 mL/g/day ethanolic extract	Decreased expression of inflammatory cytokines including TNF-α, IL-6, IL-1β, and MCP-1 and decreased infiltration of macrophages in adipose tissues	(Zhou et al., 2020)
		Animal model (induced arthritic rats)	Petroleum ether extract (0.5 ml/kg)	Decreased edema and decreased inflammatory cytokines, also modulating cyclooxygenase enzyme (COX)	(Almatroodi et al., 2021)
	Galactagogue	Human (women)	580 and 610 mg in capsules (3 times per day)	Increased secretion of breast milk in 24-72 hours	(Yao et al., 2020)
	Antimicrobial and antiviral	Animal model (rats)	0.05-1.6 µg/mL	Decreased microbial growth	(Mohamadi et al., 2018)
	Anti-carcinogenic	Animal model (rats) induced breast cancer	200 mg/kg ethanolic extract	Inhibited hyperplasia of mammary glands	(Jhajhria and Kumar, 2016)
		A-549 male lung carcinoma and MCF-7 female breast cancer cell lines	Ethanolic extract	Induced apoptosis and decreased tumor activity	(Jhajhria and Kumar, 2016)
		Animal model (mice)	Seeds powder	Protects against cyclophosphamide-induced apoptosis and lipid peroxidation in the urinary bladder of experimental mice	(Jhajhria and Kumar, 2016)
	Hepatoprotective	Thiamethoxam induced liver injury cell line	Polysaccharide fenugreek extract	Reduced liver toxicity and induced healing	(Yao et al., 2020)
		Animal model (carbon tetrachloride-induced liver injury in rats)	Ethanolic extract	Decreased liver injury through radical scavenging activity	(Almatroodi et al., 2021)
		Animal model (high-fat diet-induced mice)	Seed powder	Decreased liver enzymes (ALT and AST) and improved histopathological analysis	(Almatroodi et al., 2021)

Saponin, 20-hydroxyecoyson, and dietary fiber found in quinoa, as depicted in Table 3, were reported to have an anti-obesity effect. It was reported that saponins in quinoa seeds inhibit triglyceride (TG) accumulation in mature adipocytes (Ellulu et al., 2017). It was also stated that mice treated with quinoa seed extract showed lower levels of inflammation manifested in less inflammatory markers as well as decreased insulin resistance. Quinoa administration may prevent diet-induced obesity and control adipocyte-specific obesity expression of a gene in mice (Foucault et al., 2012).

It is reported that high-risk patient groups will benefit from quinoa, for example, people with diabetes, dyslipidemia, and obesity, due to its high nutritional value characteristics, therapeutic characteristics, and being a material free of gluten. Such characteristics are directly linked to the quinoa seed levels of minerals, fibers, vitamins, fatty acids, antioxidants, and phenolics that significantly impact human nutrition and well-being maintenance conditions (Navruz-Varli and Sanlier, 2016).

According to recent studies, it was found that quinoa seeds have a significant ability to enhance the health conditions related to obesity as well as reduce body weight. A study performed on induced obesity in Wistar rats showed that the test group subjected to quinoa seeds had lower glucose levels and an enhanced lipid profile manifested in decreased levels of LDL, total cholesterol, and triglycerides proving the significant impact of quinoa seeds on obesity (Paśko et al., 2010).

4.2. Chia seeds

Chia (*Salvia hispanica* L.) seeds, as depicted in Figure 2B, belong to the family Lamiaceae. It is an annual herbaceous plant native to Northern Guatemala and Southern Mexico. Its name comes from the word "salvere" in Latin related to the healing properties of the well-known *Salvia officinalis* herb for culinary and medicinal purposes, also called Mexican chia or salba chia. (de Falco et al., 2017).

Chia seeds play a significant role as a functional food and nutritional supplement shown in Table 2. The composition and concentration of their bioactive compounds, as shown in Table 3, depending on several factors: climatic conditions, geographical origin, and extraction methods. Moreover, chia seeds do not produce toxic compounds and are gluten-free (de Falco et al., 2017).

Chia seeds are of high interest nowadays as anti-obesity nutraceuticals. It was reported that chia seed extracts directly relate to the downregulation of the expression of genes related to lipid synthesis (Chooi et al., 2019).

Chia seeds are rich in dietary fibers, which decrease the sense of hunger and omega-3 necessary for the emulsification and absorption of many essential nutrients, including liposoluble vitamins A, D, E, and K. Moreover, it was reported that chia seeds also improve the metabolism of glucose that could be an excellent alternative strategy to develop successful, safe anti-obesity nutraceuticals for the future (Rubavathi et al., 2019).

According to recent studies, it was stated that chia seeds are rich in α-linolenic acid (ALA), which was believed to be related to decreasing body weight. Test subjects treated with chia seeds showed a significant decrease in body weight compared to those fed with a high-fat diet that suggested that α-linolenic acid decreased lipoid accumulation and improved lipid profile of these subjects. The exact mechanism behind the ability of chia seeds to reduce body weight is still under investigation, but it is considered a promising weight loss herbal nutraceutical (Han et al., 2020).

Table 2. The nutritional profile of phytotherapeutic seeds

	Fibers		Ash		Protein		Fat		Moisture		Reference
Quinoa	14.40	Avg% 17.02	1.58	Avg% 1.56	16.71	Avg% 16.78	5.5	Avg% 5.9	8.35	Avg% 8.225	(Nowak et al., 2016)
	19.651		1.53		16.85		6.3		8.10		
Chia	29.80	Avg% 30.3	4.32	Avg% 4.33	17.51	Avg% 17.405	16.05	Avg% 16.125	4.5	Avg% 4.425	(Kulczyński et al., 2019)
	30.83		4.34		17.3		16.2		4.35		
Fenugreek	10.36	Avg% 10.615	3.43	Avg% 3.45	24.5	Avg% 25.05	6.5	Avg% 6.85	2.77	Avg% 2.89	(Afzal et al., 2016)
	10.87		3.47		25.6		7.2		3.01		
Pumpkin	14.80	Avg% 15.16	4.15	Avg% 4.10	18.5	Avg% 18.195	17.85	Avg% 17.675	5.97	Avg% 6.12	(Syed et al., 2019)
	15.52		4.04		17.89		17.5		6.27		
Hab El-Rashad	29.85	Avg% 30.035	4.31	Avg% 4.34	20.65	Avg% 20.88	17.67	Avg% 18.35	7.86	Avg% 7.91	(Gokavi et al., 2004)
	30.22		4.36		21.10		19.03		7.95		

Chia seeds are a healthy source of fibers, proteins, antioxidants, essential fatty acids, and minerals. These seeds are considered by many to be a "superfood" that contributes to human nutrition and fights obesity by helping to raise the satiety index. Furthermore, chia seeds are considered gluten-free, making them a safe alternative for many food products that increase the obesity risk (Caruso et al., 2018).

Figure 2. Dietary seeds (A); quinoa (*C. quinoa*), (B); chia (*S. hispanica*), (C); Hab El-Rashad (*L. sativum*), (D); pumpkin (*C. pepo*), (E); fenugreek (*T. foenum-graecum*)

4.3. Hab El-Rashad seeds

Hab El-Rashad seeds, as demonstrated in Figure 2C, is originally called *Lepidium sativum* L. and is considered to be edible plant that belongs to cruciferous plants. This species was grown in ancient Greece as a grain. *L. sativum* was a nutritional source for ancient Egyptians who used it as an essential food source long before the invention of bread (Al-Fuhaid, 2018). Hab El-Rashad is also well known as garden cress which is widely used in food industry and in dietetic products (Rafińska et al., 2019).

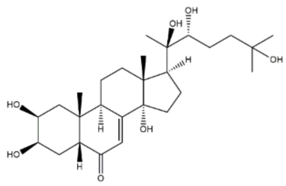
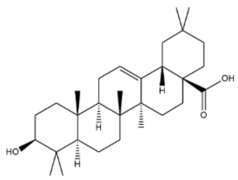
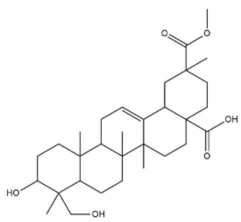
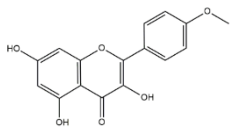
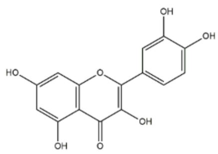
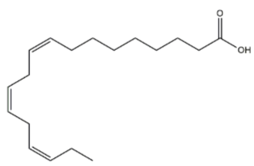
In Egypt and Saudi Arabia *L. sativum* is widely known with its Arabic name Hab El-Rashad. It is a widely spread medicinal plant cultivated in different temperate climates around the world. It has different names according to the place of origin, such as Garten-Kresse in Germany, Shahi in Iran and Agretto in Italy (Al-Fuhaid, 2018).

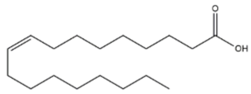
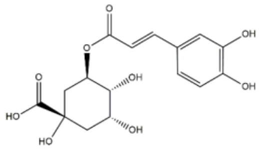
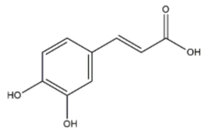
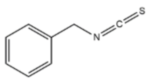
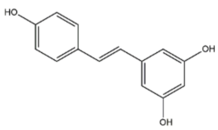
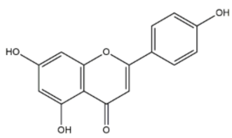
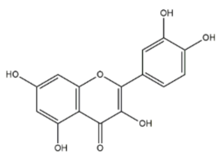
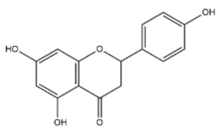
Hab El-Rashad seeds are mainly used in traditional medicine to treat asthma, hypertension, hepatotoxicity, and hyperglycemia. It is also known as Haliv in India and has been historically used in the lactating women's diet as well as treating diarrhea and dysentery (Rafińska et al., 2019).

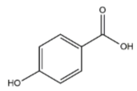
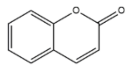
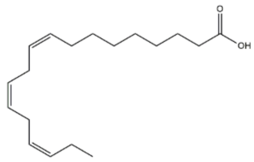
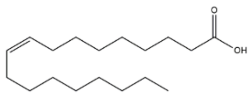
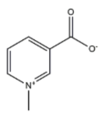
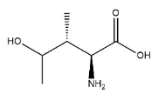
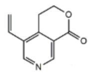
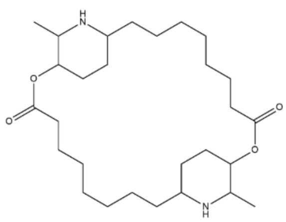
L. sativum seeds has drawn great attention in the recent years for many research aspects, especially its high nutritional content as shown in Table 2 and its biological effect in reducing the risk of obesity and its related health problems. It was reported that the Hab El-Rashad seeds had hypercholesterolemic and hypoglycemic effect which help decreasing the onset of obesity. The exact mechanisms are still under investigation; however, these seeds are promising remedies for treatment of obesity (Abdulmalek et al., 2021).

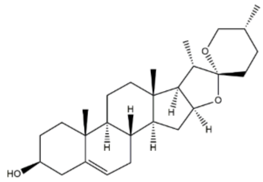
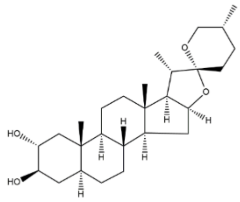
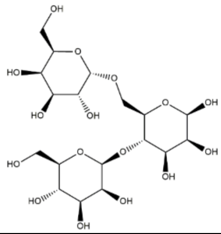
A recent study revealed that dietary supplementation with Hab El-Rashad seeds powder (*L. sativum*) had a tremendous positive effect on metabolic rate, oxidative stress, and related histopathological injuries manifested in obesity. It was also reported that Hab El-Rashad seeds induced weight loss in test subjects along with the enhancement of the lipid profile through lowering the levels of total cholesterol, triglycerides and LDL in Sprague Dawley rats that were exposed to high-fat ratios nutrition (L'hadj et al., 2019). Several authors attributed this beneficial effect to the phytochemical molecules, especially the flavonoid group which has the mimetic insulin property of improving sensitivity to insulin playing a significant role in enhancing the condition of obesity (Alharbi and Hanan, 2017).

Table 3. Anti-obesity main bioactive compounds in phyto-therapeutic seeds

Seed	Bioactive compound	Structure	Reference
Quinoa (*C. quinoa*)	20-Hydroxyecoyson		(Ellulu et al., 2017)
	Oleanolic acid		(Ellulu et al., 2017)
	Phytolaccagenic acid		(Tang and Tsao, 2017)
	Kaempferol		(Tang and Tsao, 2017)
	Quercetin		(Tang and Tsao, 2017)
Chia (*S. hispanica*)	α-Linolenic acid (ALA)		(Han et al., 2020)

Seed	Bioactive compound	Structure	Reference
	Oleic acid		(Han et al., 2020)
	Chlorogenic acid		(Marcinek and Krejpcio, 2017)
	Caffeic acid		(Marcinek and Krejpcio, 2017)
Hab El-Rashad (*L. sativum*)	Benzyl isothiocyanate (BITC)		(Yokoyama et al., 2020)
	Resveratrol		(Marrelli et al., 2020)
	Apigenin		(L'hadj et al., 2019)
	Quercetin		(L'hadj et al., 2019)
	Naringenin		(L'hadj et al., 2019)

Seed	Bioactive compound	Structure	Reference
Pumpkin (*C. pepo*)	*p*-Hydroxybenzoic acid		(Dotto and Chacha, 2020)
	Coumaric acid		(Dotto and Chacha, 2020)
	Linoleic acid		(Hernández-Pérez et al., 2021)
	Oleic acid		(Hernández-Pérez et al., 2021)
	Trigonelline		(Hernández-Pérez et al., 2021)
Fenugreek (*T. foenum-graecum*)	4-Hydroxyisoleucine		(Zhou et al., 2020)
	Gentianine		(Kandhare et al., 2018)
	Carpaine		(Kandhare et al., 2018)

Seed	Bioactive compound	Structure	Reference
	Diosgenin		(Kandhare et al., 2018)
	Gitogenin		(Kandhare et al., 2018)
	Galactomannan		(Kandhare et al., 2018)

Insulin resistance, type 2 diabetes, dyslipidemia, and cardiovascular disorders are associated with obesity. It is understood that adipokines, adipose tissue markers, and other adipose-derived peptides influence the intake of foods where insulin controls their expression (Achari and Jain, 2017). According to recent studies it was reported that Hab El-Rashad seeds are rich in phenolic compounds and flavonoids that may aid to its anti-obesity action as shown in Table 3 (Elshawwa, 2020).

Hab El-Rashad seeds were found to be rich in benzyl isothiocyanate (BITC) which belongs to the glucosinolates. These are sulfur-containing phytochemicals abundant in various cruciferous crops and edible herbal plants. According to recent studies the elevated level of BITC found in Hab El-Rashad seeds plays an important role in increasing the body libido and balancing the thyroid hormone and consequently increasing the metabolic rate which has a positive effect on obesity (Yokoyama et al., 2020).

4.4. Pumpkin seeds

Pumpkin (*Cucurbita pepo* L.) seeds as shown in *Figure 2D*, belongs to family Cucurbitaceae. They are commonly used edible seeds all over the world, as they are rich in phytosterols, proteins, vitamins and minerals (Ademiluyi et al., 2019). *C. pepo* is widely known as pumpkin, pompom in France and pepon or larger melon in Greece. It was originally cultivated by ancient Americans, and it is also cultivated in many other regions including India, Brazil, Argentina and Mexico (Joebstl et al., 2010).

This plant has been employed in the food industry for the production of purees, juices, jams, and alcoholic beverages. Pumpkin seeds as a rich source of bioactive compounds have been used frequently as functional foods or medicines. Moreover, the pumpkin seed has gained attention not only as an edible seed, but also as a potential nutraceutical supplement (Montesano et al., 2018).

The potential of pumpkin seeds to have anti-obesity effect was recently investigated, where a recent study reported that rats fed on high fat diet along with pumpkin seeds showed improvement in body weight and fat accumulation compared to control group which was fed on only high fat diet. The addition of pumpkin seeds showed a more notable decrease in the gaining of body weight, where the control of body weight gain could be due to a variety of mechanisms, including unusual food assimilation or decreased body energy storage. The exact mechanism is still not known but pumpkin seeds are considered to be a promising anti-obesity nutraceutical (Kalaivani et al., 2018).

According to recent studies the pumpkin seeds were found to be of high interest for the food industry serving healthier food products. The seeds were found to have rich nutritional profile as shown Table 2, including proteins, crude fibers, calcium, carotene, and vitamin C which help in weight reduction. Also, it was reported that pumpkin seeds are gluten free which serves as an alternative for many food products, that help in decreasing the burden of obesity and related health problems especially liver diseases resulting from untreated obesity demonstrated in Table 3 (Mala et al., 2018).

It was reported that the ingestion of natural bioactive compounds with a recognized anti-obesity effect, became of special importance in scientific communities as it can help in replacing other medical interventions owing to its ability to control weight gain and help in weight loss (Ghahremanloo et al., 2018). Based on recent studies it was found that pumpkin seeds chloroform extract has a potent effect on adipogenesis, and downregulation of some genes related to obesity including FABP4, PPARGC1A, CEBPB, respectively (Alshammari and Balakrishnan, 2019).

4.5. Fenugreek seeds

Fenugreek (*Trigonella foenum-graecum* L.) seeds as depicted in Figure 2E, is an annual legume crop mainly grown for use as a spice in many parts of the world. The plant is an aromatic herbaceous annual, widely cultivated in Mediterranean countries and Asia (Rafiqi et al., 2019). Fenugreek is one of the oldest and widely spread seeds used by ancient Egyptians and Hippocrates as an herbal medicine decades ago (Yao et al., 2020).

Fenugreek has many names such as Helbeh in Arabic, Methi, Sag methi and Kasuri methi in Hindi, Fenugreek, Bird foot and Greek hayseed in English and Fieno Greco or Trigonella in Italian. Fenugreek has very rich nutritional constituents as shown in Table 2. Also, it is a rich source of calcium, iron, carotene and other vitamins (Kimbonguila et al., 2019).

According to recent pharmacological studies fenugreek has shown that it contains a number of active ingredients that regulate the metabolism of glycolipids and enhance insulin resistance. In addition, it was found that 4-hydroxyisoleucine shown in Table 3 has a strong impact on lowering insulin resistance and therefore helps in decreasing the obesity in test subjects. However, the exact mechanism is still unclear and further research is needed on this seed to investigate its anti-obesity effect (Zhou et al., 2020).

A number of chemical components are present in fenugreek seeds which are responsible for its biological activity including alkaloids (such as trigonelline, gentianine and carpaine), furastanols (such as vicenin-1, vitexin, diosgenin, gitogenin, yamogenin), essential oils, proteins, steroidal saponins, mucilaginous soluble fiber and insoluble fibers. These constituents help in decreasing serum glucose levels, inflammatory mediators causing minor inflammation associated with obesity and insulin resistance in test subjects. All of this makes the fenugreek seed a promising anti-obesity phytomedicine (Kandhare et al., 2018).

It was reported that fenugreek seeds have a potent efficacy in lowering lipids including low-density lipoprotein (LDL) and cholesterol due to the high fiber content when it was compared to other dietary fibers. There has been a suggested mechanism in decreasing blood cholesterol, where fenugreek gum thickens in the stomach in the presence of moisture and forms a gel. This gel appears like fat inside the body where it gives signals to the brain to send a message to the gall bladder to empty its content of bile in the stomach, where the gel traps the bile. This bile should act as a lipid-emulsifying agent, therefore when it is trapped, it would not perform its function, and this prevents the reabsorption of the lipids. Thus, the emulsification and absorption of lipids, including cholesterol, results in the lowering of blood lipid and this, respectively, reduces the risk of many disorders related to obesity, as well as helping in weight loss (Gurunath, 2019).

5. Molecular anti-obesity effect of the seeds

In the shadow of this review, the molecular processes through which bioactive substances found in herbal extracts, functional foods, or dietary supplements exhibit anti-obesity benefits are addressed. Several studies, including clinical trials, animal tests, *in vitro* cell culture, and *in vivo* alternative model systems, have identified specific bioactive compounds that aid in demolishing obesity as shown in Figure 3.

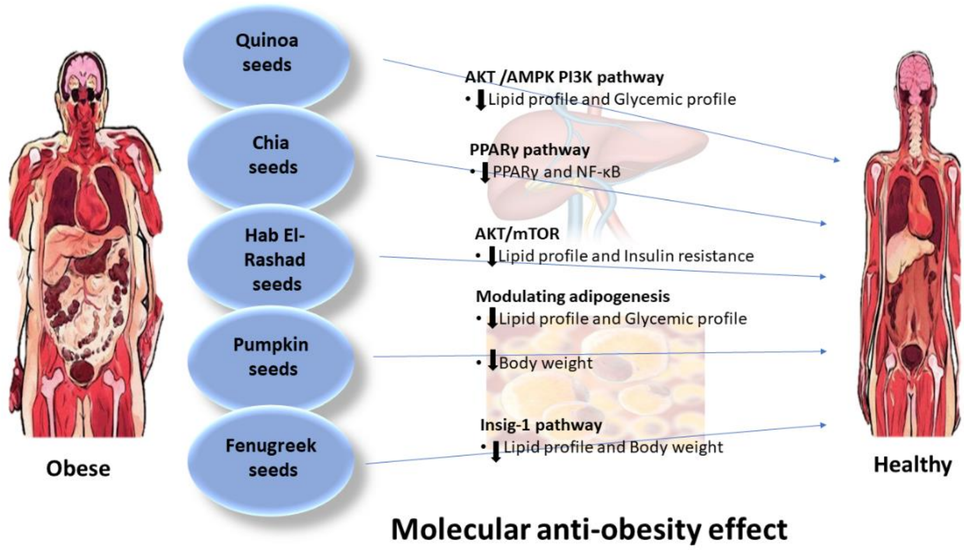


Figure 3. Common pathways involved in the anti-obesity effect of natural products

According to Obaroakpo et al. (2020), quinoa formulated in the form of yogurt showed anti-obesity effect through lowering lipid and glycemic profiles via AKT (protein kinase B)/AMPK (Mitogen-activated protein kinase)/PI3K (phosphatidylinositol 3-kinase) signaling pathway (Obaroakpo et al., 2020). *In vitro* studies on 3T3-L1 adipocytes treated with chia seeds extract showed anti-obesity effect through modulating adipogenesis process via the inhibition of the expression of PPARγ (peroxisome proliferator-activated receptor γ) and NF-κB (nuclear factor kappa light chain enhancer of activated B cells) (Grancieri et al., 2021). Moreover, an *in vivo* study performed on male Wistar rats treated with chia seeds showed decrease in body weight and visceral fat weight through modulating adipogenesis via AMPK (adenosine monophosphate-activated protein kinase) signaling pathway (Oliva et al., 2021). A study performed on obese rats suggested that Hab El-Rashad ethanolic extract showed anti-obesity effect manifested in modulating lipid profile and decreasing insulin resistance along with decreased body weight through regulating AKT (protein kinase B)/mTOR (mammalian target of rapamycin) signaling pathway (Abdulmalek et al., 2021). A study done on Wistar male rats using pumpkin seed oil demonstrated anti-obesity effect through enhanced lipid profile, glucose and insulin levels, and decreased body weight through modulating lipogenesis and adipogenesis process (Kalaivani et al., 2018). Another study was done on Wistar male rats where pumpkin seeds oil was found to decrease total cholesterol, triglycerides and LDL, also decreasing oxidative stress associated with obesity via modulating adipogenesis process (Kalaivani et al., 2020). An *in vivo* study carried out in obesity-induced rats supplemented by fenugreek seeds was found to have anti-obesity effect through modulating lipid profile and decreasing body weight via controlling lipogenesis process through insulin-inducible gene-1 (Insig-1) signaling pathway (Khound et al., 2018).

6. Pharmacological activity of the seeds

6.1. Antioxidant activity

Quinoa seeds are considered to be one of the most important medicinal plants all over the world due to its significant antioxidant activity as it is rich in phenolic compounds including chlorogenic acid and rosmarinic acid, also flavonoids including quercetin and glycosides, which contribute to the antioxidant activity of the seeds (Fernández-López et al., 2020). Phenolic acids and flavonoids are the most abundant polyphenols in quinoa responsible for its antioxidant effect. Several phenolic acids have been reported in quinoa seeds samples including protocatechuic, *p*-hydroxybenzoic, vanillic, syringic, *p*-coumaric, ferulic, sinapic and isoferulic, cholorogenic, rosmarinic and caffeic acid, where ferulic acid and its derivatives were the most abundant phenolic compounds in quinoa seeds (Stikić et al., 2020). Phenolic compounds found in quinoa seeds had a significant ability to scavenge the 2,2-diphenyl-1-picrilhidrazil (DPPH) (Liu et al., 2020). The antioxidant effect of compounds containing phenols is due to the existence of a hydroxyl group connected to an aromatic ring which, through its inhibitory capacity of reactive oxygen species, can provide a defensive barrier against oxidative stress (ROS) which alter many biological actions of the body leading to many diseases including obesity, diabetes, cardiovascular diseases and cancer. Therefore, quinoa seeds were found to have a significant effect as antioxidants to prevent that cascade of events leading to severe illness (Buitrago et al., 2019).

Also, chia seeds were reported to have a potent antioxidant effect. It was shown that ingestion of chia seeds extract decreased oxidative stress that was manifested in reducing MDA (malondialdehyde) levels and increasing GSH (glutathione) levels indicating a potent antioxidant ability (Tamargo et al., 2020). This is linked to the presence of high levels of antioxidant nutrients such as chlorogenic acid, caffeic acid, myricetin, quercetin, kaempferol and omega-3. These nutrients aid in decreasing the oxidative stress and activating hepatic antioxidant enzymes leading to reduction of lipid peroxidation (Mukthamba and Srinivasan, 2016). Chia seeds are considered to be one of the most important antioxidant herbal nutraceuticals, since they represent a very good source of polyphenols and antioxidants such as caffeic acid, rosmarinic acid, myricetin and quercetin. The advantages of chia seeds being a potent antioxidant, have been explored in various fields of study worldwide including the medical, pharmaceutical and food industry. They have shown a great help in decreasing and delaying the onset of many diseases including obesity and related health disorder, aging, cancer and inflammatory diseases (Knez Hrnčič et al., 2020).

It was reported that Hab El-Rashad seeds have potent antioxidant effect where they showed a potential in being a hepatoprotective agent against oxidative stress. Studies revealed that this action might be related to the high content of linolenic acid and phytosterols along with phenolic compounds in the seeds (Alqahtani et al., 2019). A related analysis discovered that providing Wistar rat with Hab El-Rashad seeds for 60 days, increased tocopherol levels and the activity of antioxidant enzymes proving that Hab El-Rashad seeds are a promising herbal antioxidant agent (Umesha and Naidu, 2015). The plant's seeds and leaves have volatile oils and are a good source of amino acids, fatty acids, and minerals. Owing to their high content of phenolic compounds, they have the ability to act *in vitro* as antioxidants, and thus they may have significant preventive effects against chronic disorders (Balgoon, 2019). A recent study showed great potential in Hab El-Rashad seeds being a potent antioxidant, where the levels of glutathione (GSH) and catalase levels were elevated on administration of the seed extract which decreased the lipid peroxidation level and acted as a shield against tissue damage by oxidative stress (Feng et al., 2016).

It was stated that the serviceability of the pumpkin lies in its functionality, containing variant constituents, each of which has an excellent nutritional composition, which can be used in food formulations and is functional in the treatment and prevention of many illnesses related to high oxidative stress, where pumpkin seeds were reported to be a promising anti-oxidant agent due to the presence of triterpenoids, flavonoids, coumarins, cucurbitacins, and carotenoids which were reported to have a direct relation with the antioxidant activity of pumpkin seeds (Sharma et al., 2020). Based on various research works underlying the high levels of polyphenolic compounds in pumpkin ethanolic extract, pumpkin seeds are regarded as a functional food. Species of *Cucurbita* contain numerous nutrients that are important for human wellbeing, including carotenoids and tocopherols present mainly in peels and seed fractions, respectively (Achilonu et al., 2018).

Based on recent studies, it is understood that dietary fenugreek seed counters surplus lipid peroxidation and induces changes in the content of antioxidant molecules in test subjects. It was also reported that an antioxidant property is correlated to the soluble portion of fenugreek seeds. Administration of fenugreek to test subjects reversed the altered levels of antioxidants and antioxidant enzymes behavior indicating that fenugreek seeds have a positive antioxidant activity that can be used to treat many health complications related to the presence of high oxidative stress in body (Srinivasan, 2019). Latest biological studies have shown that fenugreek has antioxidant associated with anti-inflammatory activities which are directly related to the presence of bioactive phytochemicals including flavonoids which were reported to have a potent antioxidant activity through their radical scavenging effect and LDL-antioxidant properties. Moreover, fenugreek seeds rich in glycosides decreased the production of nitric oxide (NO) which increases oxidative stress in cells (Wu et al., 2020).

6.2. Anti-diabetic activity

According to recent studies quinoa, a pseudo cereal free of gluten, high in nutrients, fibers and phytochemicals, including saponins, phytosterols, phytoecdysteroids, phenolics and bioactive peptides, may be a key solution for dietary intervention to combat obesity, metabolic syndrome, type 2 diabetes and non-alcoholic fatty liver disease (NAFLD). This diversity in combination of phytochemicals makes quinoa one of the greatest phenolic compounds associated with anti-diabetic activity (Noratto et al., 2019). It was stated that quinoa intake decreased the glucose levels and enhanced insulin resistance in test subjects which by far had a significant role in diabetic treatment (Paśko et al., 2010). Furthermore, human studies have also shown that the ingestion of quinoa lowered the levels of BMI and glycosylated hemoglobin (HbA1c) and improved satiation and fullness in patients with pre-diabetic condition (Ruiz et al., 2017).

Regarding chia seeds, they are a rich source of α-linolenic acid (ALA) which was found to decrease insulin resistance in type 2 diabetes and the related health conditions. It also decreased the serum glucose level, total cholesterol and triglycerides levels, aiding in the treatment of diabetes, and also delaying the onset of diabetes in borderline test subjects (Akinfenwa et al., 2020). Also, chia seeds have been the subject of recent research due to their promising chemical composition and nutritional value; they contain high amounts of dietary fibers, minerals, proteins, and essential fatty acids such as linolenic acid. Chia seeds have recently been described as the best source of fatty acids and omega-3. They also have a high content of bioactive ingredients, such as phenolic compounds and tocopherols, which have an anti-diabetic effect (Scapin et al., 2016). Some experiments on rats have shown that six and 12 weeks of consumption of chia seeds can promote health benefits, such as decreased glucose levels, however, the exact mechanism is still unknown (Alamri, 2019).

According to recent studies, in a high fat diet rodent model, Hab El-Rashad seed powder and alcoholic extracts showed a cytoprotective action in pancreatic islets to maintain the integrity of the β cell which control adequate insulin secretion and maintain glucose levels to normal in test subjects (Desai et al., 2017). Furthermore, Hab El-Rashad seeds were reported to contain flavonoids, sulfur, coumarin, triterpenes, sterols, glycosides, and various imidazole alkaloids, where alkaloids exert its action through alpha-glucosidase inhibition and reduce transporting glucose through the intestinal epithelium (Roughani and Miri, 2018). It was reported that Hab El-Rashad seeds ethanolic extract stabilize diabetes through enhancing antioxidant effect, decreasing oxidative stress and improving lipid profile, also regulating insulin pancreatic secretion from the pancreatic islet β cells which is related to decreased levels of glucose, urea, triglycerides, and cholesterol (Jain and Grover, 2018).

Pumpkin seeds were reported to have anti-diabetic effect due to their hypoglycemic and hypolipidemic activity. According to recent studies it was found that in diabetic rats, cellular insulin uptake was increased demonstrating that the capacity of cells to utilize insulin and glucose was increased significantly. It was also reported that pumpkin seeds alcoholic extracts showed a potential in α-amylase inhibition, and aqueous extracts showed significant inhibition of α-amylase and α-glucosidase which are directly linked to the anti-diabetic effect that was recently taken in consideration for pumpkin seeds (Kushawaha et al., 2017). According to recent studies, the use of natural products is increasing in the field of diabetes including the using of pumpkin seeds extracts in the past few years, due to the presence of polysaccharides which were found to be highly active in combating blood sugar content. The polysaccharides were evaluated for their mechanism of action where it was found that pumpkin polysaccharides can stimulate endogenous GLP-1 secretion, decrease oxidative damage, and delay the onset of diabetes. These are considered to be the key steps that explain the anti-diabetic mechanism of pumpkin polysaccharides (Lu et al., 2019).

Fenugreek seeds were also found to have hypoglycemic effect due to a variety of constituents including galactomannan, phenolic compounds and fibers. Clinical studies have shown that 2 to 3 g/day of fenugreek gum is effective in controlling blood sugar, whereas the requirement of other food fibers is much larger (~ 20 g). When ingested, the fenugreek gum thickens and forms gel trapping sugars, fats and starch-hydrolyzing amylase enzymes in the stomach; thus, leading to the slowing down of the sugar absorption and that is of high benefit for diabetic and obese patients (Zameer et al., 2018). According to updated studies it was found that the soluble fiber content including galactomannan was stated to be responsible for the anti-diabetic activity of the fenugreek seeds and clinical data showed that the glycemic control was improved in a small study of mild type-2 diabetes mellitus patients. A reduction in glycosylated hemoglobin (HbA1c) levels and an increased insulin sensitivity was observed in patients receiving fenugreek (Srinivasan, 2019). It was also reported that the hypoglycemic effect was demonstrated in a study that fenugreek inhibited in vitro α-amylase activity in a dose dependent manner and that it was found to be effective and considered of high potential as anti-diabetic agent (Wu et al., 2020).

6.3. Anti-inflammatory activity

Regular consumption of quinoa seeds was reported to have a potent anti-inflammatory effect that takes place by lowering the levels of circulating inflammatory mediators including interleukin-6 (IL-6) and tumor necrosis factor (TNF)-α. This is due to the high fiber content found in quinoa seeds (Noratto et al., 2019). The anti-inflammatory effect of quinoa seeds is directly related to being a potent antioxidant, which is manifested by the high levels of phenolic compounds where, two major groups are classified as phenolic acids and polyphenols (Carciochi et al., 2014). Inflammation is complementary to chronic diseases associated with obesity and dietary changes have shown that inflammation has decreased, with implications for slowing or preventing the onset of certain diseases. The overproduction of ROS in obesity promotes cell injury, secretion of pro-inflammatory cytokines and their development, consequently contributing to inflammation-signaling pathways. Quinoa seeds were reported to decrease chronic inflammation associated with obesity and related health problems through decreasing the oxidative stress and so decreasing the inflammatory mediators onset leading to minor inflammation (Garcia-Mazcorro et al., 2018).

According to recent studies, it was reported that chia seeds exert anti-inflammatory effect that could treat minor inflammation associated with obesity. The seed extracts inhibit the macrophages recruited by adipocytes that aggravate immune response and decrease the expression of MCP-1 (monocyte chemo attractant protein-1), PGE2 (prostaglandins E2), IL-6 (interleukin-6), PAI-1 (plasminogen activator inhibitor-1) and TNF-α (tumor necrosis factor-α) and so it was reported to have a great potential in treating minor inflammation associated with obesity (Marcinek and Krejpcio, 2017). It was also found that chia seeds intake has been able to inhibit NF-κB and TNF-α activation, reducing inflammatory cytokines such as TNF-α, leading to enhanced anti-inflammatory body ability in the normal diet and high-fat diet, resulting in a low-grade inflammatory state. This may be due to the fatty acids, phenolic acids, and other bioactive compounds that are found in chia seeds, including vitamins, minerals, and antioxidant substances. The bioactive compounds in the seeds results in upregulation of PPAR-α expression which control variant gene expression, and cell signaling pathways, reducing inflammation in that way (da Silva et al., 2019).

Hab El-Rashad seeds are used in folk medicine to treat some inflammatory diseases including hepatitis, diabetes mellitus and arthritis (Alqahtani et al., 2019). According to recent studies it was reported that Hab El-Rashad seeds have shown synergistic effects of platelet aggregation inhibition and decrease thromboxane B2 levels in Wistar rats' spleen and lung tissues decreasing the accumulation of inflammatory mediators (Raghavendra and Akhilender Naidu, 2011; Alqahtani et al., 2019). According to recent studies (Akbar, 2020) evaluating the anti-inflammatory effect of Hab-El-Rashad seeds extract on inflammatory shock it was suggested that the presence of lipopolysaccharides (LPS) aggravated an immune response manifested in releasing inflammatory mediators released by macrophages, especially tumor necrosis factor alpha (TNF-α) which cause fever, shock, and could lead to death if not treated. Hab El-Rashad seeds were found to decrease the levels of circulating TNF-α leading to reducing the inflammation effect on the human body. Further research is required to reveal the exact mechanism for more clinical implications (Ahmad et al., 2018).

It was stated that pumpkin seeds extracts possess a potent anti-inflammatory action where 3β-hydroxycholest-7-en-24-one extracted from pumpkin seeds had a direct effect on inhibition of nitric oxide (NO) production and decreased inflammatory macrophages circulation through inhibiting the activation of macrophages, decreasing thereby the onset of inflammation. Accordingly, they can be considered promising anti-inflammatory agents (Ratnam et al., 2017). The anti-inflammatory function of pumpkin seeds was evaluated where the administration of low and high doses of pumpkin seed extracts of various origins showed that different cellular markers such as DNA damage and chromosomal damage as well as inflammation regulation index improved significantly in relation to normal subjects. The lipoxygenase inhibitory activities of pumpkin seed extracts may partly explain this fact (Al-Okbi et al., 2017).

Recent studies showed that fenugreek seeds contained diosgenin which played an important role in inflammation linked to obesity, where it inhibits filtration of macrophages of adipose tissues and decrease inflammatory mediators and cytokines produced in obese test subjects. Further studies are needed to investigate the exact mechanism where diosgenin extracted from fenugreek seeds exerts its anti-inflammatory effect (Zhou et al., 2020). Moreover, fenugreek seeds were reported to exert anti-inflammatory effect through inhibition of the inflammatory biomarkers including TNF-α, IL1β, LT-B4. It was also suggested that it inhibits macrophages and pro-inflammatory cytokines along with decreasing the oxidative stress leading to decreased inflammatory response. The exact mechanism is still under investigation, but fenugreek seeds are considered to be a promising nutraceutical as an anti-inflammatory herbal medicine (Tavakoly et al., 2018).

6.4. Effect on appetite

It was recently reported that quinoa delayed the weight gain in test subjects fed quinoa along with high caloric intake diet through suppressing appetite. The exact mechanism is still not clear, but it was suggested that quinoa boosts satiety and fullness. Studies showed high potential in quinoa seeds as an appetite suppressor (Noratto et al., 2019).

According to recent studies, chia seeds were also found to reduce appetite in a significant way and so it's a promising appetite suppressor that can be used as a safe herbal nutraceutical supplement (Shende and Narvenker, 2020).

Pumpkin seeds were reported to have a potent effect on digestive disorders, stabilizing the appetite and decreasing sugar craving, which also plays a significant role in enhancing glycemic profile and modulating insulin resistance in test subjects (Rajasree et al., 2016).

Recent studies suggested that high content of soluble dietary fibers found in fenugreek seeds lowered the level of blood sugar in diabetic test subjects by postponing carbohydrate gastric emptying leading to appetite suppression for longer duration of time (Yao et al., 2020).

7. Edible seeds in anti-obesity supplements

Nowadays obesity is a high-risk chronic disease, which encouraged the Food and Drug Administration (FDA) to approve many drugs and supplements of natural products to help in decreasing the risk which became a threat to a lot of people. Pharmacotherapy treatments for obesity is of high importance to reduce the risk of many chronic diseases, improve the lifestyle of patients suffering from obesity, and decrease the need for the bariatric surgeries (Gomez, 2017).

The health benefits of human nutrition from quinoa seeds have been extensively documented, such that this crop is now indicated as an important herbal dietetic to produce functional foods and nutraceutical products. It is reported that several food-derived molecules, including proteins and peptides, can show bioactivities and disease prevention in humans and enhancing the quality of life (Capraro et al., 2020).

Chia seeds are a healthy source of fiber, protein, antioxidants, and essential fatty acids, proteins, and minerals. These seeds, considered by many to be a "superfood" that contributes to human nutrition and fights obesity by helping to raise the satiety index. They also have many biological characteristics, and are considered to be gluten free which can be a safe alternative for many food products that increase the obesity risk (Caruso et al., 2018).

A recent study revealed that dietary supplementation with Hab El-Rashad seeds powder (*L. sativum*) had a tremendous positive effect on metabolic rate, oxidative stress, and related histopathological injuries manifested in obesity. It was also reported that Hab El-Rashad seeds induced weight loss in test subjects along with enhancement of the lipid profile through lowering the levels of total cholesterol, triglycerides and LDL in Sprague Dawley rats exposed to high-fat ratios nutrition (L'hadj et al., 2019). This beneficial effect has been attributed by several authors to phytochemical molecules, especially the flavonoid group which has the mimetic insulin property of improving sensitivity to insulin which had a significant role in enhancing the condition of obesity making it a promising weight loss supplement (Alharbi and Hanan, 2017).

It was reported that the ingestion of natural bioactive compounds with a recognized anti-obesity effect, such as pumpkin seed extract became of high interest as it can help in replacing other medical interventions owing to its ability to control weight gain and help in weight loss (Ghahremanloo et al., 2018). Based on recent studies it was found that pumpkin seeds chloroform extract has a potent effect on adipogenesis, and downregulation of some genes related to obesity including FABP4, PPARGC1A, CEBPB, respectively (Alshammari and Balakrishnan, 2019). Moreover, this plant has been employed in the food industry for the production of purees, juices, jams, and alcoholic beverages. Pumpkin seeds as a rich source of bioactive compounds have been used frequently as functional foods or medicines. Moreover, pumpkin seed has gained attention not only as edible seed, but also as a potential nutraceutical supplement (Montesano et al., 2018).

Fenugreek seeds were reported to be one of the most used seeds all over the world, due to the rich nutritional content and various phytochemical active compounds. The seeds are used as dietary supplement as it has shown to promote lean body mass and decrease cholesterol in recent research. Moreover, enhance digestion, glycemic profile and lipid profile. The seeds have high potential as functional food to be also a weight loss agent (Yao et al., 2020).

8. Role of dietary seeds in food industry

Quinoa seeds are abundant in fiber, which adds to the product's health advantages. Furthermore, quinoa's overall nutritional content has aided in increasing demand in the global market. Quinoa rice and flour recently replaced the traditional white rice and flour, also quinoa pasta is used recently replacing the pasta done with white flour, it is also used in bakery and cakes owing to the nutritional content of the quinoa seed, offering a better and healthier option that can be used in daily diet. Moreover, quinoa seeds are rich in saponins which can be utilized in a variety of commercial applications in the agricultural (e.g., as a bio-insecticide), food, cosmetic, and pharmaceutical sectors due to their physicochemical and biological characteristics (Angeli et al., 2020).

Chia seeds is used in the market in many categories including food, beverage, bakery, morning cereals, soups, and gravies. The seeds provide a healthier and gluten free option for many bakeries and cereals in the market. Moreover, chia seeds have a high concentration of gum and mucilage, making them potentially helpful in the food and cosmetics business. Bread, spaghetti, cookies, and cakes are just a few of the goods that contain chia seeds in them. Chia seeds can also be added to drinks, snacks, and other foods (Katunzi-Kilewela et al., 2021). A lot of interest is invested in the incorporation of the seeds in food industry owing to its high nutritional value and health benefits.

Hab El-Rashad is used in many food products especially in Saudi Arabia, it is used in cereals, bread, cookies, muffins, and noodles as a healthier option. Hab El-Rashad seeds may be utilized to make a variety of functional and nutritionally enhanced foods including dahiwala bread, omega-3-fatty acid-rich biscuits, iron-rich biscuits, health drinks, vegetable oils mixed with alpha-linoleic acid-rich Hab El-Rashad oil, fortified burfi, and fortified chikki. Moreover, Hab El-Rashad oil is used as a native medicine where it is used in relieving inflammation and pain (Lahiri and Rani, 2020).

Pumpkin seeds are popular to be used as a healthy snack, unsalted seeds are used as healthier option as a topping in many bakeries and used with oats to make healthy and nutritionally rich snacks. The seeds in raw or roasted form are used in cakes, breads, cereals, and salad dressings, while seed oil is used as a cooking oil. Also, pumpkin seed oil may be used in a variety of dishes, including pasta, salads, and soups. Moreover, the seeds powder is used in cookies preparation for a healthier recipe (Adsul and Madkaikar, 2021).

Fenugreek is widely used as a spice in many food products, whereas its seeds are used in many bakery products including bread, cookies and cakes. Also, it is used as an infusion powder or added to black and green tea. Moreover, seed powder is used in capsules to increase breast milk (Yao et al., 2020).

9. Technological perspective and future trends

Dietary seeds rich in phytochemicals show great promise as a natural source of nutrients and additives for contributing to modern diets. Moreover, seeds have a promising role in the production of functional foods and nutraceuticals in the forthcoming years. The nutritious and bioactive components have the potential to be used in food, cosmetics, and pharmaceutical manufacturing. Nowadays, many technologies are utilized for extraction of bioactive compounds from the seeds, also the seeds are used in different forms such as flour and seed powder to be incorporated in dietary supplements and food industry owing to the fact that these seeds are rich in bioactive compounds and nutritional components (Akbar, 2020). Seeds include a variety of components, including proteins, omega 3 fatty acids, dietary fiber, minerals, flavonoids, and polyphenols, all of which are appealing to the food industry and customers seeking healthy meals.

10. Conclusions

In conclusion, alternative medicine and dietary supplements are required to address the most pressing issues linked with obesity. In the past years dietary seeds have been used widely against the battle of many chronic diseases including obesity and related diseases. There is growing evidence everyday about the usage of dietary seeds and natural products either in food industries or in drugs and supplement products.

Food industries around the world is now moving towards more healthy options and widely using medicinal plants in the daily diet along with food supplements to help decrease the worldwide catastrophe of obesity. These seeds showed a promising potential to be used as a weight reducing nutraceutical. The exact mechanism by which these seeds exert their action against obesity is still not fully discovered, therefore, further research and clinical trials should be conducted to assess their efficiency and mode of action.

This review contributes to a deeper understanding of the cellular and molecular processes that mediate the anti-obesity impact of some dietary seeds used nowadays. Furthermore, it prompts understandable knowledge to practitioners, and consumers who are seeking safe and economical natural product with anti-obesity effect. Seeds have been shown to have potent pharmacological effects with little or no toxicity, and their intake as a dietary supplement appears to lower the risk of many human health problems. Taken together, the suggested optimum strategy to achieve long-term loss in body weight seems to be the use of potential anti-obesity natural products and to be incorporated into the daily low-fat diet.

Acknowledgments

None.

Conflict of interest

The authors declare that they have no conflict of interests.

CRediT authorship contribution statement

Heba Hosny: Data analysis, Manuscript writing, Revision
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Supplementary File

None.

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