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## Nutritional and functional profile of carob bean (*Ceratonia siliqua*): a comprehensive review

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### ABSTRACT

Carob (*Ceratonia siliqua*) is one of Asia and Africa's popular nutritional and medicinal crops. This unique plant has an outstanding functional properties and nutritional profile. Carob has high sugar content, drought resistance and is very economical. Carob fruit consists of pulp and seed that are rich sources of different bioactive components. Carob has wide applications in various industries (food, pharmaceuticals and cosmetics) as an anti-oxidant, thickener, stabilizer, lactic acid production and emulsions. The trend of moving toward natural products further highlights the use of carob in different fields due to its excellent nutritional and therapeutic profile. Carob bean gum is widely used in the food industry. The current review has highlighted the nutritional composition, bioactive profile, functional properties, and recent findings on the subject.

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## Introduction

The carob tree (*Ceratonia siliqua*) is an evergreen member of the Caesalpinoideae subfamily of the Leguminosae family. *Ceratonia siliqua* L. is the scientific name of carob originated from the Greek word “Kera,” which correlates to the keratomorphic fruit shape, and the Latin word “siliqua,” it relates to the firmness and shape of pods. Western parts of Asia are its original habitat after it extended to the Mediterranean basin and western shore of America, South Africa, and Southern regions of Australia. Nowadays it is extensively cultivated along the area of Mediterranean.<sup>[1]</sup> Carob bean is considered to be of great economic and environmental importance in this region.<sup>[2]</sup> According to FAO estimates (Food and Agriculture Organization of the United Nations), production of carob has dropped from 165,990 tonnes in 2013<sup>[3]</sup> to 136,612.75 tonnes in 2018.<sup>[2]</sup><sup>[4]</sup> Around the globe top, carob producers were Portugal (28.83%), Italy (23.11%), Morocco (16.11%), and Turkey (10.39%), from 2015 to 2018.<sup>[4]</sup> The different factors such as variety, area, cultural practices, and environmental condition affect the yield of carob pods. The edible fruit is sometimes referred to as locust bean. The fruit (pod) is elongated, compressed, straight or curved, with a length, width, and thickness of 10–30, 1.5–3.5 and 1 cm, respectively. The pods are green in color that become dark brown and wrinkled with a leathery appearance on maturation; then harvested. The fruit has two main components: pulp and seeds holding 90% and 10%, respectively. In the case of Pulp, the outer leathery pericarp is followed by an inner mushy mesocarp that separates the seeds that are present transversely in a pod. Morphological characteristics of pods such as color, density, dimension, seed-to-pulp ratio, shape, and size vary

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significantly due to variety and climatic conditions.<sup>[5]</sup> The total fruit composition is sugars (48% to 56%), mainly fructose, glucose, sucrose, and protein content is 3%–4%, low-fat content of 0.2%–0.6% and high dietary fibers content particularly in the seeds.<sup>[6]</sup> Carob fruit is a significant source of bioactive-components, as well as macro and micronutrients<sup>[7]</sup> especially, the pulp contains sugars, minerals (such as Zn, Mg, Mn, K, Fe, Ca, Cu, and Na), and polyphenols (includes phenolic acids, tannins, and flavonoids), cellulose, and hemicellulose. The seed contains gum, proteins, dietary fibers, minerals, polyphenols and is gluten-free. Carob powder is high in folic acid, niacin, vitamins E, B<sub>6</sub>, C, and D, and provides low levels of vitamins A, B<sub>2</sub>, and B<sub>12</sub>. Carob powder oil contains 17 fatty acids, the majority of which are oleic, linoleic, palmitic, and stearic acid, accounting for 40.45%, 23.19%, 11.01%, and 3.08%, respectively. Carob pods were utilized by Egyptians to feed livestock and gum for mummy-binding, whereas Arabs used carob seeds as weight unit Qirat/Karat that later on became unit of Gold<sup>[8]</sup> The most common usage of LBG (Locust Bean Gum) is a thickener, stabilizer, gelling and dispersing agent in the food industry. It is associated with many health benefits, and LBG as well as other carrier molecules, are responsible for controlled drug release.<sup>[9]</sup> It has wide applications in adhesives, ceramics, cosmetics, film emulsions, oil drilling, pharmaceuticals, paints, and polishes<sup>[10]</sup> It is utilized as a food because of the high sugar content that makes it energy-rich<sup>[11]</sup> It is added as an alternative to cocoa or extender in many confectionery and bakery products,<sup>[1,12]</sup> milk formulations,<sup>[13]</sup> and decoctions.<sup>[14]</sup> Carob pods are used in the manufacturing process of different organic acids,<sup>[15,16]</sup> alcohols,<sup>[17]</sup> and enzymes by fermentation with algae, fungi, and bacteria.<sup>[18]</sup> Carob and its products are associated with a large number of beneficial health effects such as anti-diarrheal, anti-diabetic, and anti-hyperlipidemic effects<sup>[19]</sup> and anti-proliferative or anti-apoptotic activity against cancer cells.<sup>[20]</sup> It cures neurodegenerative disease, hyperpigmentation, and atherosclerosis<sup>[21,22]</sup>. Carob flour is used to manufacture dietetic and gluten-free products.<sup>[23]</sup> Many findings claim that carob fruit and its byproducts are utilized as a functional food and food additive.<sup>[24]</sup> This review article highlights the nutritional composition, phytochemical profile, functional properties of Carob bean including the products made from it in detail.

## Importance of carob beans

The extensive use of carob beans is attributed to their unique nutritional profile. Carob pod is edible and used as a natural sweetener and cocoa alternate. Carob is available as chips, powder, syrups, extracts, and dietary pills. It provides low calories with a dense amount of bioactive compounds (polyphenols, flavonoids, dietary fibers, tannins, etc.), vitamins, and minerals such as calcium, sodium, phosphorous, zinc, and selenium.<sup>[25]</sup> Seeds are the reservoir of LBG native food-additive (E-410), with broad applications in the food and cosmetics industries as a thickener and stabilizer. The cultivation replacements for LBG that are less expensive (guar or xanthan gum) is not effectively compelling toward increasing carob seeds' utilization for LBG extraction. Dietary fiber and polyphenols in the carob prevent hypercholesterolemia by reducing and maintaining LDL (low density lipoproteins), reducing the risk of CVDs, stroke, high blood pressure, and atherosclerosis.<sup>[20,26]</sup> Carob extracts and powder showed significant anti-diabetic<sup>[27]</sup> and improved gastrointestinal effects of carob tannins and fiber. These bioactive compounds ensure healthy bowel moments by elevating constipation and maintaining ideal body weight by providing satiety.<sup>[28]</sup> Anti-proliferative, anti-apoptotic, and anti-cancer properties are due to polyphenols and flavonoids that counter oxidative stress, preventing the different types of cancers.<sup>[29,30]</sup> Furthermore, carob is gluten, caffeine, and tyramine free, thus making it an effective coca substitute for celiac patients, children, caffeine sensitivity, and migraine patients.<sup>[31]</sup> 2Tbsp of carob provides 42 mg of calcium, a vital mineral for bone health, normal nerve, and heart function; therefore, it cures osteoporosis.<sup>[32]</sup> Carob didn't have oxalates; hence, no calcium-binding reduces the risks of kidney stones.<sup>[33]</sup> Buyukcapar et al.<sup>[34]</sup> explored utilization of carob kibbles as animal feed and its effect on growth performance. Carob plants are used as ornamentals and drought, salt, as well as fire-resistant in nature.

## Physicochemical screening of carob beans

Carob fruit bears a rich nutritional profile with the presence of sugars, dietary fibers, minerals, vitamins, and a diversity of polyphenols that makes it a functional food.

### Carbohydrates

According to previous studies, nutritional value of carob beans is due to their high sugar content that ranged between 40–55 g/100 g.d.m in different cultivars as far as sugar composition is concerned major carbohydrates are sucrose with a concentration up to 52 g/100 g.d.m, whereas fructose and glucose concentrations are 1.8–12.5 g/100 g.d.m and 1.8–10.2 g/100 g.d.m respectively.<sup>[35,36]</sup> Natural carob syrup is produced by sugar extraction.

### Carob bean gum

Locust bean gum or carob bean gum is obtained due to alkaline or aqueous extraction of the carob seed. Chemically LBG is galactomannan, and up to 85% of it is present in seeds.<sup>[37]</sup> Linear polysaccharides are galactomannans with a -(1-4)-mannose backbone and a single d-galactopyranosyl unit linked as a side branch through -(1-6) linkages. Like other polysaccharides, these are significantly polydispersed, with a molecular mass of roughly 310,000 Da.<sup>[10]</sup> Chromatography through gel permeation suggests that the average locust molecular weight galactomannan mostly ranges from 0.3 to 2.0 million, which varies remarkably due to several aspects such as growth conditions and manufacturing procedures, and seed source.<sup>[38]</sup> In CBG, galactose and mannose contents are 21–23% and 77–78% respectively, whereas the galactose to mannose ratio was reported between 1:3.1 and 1:3.9.<sup>[37]</sup> Its Molecular size and structure have considerable effects on functional properties. The different physiochemical aspects of galactomannans, including water adsorption, rheology, viscosity, solubility, and synergistic-gel formation have all been investigated for a better understanding of their functional qualities.<sup>[39,40]</sup> LBG found wide applications as an additive in the food industry in frozen foods and baby foods, as well as in the pharmaceutical, paper, and cosmetic industries<sup>[10]</sup> Figure 1.

### Carob fiber (dietary fiber)

Carob fiber production starts with the seed. Aqueous extraction of carob is done to remove dissolved carbohydrates and recover fibers that range from 30% to 40% of pulp.<sup>[41]</sup> More than 70% of carob fiber is an insoluble fraction including insoluble polyphenols, hemicelluloses, lignin, and cellulose. The high polyphenol fiber content in carob differentiates it from other dietary fiber sources. It is chiefly dietary fiber that is insoluble and basically non-fermentable.<sup>[5]</sup> A low amount of soluble fraction (max 10



Figure 1. Schematic depiction of carob beans life cycle.

grams per 100 grams' carob fiber) is also present and is high in simple carbs. Cellulose has thousands of glucose units in a linear-chain linked by  $\beta$ -1-4 linkages, whereas hemicellulose is a branched polymer.<sup>[42]</sup> Different subclasses (arabinoxylans, galactomannans,  $\beta$ -glucans) are found based on plant species.<sup>[43]</sup> According to Owen et al. carob fiber has a variety of phenolic compounds; both are linked by hydrogen bonding, hydrophobic interactions, and covalent bond. These maintain intestinal health on reaching the colon<sup>[44]</sup> Table 1.

### Cyclitols

A group of Cyclitols with functional properties has been confirmed in carob beans. D-pinitol (3-O-Methyl-D-chiro-inositol) is the major Cyclitols of carob bean. Its concentration shows abundant range (1.0 to 8.5 g /100 g-1 d.m) affected by genetic and environmental factors. Wild cultivars have higher D-pinitol content than others.<sup>[35]</sup> D-pinitol is of great significance as it can be used to detect adulteration of carob by cocoa.<sup>[20]</sup> Recently, separation of D-pinitol from carob has been done by using supercritical fluid extraction or ultrasound-assisted extraction; another procedure has been patented. A trace amount of bornesitol (1-O-methyl-myoinositol), D-(+)-chiro-inositol, Myo-inositol, ononitol (4-O-methyl-myoinositol), sequoyitol (5-O-methyl-myoinositol) have been detected.<sup>[14]</sup>

### Polyphenols

Polyphenols are a widespread group of substances present in plants. Structurally these feature one or more aromatic rings to varying degrees of glycosylation, hydroxylation, and methoxylation.<sup>[47]</sup> Flavonoids, gallotannins, and phenolic acids are the major classes of phenolic acids found in carob fruit. The concentration of polyphenols in carob fruits ranges between 45–5376 mg Gallic-acid equivalents per 100 g and is influenced by extraction methods, environmental and genetic factors.<sup>[45]</sup> According to Novotni et al.<sup>[48]</sup> carob phenolics are covalently bonded to dietary fiber, whereas some are present as free or soluble conjugated forms. Almasrah et al.<sup>[49]</sup> suggested that carob germ and seeds are a good source of phenolics extracted using different methods. Gallic acid ranges between 23.7–164.7 mg per 100 g of carob fruit; hence it is considered as richest Gallic acid source<sup>[50]</sup> after chestnut and cloves according to the phenol-explorer database. Benzoic acid and its derivatives (Gentisic acid, 4-hydrobenzoic acid, and Syringic acid) are an abundant-class of polyphenols found in carob fruits whereas the low concentration of cinnamic acids, coumaric acid, chlorogenic acid, and ferulic acid have also been reported.<sup>[46,51]</sup> Flavonoids are the most divergent phenolics with two aromatic (X and Y) rings connected via a 3 C oxygenated heterocycle through C-C bonds. Based on the oxidation state of the central ring, flavonoids are further categorized as flavonols, anthocyanins, flavonols, flavanones, flavones, and iso-flavonoids. Flavonols (kaempferol, myricetin, and quercetin) and their glycosidic derivatives (quercetin, myricetin, rhamnosides) are significantly ample in carob fruits whereas flavones (apigenin, chrysoeriol, luteolin), flavanones (naringenin), and isoflavones (genistein) are found in low concentration.<sup>[20,52]</sup> Tannins comprise the most distinctive group of polyphenols that contribute to the astringency of the carob fruit. Carob juice contains a ten-fold higher concentration of tannins than grape juice.<sup>[53,54]</sup> Tannins are classified

**Table 1.** Physicochemical Composition of carob beans.

Chemical constituent	Concentration (g.100 g-1)	References
Polyphenols	0.5–20	[36,41,45,46]
Total sugars	32–60	
Carbohydrates	48–88.9	
Protein	1–7.6	
Fat	0.2–2.3	
Ash	1–6	
Dietary Fiber	2.6–39.8	
Moisture	3.6–18	

into hydrolyzable and non-hydrolyzable (condensed). Hydrolyzable tannins are, also called ellagitannins, and galloyl tannins that are formed on esterification of Gallic or ellagic acid with glucose. The condensed tannins are non-hydrolyzable that are polymeric proanthocyanidins and oligomeric.<sup>[55]</sup> Tannin content varies in different parts of the carob fruit. Germ comprises the highest concentration of tannins which is 16.2 mg condensed tannins/g and 2.98 mg hydrolyzable tannins/g, pods contain 2.75 mg condensed tannins/g and 0.95 mg hydrolyzable tannins/g whereas trace amounts are present in seeds.<sup>[56]</sup>

### **Minerals**

Carob fruits are a tremendous reservoir of macro minerals (K, Ca, Mg, and P) and trace (Mn, Fe, Zn, and Cu,) minerals.<sup>[57]</sup> In the case of major minerals, potassium is at a peak level, followed by calcium, ranging between 970 to 1120 mg per 100 g of dry weight and 300 mg per 100 g of dry weight, respectively.<sup>[36,46]</sup> A low concentration of phosphorus and magnesium is also present which is around 75 and 94 mg/100 g dry weight, respectively. On the other hand, iron is at the highest concentration among micro minerals with a value of 2.01 mg/100 g dry weight whereas Mn, Zn, and Cu are found in 0.29, 0.46, and 0.29 respectively.<sup>[57]</sup> The literature of Papaefstathiou et al.<sup>[58]</sup> showed detailed studies on the mineral profile of carob and its traditional products.

### **Amino acids**

Carob pods provide two essential products: carob kibbles and carob seeds that are processed to obtain multiple functional products. Ayaz et al.<sup>[59]</sup> suggested carob as a good amino acid source because it provides all of the necessary amino acids in the required concentrations recommended by World Health Organization (WHO). Literature showed diversity in crude protein values of different carob fractions, protein percentage for carob kibbles, carob seeds and carob germ meal is 2.47%, 1%, and 54.7%, respectively.<sup>[24,57]</sup> On the other hand, carob fruit has a heterogeneous amino acid profile; consisting of 17 different amino acids phenylalanine, alanine, threonine, isoleucine, aspartic acid, leucine, glutamic acid, valine, methionine, arginine, glycine, serine, proline, cysteine, lysine, tyrosine, and histidine.<sup>[36,59]</sup> All these essential amino acids are as per FAO guidelines except tryptophan. However, the CP value varies with processing and isolation methods.<sup>[60]</sup> According to the studies Ayaz et al.,<sup>[59]</sup> commercially made carob powder contains 40% less protein than home-prepared carob powder due to the loss of particular amino acids caused by high shear mechanical methods.

## **Functional properties of carob beans**

### **Anti-proliferative activity**

Carob is rich in phytochemical compounds; a literature study indicates that these compounds have antitumor, anti-proliferative, and pro-apoptotic properties. Quercetin, a polyphenol, boosts apoptosis (programmed cell death) in T-leukemic cells by directly hitting the anti-apoptotic protein Bcl-xL.<sup>[61]</sup> It is also effective in the tumor microenvironment. It reduces the tumor size and prohibits angiogenesis (new blood vessel formation) as indicated by pancreatic and breast cancer xenograft models.<sup>[62]</sup> Carob fruit also contains Gallic acid (phenolic acid) that decreases the development of osteosarcoma (bone cancer) MNNG/HOS xenograft tumors in mice. On application in osteosarcoma cell lines, it inhibits proliferation and causes apoptosis.<sup>[63]</sup> Delphinidin (anthocyanidins) is effective in regulating of the NF-B proteins (control DNA transcription and cell survival) expression and preventing tumor growth in PC<sub>3</sub> xenograft mice models.<sup>[64]</sup> Forester et al.<sup>[65]</sup> explored that Gallic-acid and its derivatives are responsible for anti-proliferative action in human colon cell lines that block DNA synthesis and protect against human colon cancer. Theophylline (alkaloid), present in the methanolic extract of carob flour, causes a reduction in breast cancer and HeLa cell lines through apoptosis.<sup>[14]</sup> Carob fiber extract

and tannins are also effective against cancer and prevent adenoma and adenocarcinoma cells proliferation in the human colon by protecting against oxidative-stress in these cells. The literature Hsouna et al.<sup>[66]</sup> showed that the ethyl acetate fraction of carob leaves has a marked protective effect against induced hepatotoxicity and nephrotoxicity in rats.

### **Anti-diarrheal**

Carob fruit contains tannins and phenolic that ensure the health of the gastrointestinal tract. Carob pulp has free and bound phenolic during in-vitro digestion; these phenolic compounds are metabolized to produce certain anti-oxidants that prevent carbohydrates metabolism by inhibiting enzyme activity. In addition to it, the non-digestible fraction of carob that reaches to colon imparts health-promoting benefits.<sup>[67]</sup> Carob's tannins are responsible for its anti-diarrheal properties by regulating water control inside the cell. Regular plant tannins dissolve in water and prevent digestion, but carob's tannins don't. Instead, they have a drying effect on the digestive tract that helps to tackle toxins and prevent the growth of harmful bacteria within intestines. The natural sugars in the carob also support thicken loose stool inspected the efficiency of the carob's tannins in the therapy of acute onset of diarrhea. Past studies also revealed that administration of 2% carob solution results in the prevention of hem agglutination and *E. coli* adherence on intestinal cells that is effective against diarrhea.<sup>[20]</sup> Asgari et al.<sup>[68]</sup> explored the efficacy of carob against oral rehydration solution (ORS) for treating acute diarrhea which is a leading cause of death and morbidity among children and adults. Studies revealed that carob preparations showed significant anti-diarrheal properties by functioning as a detoxifier and constipator, as well as a good source of calories. High pectin and dietary fiber content in the carob act as a prebiotic that feeds gut microbiota and hence soothes intestinal track.<sup>[69]</sup>

### **Anti-regurgitation**

Regurgitation is a frequent manifestation of gastro-esophageal-reflux (GER). It is considered a self-limiting physiological condition in infants that is the major source of parental concern, feeding issues, milk formula change, and physician referral. It does not require any treatment; nutritional management is enough for controlling frequent regurgitation or reducing multiple episodes.<sup>[70]</sup> The prevalence of GER is 30% around the globe.<sup>[71]</sup> Non-pharmacological methods are considered the best treatments for regurgitation that include infant positioning, gastric clearance, proper feeding volume, frequency, removing obesity, and thickening agents.<sup>[72]</sup> Various anti-regurgitation formulas are available in the market. Infant formulas are thickened with CBG, corn starch, xanthan guar gum, and soybean polysaccharides. All thickening agents confer certain health benefits such as reduced regurgitation, increased weight gain, and improved reflux-associated symptoms, whereas CBG has several advantages over others it is indigestible fermentable fiber with prebiotic effects that supports microbiota growth that lowers pH hence resulting in reduced acid reflux<sup>[73]</sup>. Tounian et al.<sup>[74]</sup> explored that LBG thickened formula is well tolerated in infants and reduces regurgitation episodes with increased value of life. Stool content and frequency remain within the normal physiological range. According to the literature Gatcheco et al.,<sup>[75]</sup> nutritional intervention such as the intake of anti-regurgitation thickened formulae enhances the quality of life for new-born's by preventing sleep disturbance and screaming, as well as less regurgitation and regular softer stool. The above studies coincide with previous studies of<sup>[76]</sup> that administration of CBG based thickened formulas considerably reduces the amount of regurgitation episodes and ameliorates the other signs gastro-esophageal-reflux in infants.

### **Anti-hyperlipidemia**

Hyperlipidemia is characterized by elevated blood levels of cholesterol, triglycerides, or both that may promote atherosclerosis and become the major cause of cardiovascular diseases<sup>[77]</sup>. In the United

States, 38% of deaths are attributed to coronary heart diseases and stroke.<sup>[78]</sup> McRae<sup>[79]</sup> suggested that high dietary fiber consumption reduces the incidence of cardiovascular diseases and mortality rates by lowering total serum and LDL concentration in blood. The carob tree has a high dietary fiber that can reduce human serum cholesterol. Administration of IFC to rabbits fed with a cholesterol-rich diet showed a reduction in serum cholesterol and triglycerides. The hypolipidemic effect of fiber was attributed to bile acid binding, resulting in an increased fecal loss of bile acids and enhanced consumption of cholesterol. Furthermore, fiber consumption hampers triglyceride absorption, which lowers serum concentrations.<sup>[22]</sup> Macho-Gonzalez et al.<sup>[80]</sup> explored that carob fiber extract (CFE) reduces postprandial lipemia levels in rats by inhibiting pancreatic lipase activity that leads to reduced fat digestion and absorption along with enhanced fecal excretion of fat. The carob beans are a rich source of dietary fiber as well as phenolic compounds both are responsible for anti-hyperlipidemia activity. CBG increases fiber in foods without increasing caloric counts and is administrated as an effective treatment of hypercholesterolemia. Studies revealed that higher content of anti-oxidants in carob showed hepato protective effect along with lowered lipoproteins and oxidative stress in hypercholesterolemic rats.<sup>[81]</sup> Another study showed that carob pods' insoluble fiber abrogates the harmful effects of hepatic dyslipidemia by modifying SIRT1 and PGC-1 $\alpha$  pathways that play a vital role in the metabolism of cholesterol and triglycerides in the liver. These effects were linked with lower hepatic fibrosis, plasma levels of total cholesterol and triglycerides in rabbits fed with cholesterol and a coconut oil-rich diet.<sup>[82]</sup>

### **Nephron protection**

Kidney disease is the most common health problem linked with severe pain and suffering in individuals. The studies of Bencheikh et al.<sup>[83]</sup> reported that medicinal plants are used to treat renal diseases in underdeveloped countries. Carob fruit is of medicinal plant loaded with many bioactive compounds that confer health effects. Kidney stones are mineral deposits found free or attached to the renal papillae, calcium oxalate is the main constituent of most stones.<sup>[84]</sup> Carob is oxalate free, making it highly suitable to use as a coca replacer in confectionery. The absence of oxalate prevents calcium binding hence ameliorating risks of kidney stones.<sup>[33,85]</sup> Arribas et al.<sup>[23]</sup> reported that carob fortified rice-based gluten-free extruded products are rich in many bioactive compounds like phenols that act as anti-cancer and anti-inflammatory because of high anti-oxidant potential and inositol phosphates that promote mineral absorption hence preventing the formation of kidneys stones. El-Haskoury et al.<sup>[86]</sup> suggested that carob honey can be used as an active diuretic in rats because of its rich flavonoid content. The literature of showed that 70% ethanol/water extract of carob improves kidney function in diabetic rats. The anti-oxidant and anti-inflammatory properties of the extract are due to polyphenolic compounds that are effective against dextran sulfate sodium-induced hepatic and renal injuries in rats.<sup>[87]</sup> Different fractions of carob leaves were prepared using ethyl acetate and n-hexane; tested for their efficacy against oxidative stress. The fractions showed a positive response against renal failure caused by CCl<sub>4</sub>-induced oxidative stress.<sup>[88]</sup>

### **Anti-diabetic effect**

Diabetes is a chronic condition in which the pancreas malfunctions is unable to produce sufficient insulin or when the body is unable to utilize produced insulin. Uncontrolled diabetes is responsible for hyperglycemia and raised blood glucose levels as well as leads to severe damage to other body systems, including kidneys, liver, blood vessels, and nerves over time. There is a drastic increase in the number of diabetics. The number of diabetes patients is expected to climb to 300 million by 2025. Diabetes is also expected to be the seventh biggest cause of mortality by 2030, according to the World Health Organization.<sup>[89]</sup> Diabetes pathogenesis is controlled with insulin or oral medication of hypoglycemic medicines. Novel treatments focus on diminishing or inhibiting glucose absorption from controlling hyperglycemia.<sup>[90]</sup> Many therapeutic herbs and extracts have been used as effective anti-diabetic due to

the high content of flavonoids and polyphenols.<sup>[91]</sup> Carob fruit and its extract are also responsible for the anti-diabetic effect because of its diverse phytochemical composition. These compounds can be used as food supplements in hyperglycemia and treat diabetes by inhibiting transportation and absorption of intestinal glucose.<sup>[92]</sup> Custódio et al.<sup>[14]</sup> reported that decoctions made from carob leaves and barks exert significant inhibitory activity on  $\alpha$ -amylase and  $\alpha$ -glucosidase, both are carbohydrate-hydrolyzing enzymes that digest carbohydrates and increase postprandial hyperglycemia in diabetics. Another study showed that carob could be used for treatments of diabetes as it improves glucose tolerance, inhibits glucose absorption, and protects against alloxan-induced diabetes in rats.<sup>[93]</sup> Prediabetes state is impaired glucose tolerance (IGT) or impaired glucose fasting that is commonly characterized by abdominal or visceral obesity. Prediabetic subjects are at higher risk of diabetes. Obesity contributes to developing insulin resistance, a hallmark of type 2 diabetes-mellitus (T2DM).<sup>[94]</sup> Defective metabolism of inositol can cause impaired insulin action and resistance, inositol therapy regulates the metabolism of T2DM. Consumption of carob pod inositol enriches beverage produces a BMI-dependent response in Prediabetic subjects with improved insulin resistance.<sup>[95]</sup> Pintel or specifically D-pintel is another inositol extracted from carob and has significant anti-diabetic effect.<sup>[96]</sup> In addition to it, the literature of also showed that substitution of sucrose with natural pintel rich sweetener attenuates glucose metabolism disruption and normalizes impaired glucose metabolism in IGT subjects. At early stages, pancreatic  $\beta$  cells can counterbalance insulin resistance by increased insulin production, with time, Pathology causes pancreatic -cell malfunction, which manifests as hyperglycemia with insufficient insulin. Carob fruit extract (CFE) enriched functional meat is an effective tool to manage late-stage T2DM that relieves the dysfunction of  $\beta$ -cells of pancreas, leading to higher insulin levels and a reduction in hyperglycemia.<sup>[97]</sup> The most common endogenous cause of lipid metabolism problem is insulin resistance leading to higher risks of cardiovascular diseases. Furthermore, it contributes to alternations in plasma lipid levels that result in the presence of big VLDL particles, tiny and dense LDL particles, and HDL enriched in triglycerides. All these modifications of T2DM are linked to hepatic insulin signaling alterations.<sup>[98,99]</sup> CFE formulated meat intake improves lipoprotein metabolism and insulin signaling effectiveness by reducing VLDL and plasma triglyceride levels as a result of increased fecal fat excretion.<sup>[97]</sup>

### **Prevents migraine**

Migraine is a neurological disorder and classified as primary headache, according to

Number four of the Trøndelag Health Survey (HUNT4 study), approximately 18.1% of the studied population experienced active migraine.<sup>[100]</sup> Migraine is defined by the International Headache Society as a recurring primary headache disease characterized by bouts lasting 4 to 72 hours. Usually, migraine is characterized by headache followed by fatigue, neck discomfort, gastrointestinal disturbances, Nausea, sensitivity to light, sound, and touch, and mood swings.<sup>[101]</sup> It is categorized based on attack frequency. It can be episodic migraine if the headache lasts for 1–14 days, otherwise called chronic; less than 15 days or at least 8 days of headache.<sup>[102]</sup> Migraine can be triggered by many factors like external triggers, including lifestyle, diet, stress, sleep, exercise, and geographical location, whereas internal triggers are metabolism, hormonal disturbance, and genetics. Diet modifications and nutraceutical interventions have had a significant affect in migraine patients<sup>[103]</sup> Generally, it is observed that migraines are sensitive to diet and triggered by some dietary ingredients like chocolate, citrus fruits, coffee, caffeine, dairy products, monosodium glutamate(MSG), histamine, tyramine, nitrate, aspartame, and gluten.<sup>[31,104]</sup> Dietary modifications play an important role in the avoidance of migraines. One such modification is elimination diet therapy, which includes identifying and eliminating proactive ingredients from the diet for a particular disease. The identification is a complex process due to food complexity and judgment precession. Furthermore, eliminating food from the diet results in malnourishment<sup>[103,105]</sup> Another modification is dietary interventions or specific diets for migraines that work through different mechanisms and pose anti-migraine effects.<sup>[105]</sup> Literature showed that a low glycemic index diet, average or low lipid diet, or vegan diet

decreases attacks. As in the case of menstrual migraine that is managed by dietary intakes that alter estrogen levels in patients. Being low in fat and high in fiber, plant-based diets are loaded with bioactive ingredients that act as an anti-inflammatory against migraine.<sup>[106,107]</sup> Chocolate consumption is also considered a migraine trigger<sup>[108]</sup> possibly due to caffeine and tyramine<sup>[109]</sup> so replacement of chocolate with carob can prevent the occurrence of migraine, as carob is free of tyramine and caffeine. On the other hand, some studies suggest there is no clear evidence for chocolate as a migraine trigger.<sup>[110]</sup> So, Dietary interventions and elimination are complex processes that require further deep insight.

### **Anti-microbial activity**

Methanolic extract of *C. siliqua* was more active against the bacterial activity, particularly *Enterococcus* sp. <sup>[111]</sup> Methanolic extract of leaves is effective against *Listeria monocytogenes* and *Geotrichum candidum* (fungus).<sup>[112]</sup> A suspension made with carob powder and methanol was found to have anti-bacterial and anti-fungal effects<sup>[113]</sup> Aqueous and methanolic extracts and anti-bacterial agents (ampicillin, gentamicin, amikacin, and clindamycin) were productive against bacteria<sup>[114]</sup> Methanol, chloroform and hydro-alcohol based extracts of dry carob were greatly effective against different microbes including 15 bacterial and 8 fungal species.<sup>[88,115]</sup> Fruits processed with 80% methanol in water showed antimicrobial and moderate anti-oxidant activity.<sup>[116]</sup> Kumar et al.<sup>[117]</sup> reported that in concentrations of 1000 and 500 g/ml, dried pod extract in dichloromethane-methanol (1:1, v/v) was effective against 11/14 bacteria types and fungi. The acetone extract was more active against *Pectobacterium atrosepticum* than ethanolic extract.<sup>[118]</sup> Ethanolic extract of leaves was partially active against Newcastle Disease Virus.<sup>[119]</sup>

### **Effects on reproductive system**

Approximately 1/7 of the world's population suffers from infertility issues at reproductive age that causes severe emotional and financial stress<sup>[120]</sup> About 50% of infertility issues arise due to male-related reproductive tissues such as semen pathologies and spermatogenesis disorders.<sup>[121]</sup> Public health studies have reported several factors that contribute to male infertility, such as diet, lifestyle, medications, and environmental and occupational exposure to toxicants.<sup>[122]</sup> All these factors affect male fertility by disrupting natural anti-oxidant defense mechanism, resulting in elevated oxidative stress due to enhanced Peroxidation of lipids, free radicals, and reactive-oxygen-species (ROS) production followed by anti-oxidant depletion.<sup>[123]</sup> Oxidative stress leads to intratesticular tissue damage, abnormal sperm function, diminished sperm activity, and impaired spermatogenesis.<sup>[124,125]</sup> Many studies suggest that the administration of herbal plants effectively treats infertility as it alleviates the oxidative stress caused by toxicants<sup>[126,127]</sup>. Carob is considered among these medicinal herbs that positively affect male fertility and spermatogenesis because of its excellent anti-oxidant potential. Ata et al.<sup>[128]</sup> reported that daily oral intake of carob extract improves semen quality in male rabbits without a negative impact on reproductive system furthermore, it enhances serum testosterone concentration without increasing abnormal sperm cells. Administration of carob improves semen parameters, morphology, and motility, particularly in terms of testosterone levels and anti-oxidant properties of semen compared to vitamin E. In addition to it, a higher pregnancy rate was observed; almost 17% of couples were able to conceive after carob treatment.<sup>[129]</sup> In other studies, carob extracts were doped along with busulfan; a chemotherapeutic agent that negatively affects the reproductive system and nicotine for 35 days to check its efficacy against male infertility.<sup>[124,130]</sup> Vafaei et al.<sup>[130]</sup> reported that a dose of 800 mg/Kg of carob extract showed positive effects on sperm quality, testosterone levels, germinal epithelium thickness, and biochemical parameters of sperms. The literature of Oztekin et al.<sup>[124]</sup> also suggested that carob extract significantly increases IL-6 and TNF- $\alpha$  level due to nicotine toxicity, improving spermatogenesis and lessening the testicular parenchymal damage, apoptosis, and angiogenesis. Mehraban et al.<sup>[131]</sup>

demonstrated the efficiency of carob extract against Cyclophosphamide (CP) induced toxicity in male rats. The results showed that CP leads to reduced sperm count with enhanced DNA fragmentation; however, carob recovers DNA damage and boosts sperm quality. Carob fruit hydro-alcoholic extract (CFHAE) alleviates lead (Pb) induced reproductive toxicity as a result of enhanced sex hormones (FSH, LH, and testosterone), total anti-oxidant capacity, and anti-oxidant enzymes the activity of serum followed by decreased levels of serum MDA. It also down-regulates testicular expression of Nrf2 gene, modulates the response of cellular resistance to oxidants<sup>[132]</sup> and iNOS gene cause an inflammatory response.<sup>[125,133]</sup> Mobli et al.<sup>[134]</sup> reported carob as an effective treatment of abnormal uterine bleeding. MSG alters the female reproductive organs (ovaries, uterus, and vagina and lowers serum estragon levels; however, feeding on a diet comprising carob powder improves the structure and function of reproductive organs which is due to phytochemical components that boost the metabolism of ovaries, uterus, and vagina<sup>[135]</sup> Ovariectomy (surgical removal of ovary) leads to significant biochemical changes such as elevated triglyceride, alanine aminotransferase, lactate dehydrogenase, and aspartate aminotransferase levels. Administration of aqueous extracts of carob powder (AACP) converse these biochemical alterations and exerts an anxiolytic-like effect linked with menopause or ovariectomy.<sup>[136]</sup>

### **Prevent obesity**

Obesity is defined as the accumulation of triglycerides in adipose tissues due to enhanced multiplication of adipocytes and adipocyte hypertrophy. Obesity is a leading cause of many chronic diseases like diabetes, cardiovascular diseases, and cancer because of abnormal adipocytokine secretions.<sup>[137]</sup> The balance between reactive-oxygen-species and oxidative reactions is lost in this state, resulting in different metabolic conditions such as hyperinsulinemia, altered lipid metabolism, and enhanced triglyceride storage<sup>[138,139]</sup>). Adverse health effects of weight-reducing drugs and surgeries shifted the attention toward the use of natural products, particularly functional foods that reduce weight and provide essential nutrients to fulfill body needs.<sup>[140]</sup> Carob is a superfood that has excellent anti-oxidant properties that exert anti-obesity effects along with treatment of other chronic life-style related disorders.<sup>[8]</sup> Fujita et al.<sup>[137]</sup> fed mice with a high-fat diet and the administration of carob pod polyphenols (CPPs) revealed that CPPs acted as anti-obesity compounds and repressed the increase in adipocyte hypertrophy and adipose tissue mass. CPP reduced triglyceride synthesis and accumulation by suppressing adipocyte proliferation and differentiation through the post transcriptional regulation of C/EBP $\beta$ . Administration of cafeteria diet enriched with carob pulp, reduce adipose tissue mass, body weight and hyperglycemia followed by improved plasma lipid profile and anti-oxidant status in male Wister rats.<sup>[141]</sup> However, the literature suggested that effective weight loss in obese men is only possible when carob supplements are taken along with certain physical activities as it increases levels of irisin hormone. This insulin-sensitizing hormone promotes glucose uptake by skeletal muscles.<sup>[142]</sup> Rico et al.<sup>[143]</sup> also reported that the high anti-oxidant potential of carob by-products made it a promising therapeutic agent for the treatment of metabolic-syndrome (MetS), is a complicated multifactorial illness characterized by abdominal obesity, hyperglycemia, elevated blood pressure, and atherogenic dyslipidemia, all of which raise the risk of heart disease and type 2 diabetes. Raised prevalence of MetS is ascribed to unhealthy dietary patterns such as frequent snacking and consumption of energy-rich foods.<sup>[144]</sup> However, adopting healthy snacking habits could improve the quality of diet as well as provide appetite control, satiety, and reduced postprandial glycaemic response.<sup>[145]</sup> Rico et al.<sup>[146]</sup> developed a functional snack by incorporating of carob and wakame to combat NAFLD (nonalcoholic fatty liver disease) is the hepatic manifestation of MetS. It is usually asymptomatic that's why its exact prevalence is unknown; however, 35% of the western population suffers from NAFLD.<sup>[147]</sup> A study by Rico et al.<sup>[146]</sup> suggested that functional snacks developed by using carob and wakame can treat fatty liver as it lowers hepatic triglycerides levels by enhancing fat oxidation and decreasing oxidative stress. Carob seed peel and pods exhibit anti-hypertensive activity and anti-inflammatory activity; however, only carob pods lessen the inflammation-promoting

mediators.<sup>[143]</sup> Carob contains a significant amount of fiber; hence, food supplemented with high fiber results in low caloric value leading to weight control<sup>[148]</sup>).

## Use of carob beans in product development

Locust (Carob) bean gum (LBG) is a non-starch galactomannan, nonionic branched heterogeneous gum extracted from carob bean seeds. LBG and its hydrogel-derived formulations found wide applications in the food, pharmaceutical, biomedical, and cosmetic industries. This wide range of usage is attributed to flexible physicochemical properties like viscoelasticity, swell-ability, and release-retarding abilities. LBG is slightly soluble in water at room temperature and highly stable at pH 3.5 to 11.0. It must be heated at 75 to 85°C for viscosity development furthermore, LBG solutions are not affected by salts commonly used in the food industry. In the food industry, major areas of usage are frozen desserts, cultured dairy products, cheese products, sauces, dips, and dressings, whereas in the pharmaceutical industry LBG has been used as a carrier in various drug delivery systems<sup>[149]</sup> Table 2.

### As a food additive (stabilizer/thickener)

In the food industry, LBG is used as a Food additive (E-410) under the thickener and stabilizer in various dairy, meat, and baked products. In addition, it is also used in dietetic products and food supplementations due to its excellent bioactive profile however its usage level in foods varies depending upon applications, mainly addition rate lies between 0.2% and 0.5%.<sup>[10]</sup> Technological roles in food include increasing shelf life by binding water, managing texture, influencing crystallization, preventing creaming or settling, improving the freeze-thaw behavior, preventing synergies and the retro gradation of starch products, retaining turbidity in juices and soft drinks, and stabilizing foam.<sup>[152]</sup> Synergistic interactions of LBG with other biopolymers are responsible for the texture development of frozen, dairy, and baked goods. Barbosa et al.<sup>[153]</sup> reported that caseinate-LBG biopolymers showed significant emulsifying properties at different pH conditions for oil in water emulsions. These emulsifying and stabilizing properties are attributed to protein and polysaccharides interactions resulting from electrostatic interactions, hydrogen bonding, and van der Waals forces. Another study suggested that LBG ameliorates the rheological properties of caprine milk yogurt as well as maintains the microbial vitality of the yogurt culture and the probiotic *Bifidobacterium spp.* Park et al.<sup>[154]</sup> According to the literature by Ravat et al.<sup>[155]</sup> irritated LBG polymer also improves probiotic survival in gastrointestinal transit conditions. Xanthan-LBG biopolymers showed high oxidative stability for O/W emulsions, making them highly suitable for encapsulated bioactive delivery in functional foods<sup>[156]</sup> Ice creams and related products are categorized as frozen desserts; major issues in the case of frozen desserts are maintained crystal size, viscosity, texture, and melting temperature of products. LBG is a source of galactomannan, which is used as a thickening to slow the formation of ice crystals and enhance the melting properties of ice cream. Chaves et al.<sup>[157]</sup> studied that LBG positively affects overrun, apparent viscosity, and melting characteristics of goat milk frozen dessert. Further studies explored that LBG lowers the overrun of ice-cream mixture, prolongs the melting time, and improves sensory characteristics in animal as well as vegan ice creams.<sup>[158,159]</sup> LBG could be used as a fat replacer in reduced or

**Table 2.** Maximum permitted usage levels of LBG in foods.

Food Category	Permitted Usage Levels
All other Food Categories	0.50%
Jams and Jellies	0.75%
Gelatins, puddings and Fillings	0.75%
Cheeses	0.80%
Beverages and beverages bases	0.25%
Baked goods and Baking mixes	0.15%

Source<sup>[150,151]</sup>.

low-fat dairy products with a marked effect on the textural and sensorial properties of the product.<sup>[160]</sup> Furthermore, it can be administrated as a natural replacement of thickeners used in the jam industry without any negative effect on the sensory and physicochemical properties of jams.<sup>[161]</sup> Siriwongwilaichat & Koedcharoenporn<sup>[162]</sup> reported that xanthan-LBG blends can be used for the preservation of fruit pulps.

### **Cocoa substitute**

Coca is a key agricultural product since it is the primary ingredient of chocolate-based products it carries excellent economic and social importance around the globe.<sup>[163]</sup> Multiple factors are responsible for reduced supply growth of coca, resulting in demand and supply imbalance that puts high pressure on coca prices. To overcome these challenges, sustainable substitutes are needed to meet customers' demand. Carob is a natural and cheap coca substitute with many similarities, which makes carob a perfect coca replacement.<sup>[164]</sup> Carob pulp is dehulled, ground and then roasted to produce carob powder. Carob is roasted at a temperature of 120–180°C for 10–60 min depending upon the desired end product.<sup>[165]</sup> During roasting sugar, caramelization and Maillard reaction develop characteristic coca like aroma, taste, and color in carob powder.<sup>[13]</sup> Thus carob can be used as a cocoa substitute, with many advantages such as caffeine and theobromine stimulants free, increased fiber supplementation, reduced fat, and excellent anti-oxidant potential.<sup>[166,167]</sup> Literature of Akdeniz et al.<sup>[168]</sup> showed that carob is the perfect replacement of coca in dark and milk chocolate formulations with no significant differences in organoleptic properties and consumer acceptance. Furthermore, carob chocolates are of high nutritional value because of their low-fat content and high levels of dietary fibers in carob. Another study reported the successful development of chocolates by substituting cocoa with carob and the product were highly accepted by the consumer that is subjected to certain disorders like diabetes, celiac disease, caffeine intolerance, or calorie-conscious group.<sup>[169,170]</sup> Carob-based glazes with good rheological and sensory properties have also been developed that can be used as the replacement of chocolate glazes and coating in confectionery and bakery products.<sup>[171]</sup> Pawłowska et al.<sup>[172]</sup> suggested that bakery products developed with carob have high nutritional and anti-radical properties with sweeter and good sensory properties compared to cocoa-based bakery products. Furthermore, cakes incorporating carob flour retained acceptable textural and sensory properties with coca reminiscent aroma due to aromatic compounds like aldehydes, lactones, furan, and pyrrole derivatives. However higher concentration of flour above 70% negatively affects the batter density and cake volume because of the high concentration of dietary fiber.<sup>[166]</sup> Carob powder can also be used to develop chocolate-flavored low-fat yogurts and low lactose yogurts with high fiber and sweetness for lactose intolerant individuals.<sup>[173]</sup>

### **Gluten-free products**

Cereal-based baked products are a major constituent of people's diet due to their sensorial and nutritional quality. However, these products can't be consumed by celiac people due to their gluten content. Celiac disease is an auto-immunological disorder triggered by the ingestion of gluten proteins which cause an inflammatory reaction in the small intestine. Celiac patients consume various products veggies, unprocessed meat, and other processed items such as pasta, breads and biscuits made with starches and gluten-free-flours. Unfortunately, there is little variety of products available in markets that can be used as an alternative to common diet by celiac. In recent years, food industries have been interested in manufacturing products according to the specific nutritional demand of consumer groups with a food disorder or food allergy. Gluten-free items come under this category, and they are in high demand increasing not only by celiac patients but also non-celiac demand GF products as these are healthier, particularly in terms of body weight management and illness prevention.<sup>[174]</sup> The development of GF products represents a few technological challenges for the food industry such as texture development due to the absence of gluten, low nutritional value, and bland taste.<sup>[175,176]</sup> GF

products require certain additives and ingredients to mimic the structural function of gluten, starches from legumes (beans) and cereals (rice and sorghum) are utilized for this purpose. Another legume with great potential for developing GF products is carob bean, carob flour showed rheological properties similar to wheat gluten along with an excellent nutritional profile.<sup>[23,177]</sup> Červenka, Frühbauerová, & Velichová<sup>[178]</sup> and Sciammaro et al.<sup>[179]</sup> explored that muffins prepared with carob flour in replacement of wheat flour exhibit high anti-oxidant potential with good sensory attributes (softness, height, weight). Carob flour cookies show higher nutritional values as compared to control cookies. It also imparts sweetness and brownish color to cookies however, higher concentrations of carob flour have a slightly negative effect on the taste, crispness, color, and fragrance of the product.<sup>[180]</sup> Functional macrons were also prepared by using carob flour and sorghum as a healthy diet alternate for celiac patients. The product presents a balance of essential and non-essential amino acids, bioactive compounds with excellent flavor.<sup>[181,182]</sup> Literature of Skaltsi et al.<sup>[185]</sup> showed the development of GF carob biscuits supplemented with apple pomace, most suitable formulations to make high-quality gluten-free biscuits with acceptable physical, textural, and sensory attributes were dried apple pomace (32.6% – 47.58%), carob flour (16.2% – 29.2%) and water (29% – 43%). Novel gluten-free fettuccine and noodles were also prepared by using carob flour with good cooking quality and better nutritional and functional value.<sup>[23,183]</sup>

### **Fermented products**

The metabolic process through which bacteria turn carbohydrates into organic compounds like acids, gases, or alcohol is called fermentation. Major and minor nutrients are required to carry out this conversion; however, utilization of pure nutrient sources makes the industrial process costly. To reduce process costs various agro-industrial waste molasses, sugar cane bagasse, maize waste, juice factory waste, lignocellulosic materials, and other substances are employed to fulfil nutritional requirements for fermentation.<sup>[184]</sup> Furthermore, these are excessively available at cheap rates, and their valorization results in reduced cost as well as efficient utilization of waste. Carob pod, with its high nutritional content, is an essential source for fermentative production. Carob is processed to produce certain carob products like CBG, carob juice, carob flour, etc. after extraction of all these fractions the leftover is still a rich sugar source that can be used for the fermentation process to produce certain organic compounds.<sup>[3,185]</sup> Citric acid, a tri-carboxylic acid, is widely used in the pharmaceutical, food, and beverage industries as an acidifying and flavor-enhancer. Researchers are focused on its production from cheap sources. The literature of<sup>[186]</sup> showed that fermentation of carob extract by *Aspergillus Niger* produced significant amounts of citric acid. After six days of incubation, citric acid production was 55.8% at a pH value of 3.16 with 10% carob extract as a carbon source. However, production reached up to 70.16% in a medium containing ammonium sulfate as a nitrogen source showing that concentration and nitrogen source affected acid production. Furthermore, adding 0.05% calcium chloride and 2% ethanol resulted in increased acid production. Carob can also be utilized as the carbon source in lactic acid production, an industrial chemical. The demand for lactic acid has risen tremendously as it is used as a monomer to produce biodegradable Polylactic acid (PLA), a sustainable bioplastic. Higher lactic acid concentrations can be obtained by using *Lactobacillus casein* and carob extract as fermentation media. However, carob extract should be treated with invertase enzymes before converting sucrose into monosaccharides that *L. casein* can efficiently metabolize 68.79% was the maximum concentration obtained by using yeast extract as a nitrogen source as compared to other nitrogen sources with 66.70% production.<sup>[187]</sup> Carob waste is valorized for lactic acid production by using response surface methodology and immobilized *Lactobacillus rhamnosus* alginate beads. To carry out fermentation, the optimum condition was 2% alginate content, 4% bacteria cells entrapped in beads, agitation speed of 80 rpm, and pH of 6.4 with 22 g/L productions of lactic acid on the consumption of 76.9 g/g sugars.<sup>[188]</sup> Carvalho et al.<sup>[16]</sup> suggested that raw carob pods are an effective feedstock for succinic acid synthesis by using in batch and fed-batch fermentation mode. 0.39 g SA/g sugars were produced by batch fermentation that was increased to 0.94 g SA/g sugars by the implementation of fed-batch mode with a reduced

yield of by-products. Due to increased prices and environmental concerns, conventional fuel resources have been replaced by renewable sources. In this regard, investigations are focused on meeting the world's energy demands by developing environment-friendly fuels through cost-effective and straightforward processes. Ethanol can be produced from food and waste sustainably.<sup>[189]</sup> Carob and its waste products can be utilized for bioethanol production because of their high sugar and mineral content.<sup>[190]</sup> Mazaheri et al.<sup>[191]</sup> reported bioethanol production from *Zymomonas mobilis* by using RSM and wheat bran mixed in carob pod as media for bacterial growth. The maximum recorded production was 0.30 g ethanol/g of initial sugar. Bioethanol production can be optimized by using immobilized *Saccharomyces cerevisiae* up to 40.10 g/L. Immobilized cells can be reused for respective five cycles; however, yield was decreased. Furthermore, immobilized cell fermentation facilitates yeast multiplication without enrichment.<sup>[189]</sup> The literature of Bindal<sup>[190]</sup> also suggested that carob pods can be effectively utilized for mass-scale ethanol production by using different strains of *Saccharomyces* sp. among them, maximum production was 20.40%, followed by 11.44% and 9.12%. Mannanases, breakdown galactomannans to mannose and found diverse applications in food as well as other industries; hence its production from cheap sources is of great economic importance. Carob extract with an initial sugar concentration of 8% showed maximum mannanases activity of 423.60 U ml<sup>-1</sup> that raised to 695.6 U ml<sup>-1</sup> by addition 0.5% nitrogen source. The optimum conditions were 0.5% yeast extract, 100 r.p.m., at a 7% inoculation rate.<sup>[15,192]</sup>

### **Non-food applications**

**Pharmaceuticals:** LBG is a biodegradable and biocompatible polymer that Food and Drug Administration, USA award GRAS (Generally recognized as safe) status. Due to these properties, LBG and its derivatives have wide applications in pharmaceutical and biomedical fields.<sup>[193]</sup> LBG act as a binder, viscosity enhancer, stabilizer, matrix former, drug release modifier, coating, emulsifier, suspending agent, gelling agents, and bioadhesives in manufacturing of several pharmaceutical formulations like solid monolithic matrix systems, films, beads, microparticles, nanoparticles, inhalable and injectable systems.<sup>[194,195]</sup> LBG is extensively used in drug delivery systems for targeted delivery and controlled release of certain substances; that is attributed to the mucoadhesive nature of this biopolymer. Furthermore, it has excellent gelling properties and synergism with other polysaccharides, due to which different formulations can be prepared like tablets, hydrogels, and multi particulate systems for drug delivery.<sup>[37,196,197]</sup> Pettinelli et al.<sup>[198]</sup> reported development of novel biocompatible drug delivery system based on Poly (hydroxybutyrate-co-hydroxy valerate) (PHBV) microparticles embedded in LBG hydrogel to release hydrophobic drugs. The composite hydrogel showed thermo-sensitive swelling behavior, good rheological properties, high affinity with fibroblastic cells, and prolonged drug release at 37C, showing that LBG hydrogels have high potential for drug use delivery carriers for hydrophobic drugs. The literature of Braz et al.<sup>[199]</sup> suggested that LBG nanoparticles prepared through chemical modification of LBG can be utilized as drug delivery systems for oral immunization. LBG incorporated agar films showed high anti-microbial and wound healing properties compared to agar films. All films were transparent allowing good observability furthermore, the tensile strength and thickness of films were under parameters for wound healing films.<sup>[200]</sup> Additionally, it is utilized as muco adhesive in buccal patches, drug release retardant in LG-alginate beads, and microspheres<sup>[201,202]</sup> and Super disintegrant and matrix former in tablets.<sup>[203,204]</sup> Hence LBG is utilized in various drug delivery systems like oral, buccal, colon, and topical drug delivery systems along with some biotechnological processes such as tissue engineering.<sup>[194,205]</sup>

### **Animal feed**

Pods of several legumes have been used in livestock diets worldwide during critical periods of the year when the quality and quantity of forages are restricted. One is carob, which is used for animals mainly ruminants feeding due to its high sugar content and is highly recommended use as feed supplement for

animal farming in drought-stricken regions.<sup>[206]</sup> Furthermore, the high cost of animal feed is a major limitation for livestock production and the use of imported concentrates cannot be avoided. Therefore, utilizing agro-industrial by-products as animal feed has emerged globally. This practice is considered a sustainable approach because of its availability at competitive prices relative to other commodities.<sup>[207]</sup> Carob and its by-products are a rich source of sugars which make it highly energetic food along with many bioactive compounds that exert certain health benefits. In addition, it has high digestibility and palatability in animals.<sup>[208,209]</sup> Literature of Beynen<sup>[210]</sup> suggested that carob treats can be used as chocolate treats replacement in animals as these are theobromine free, toxic effects of theobromine in dogs are observed at a concentration of 20 mg/kg of body weight. Due to bioactive compounds, carob meal is associated with the anti-diarrheal effect and supports gut microbiota. Carob bean gum can also be used to develop wet dog food due to its gelling properties. A study by Richane et al.<sup>[211]</sup> suggested that the nutritional profile and chemical composition of carob are affected by geographical distribution. Carob pods with supplementation can be used as ruminant feed. Medjekal et al.<sup>[212]</sup> reported that carob has a high potential to be used as a feed supplement because of its high nutrition profile. Inclusion of carob powder in the feed of weaning rabbits showed a positive effect. Growing rabbits' productive performance, protein profile, gastrointestinal function, immunity, and anti-oxidant activity were improved by lowering lipid peroxidation, critical inflammatory mediators, and protein-carbonyl residues.<sup>[213]</sup> These biological and physiological functions of carob bean can be attributed to its bioactive and phytochemical constituents, as have been reported for similar food/feed commodities.<sup>[150,151,214,215]</sup> After weaning of rabbit's administration of carob pods along with commercial feed improves growth performances by enhancing palatability and may avoid digestive problems, particularly diarrhea with reduced mortality.<sup>[208]</sup> However, the administration of carob as an animal feed source needs further investigations followed by clinical trials.

## Conclusion and future trends

As the world is facing an increasing number of health problems due to different factors including modern lifestyle and a lot of artificial products. As a result, there is a high demand for products that contributes toward a low level of economic losses as well as confers a lot of health benefits. The rich bioactive profile and high dietary fibers of carob and their related effect on obesity, diabetes, oxidative stress, hyperlipidemia, and inflammation make it an ideal food ingredient that has the potential to be used in the development of a variety of health beneficial products. Furthermore, carob products (LBG), when used as a food additive in formulations, improving rheology by imparting functional properties to foods and enhancing their nutritional profile and extending the final product's shelf life. Undoubtedly, carob is not only beneficial for human health but also of economic and environmental importance. Further studies can be done to evaluate and investigate the neuroprotective effect of carob beans.

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