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Functional Foods in Health and Disease

Different impacts of plant proteins and animal proteins on human health through altering gut microbiota

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ABSTRACT

Dietary proteins exert a wide range of nutritional and biological functions. Apart from their nutritional roles as the source of amino acids for protein synthesis, they take part mainly in the regulation of food intake, blood pressure, bone metabolism, glucose and lipid metabolism, and immune functions. The interaction of dietary proteins with the gastrointestinal (GI) tract plays a chief role in determining the physiological properties of proteins. The enzymes protease and peptidase hydrolyze dietary protein to generate dipeptides, tripeptides, and amino acids in the lumen of the gastrointestinal tract. These products digested from dietary proteins are utilized in the small intestine by microbes. Moreover, the microbes also convert the macro and micronutrients from the diet into an enormous number of compounds that may have either beneficial or adverse effects on human health. The present review discusses the various impacts caused by both dietary plant and animal protein sources on microbiota in the GI tract.

Keywords: Animal protein; Plant protein; Dietary proteins; Gut microbiota; Human health.

INTRODUCTION

Every organism needs protein to build and maintain muscles, bones, skin, tissues, and body functions. According to the Centers for Disease Control and Prevention, a woman needs 46 grams of protein and a man requires 56 grams of protein per day to maintain optimum health [1]. Among the different. proteins, dietary proteins from plant and animal sources provide essential nutrients. All 20 amino acids are present in such products of plant and animal sources, but the quantity varies. Considering the nutritional aspects of dietary proteins, they are considered essential sources of amino acids that provide energy and allow for protein synthesis. The dietary protein absorbed from the gut has a wide range of functions both nutritionally and biologically. The quality and function of proteins have been analyzed mainly on their ability to provide essential amino acids and support protein synthesis [2].

Proteins from animals are considered complete proteins, which provide all amino acids, [3] whereas, proteins from plant sources lack one or more amino acids [4]. Generally, plant proteins provide nutrients such as beta-carotene, dietary fiber, vitamin C, vitamin E, folic acid, iron, magnesium, and calcium. A person that consumes protein solely from animal sources has a greater chance of diseases related to heart and blood pressure, but this is not the case with from plant proteins [5]. Some epidemiological studies show that the risk of cardiovascular disease [6] and colorectal cancer [7] are higher following the regular consumption of red meat (beef and pork). However, meat remains an important component in the human diet because it contains high quantities of proteins, amino acids, fatty acids, minerals, and vitamins [3]. The major advantage of eating animal proteins is that they contain all 20 amino acids. Thus, plant proteins are generally taken in a combined form with animal proteins to satisfy the complete need for amino acids. This article reviews the key knowledge about the effects of plant and animal protein sources as well as their qualities and actions on microbiota in the GI tract.

Dietary Protein Sources

The dietary protein sources are mainly plant and animal sources. These sources have a complex mixture of proteins that influence physiologic regulation in different ways when consumed.

Plant Proteins

Cereals, pulses, soybeans, and seaweed are plant protein sources with varying complex characteristics.

Cereal Proteins

Cereals are the world's most important food crops which consists of seeds (rice, barley, oats, millet, sorghum, maize), flour (wheat, rye, maize), and flakes (barley, oats, maize). The metabolically active cereal proteins include mostly enzymes (protease inhibitors), which control various reactions, and storage proteins like albumins and globulins (glutelins and prolamins) which facilitate protein biosynthesis as building blocks during germination [8]. Several biological properties of cereal proteins have been reported. Especially, the hydrolyzed proteins and peptides from cereals showed potent antioxidant effects by scavenging the free radicals like DDPH, ABTS, hydroxyl radicals, followed by anti-inflammatory, and antiulcer activities [5]. Borneo and León [9] reported that a high consumption of whole-grain cereals is associated with a reduced risk of hypertension. Further, epidemiological studies have repeatedly shown that the risk for diabetes mellitus type II (T2DM) decreases with the increase in consumption of whole grains [10].

Pulse Proteins

Pulse proteins include dry peas, lentils, beans, and chickpeas from the edible seeds of legumes. In general, pulses contain 17–30% of protein. The major proteins present in pulses are albumins, and globulins. Trypsin inhibitors and chymotrypsin inhibitors are the anti-nutritional factors present in the unprocessed seeds. Improper inactivation of the anti-nutritional factors during processing will lead to a decrease in protein digestibility. The digestibility of proteins determines its nutritional value [11]. Pulse consumption also improves serum lipid profiles and positively affects several other cardiovascular disease risk factors, such as blood pressure, platelet activity, and inflammation [12]. Dahl et al. [13] also reported that a number of nutrients and non-nutrient components of pulses contributed to a reduction of cancer risk.

Soybeans

Soybeans are an oilseed and one of the least expensive sources of dietary protein with many useful nutrients including proteins, carbohydrates, vitamins, and minerals [14, 15]. They have a high protein content of 35-40% of dry weight with all amino acids being similar to animal protein except sulfur amino acids (methionine and cysteine). Thus, they are considered a good replacement for animal proteins [16]. Soy protein can lower cholesterol levels by modulating the LDL receptors in the liver [17]. However, when fed to hypercholesterolemic diabetic albino rats, pasta made of durum wheat added with defatted soy flour or soy flour supplemented with 0.3% methionine significantly lowered both serum cholesterol and glucose levels [18].

Proteins from Oil-Producing Plants

Oil-producing plants including soybeans, canola (rapeseed), sunflowers, safflowers, peanuts, corn, cottonseed, sesame, flax, and hemp are all potential sources of protein for human consumption. Oil-producing plants contain many proteins that have been isolated and proven suitable for human consumption [19].

Seaweed Proteins

Marine plants, especially brown, green, and red seaweed are mainly used for the production of phycocolloids or food. The protein content differs according to the species with, comparatively low protein content for brown seaweeds (3 ± 15% of dry weight), a moderate amount for green algae (9 ± 26% of dry weight), and high amounts for red seaweeds (maximum 47% of dry weight). Important proteins and derived peptides like phycobiliproteins, glycoproteins, phycolectins, and mycosporine-like amino acids are present in seaweed along with polysaccharides and minerals. These compounds have been shown to exert prebiotic effects, regulate intestinal epithelial cells, aid in macrophage and lymphocyte proliferation and differentiation, and modulate the immune response [20]. The recent surge of interest in seaweed is fueled by attention to its bioactive components, which have potential applications in the lucrative functional food and nutraceutical industries. These applications are targeted toward the alleviation of metabolic risk factors such as hyperglycemia, hypercholesterolemia, and hyperlipidemia [21].

Animal Proteins

Meat Proteins

Meat protein sources include red meat, poultry, and fish. These sources provide all 20 amino acids which are present in approximately 20% of the total muscle weight and 80% of the dry mass in lean tissue. Based on their solubility, the meat proteins are divided into sarcoplasmic (e.g., myoglobin), myofibrillar (e.g., myosin and actin), and stromal proteins (e.g., collagen and elastin). Enzymes are bioactive proteins, whereas proteases are a special group of enzymes that are involved in protein turnover during muscle growth and development. Calpain, cathepsins, proteasomes, and aspases are important enzymes for meat tenderization. Additionally, some proteins used as technological ingredients in food processing (e.g., collagen, gelatin, and beef plasma protein) are mainly derived from muscle and animal tissues [22].

Milk Proteins

Milk is a complex biological fluid that provides nutrients and immunity to newborns. It provides essential amino acids along with minerals and lipids used for the development and function of muscles [23]. The active proteins in milk provide antibodies, metal and vitamin-binding proteins, and several protein hormones [24]. Cow milk is composed of 3.5% protein and these proteins are divided into two major groups called caseins (80%) and whey proteins (20%). Casein exists in milk as phosphoproteins in large colloidal aggregates including αs1-, and, αs2-, as well as β- and κ-caseins known as casein micelles. Similarly, whey proteins are composed of β-lactoglobulin, α-lactalbumin, serum albumin, immunoglobulins, lactoferrin, and protease-peptone fractions. κ-Casein only contains about 5% of carbohydrates (tri- or tetrasaccharides), *N*-acetylneuraminic acid (sialic acid), galactose and N-acetylgalactosamine [25]. Milk proteins are consumed in liquid form or as dried food supplements that are widely available on the market [26]. In newborns, the milk proteins coagulate very rapidly and form a large complex with calcium phosphate [27]. From its different biological and physicochemical properties, the heterogeneity and complexity of milk proteins were determined. These properties show that milk acts as a bioactive functional ingredient to regulate food intake and metabolism [28].

Egg Proteins

Eggs are high-quality protein resource that are also considered a functional food. Along with their high nutritional value and organoleptic characters, they provide lipids, valuable minerals, carbohydrates, and vitamins. Proteins comprise about 13% of egg contents and are morphologically divided into the white (albumen) and the yolk. Egg whites have excellent foaming properties and the yolks have emulsifying properties [29]. Egg white proteins contain 15% ovalbumin, 12-13% of ovotransferrin (conalbumin), and 11% ovomucoid, while the remaining 12-13% are minor proteins like lysozyme, G2- and G3-globulins, ovoinhibitor, cystatin, avidin and others. Once the egg yolk is separated by centrifugation it contains fractions of α- and β-lipoproteins (70%), phosvitin (16%), and low-density lipoprotein (LDL) (12%) as well as some minor proteins, lipovitellin, phosvitin, and vitellogenin. The plasma from the yolk contains LDL, yolk riboflavin-binding protein, livetins, and biotin-binding protein [30]. Although the egg white protein is considered a source of high-quality protein, it contains ovoinhibitor, which is a serine proteinase inhibitor that inhibits digestive enzymes like trypsin, chymotrypsin, and elastase. This is considered an important factor which influences the GI tract regulation, especially when consuming raw egg without thermal processing [31].

The number of proteins received from animal and plant sources:

To ensure the quality and quantity of proteins received from consuming dietary fiber in an ideal human diet, both plant and animal food source should be taken in suitable proportions. In human diets, plant-based diet provides ~ 65% of proteins and animal-based diet provides ~ 35% of proteins. A sufficient amount of amino acids can be obtained through the consumption of proper combinations of both legumes and cereals, but the availability of legumes has become limited globally [32]. Although this combination provides the protein requirements for most adults it is applicable to children. In elderly subjects, the deficiency of at least one essential amino acid was identified for those who consumed less than 65% of their total protein from animal-source foods [33]. The amount of proteins present in various plants and animal sources are depicted in Table 1.

Table 1. The amount of proteins present in various plant and animal sources.

S. no	Plant Source		Value per 100 grams	Animal Source		Value per 100 grams
1	Cereal	Barley	9.91	Muscle Proteins	Beef	23.20
		Maize	9.42		Chicken	21
		Millet	11.02		Fish	21
		Rice	6.61		Lamb	21.9
		Sorghum	11.30		Mutton	21.5
		Wheat bread	10.69		Veal	24.8
		Wheat	13.68			
2	Pulse	Adzuki beans	19.87	Egg proteins/1 large		6
		Black beans	23.58	Milk proteins/cup		8
		Black gram	25.21			
		Chickpea	19.30			
		Cowpeas	23.52			
		Faba beans	26.12			
		Kidney beans	21.60			
		Lentils	25.80			
		Lima beans	20.62			
		Mung beans	23.86			
		Pigeon pea	21.70			
		Pinto beans	19.87			
		Soybeans	16.6			

HUMAN GI MICROBIOTA

The GI microbiota is an ecological community of symbiotic and pathogenic microorganisms that share our body space [34]. It is estimated that ∼1014 bacterial cells are present in the human microbiome, a number 10 times more than the total number of human cells [35]. In the human gut, there are about 300-500 different bacterial species [36] with the most common phyla being Bacteroidetes (contains genera Bacteroides and Prevotella) and Firmicutes (contains genera Clostridium, Ruminococcus, and Eubacterium) which comprise more than 90% of the microbiota [37]. Some phyla like Actinobacteria, Spirochaetes, Proteobacteria, Verrucomicrobia, Lentisphaerae, and Fusobacteria are also present in lower proportions [38]. The fungal community present in the microbiota is known as the mycobiome, which comprises only 0.001-0.1% of the microbial community and plays an important role in metabolic function, immune-priming, and maintaining the microbial community structure [39, 40]. The gut virome is the viral component of the gut microbiota, mainly the eukaryotic viruses that can replicate in human cells and the bacteriophages that replicate in gut bacteria. Myoviridae, Podoviridae, Siphoviridae, and Microviridae are the important gut phages in the microbiota [41]. The development of the microbiota begins immediately at birth when the GI tract is rapidly colonized. Life events such as illness, antibiotic treatment, or changes in diet, pH, and bile flow can cause chaotic shifts in the microbiota [42].

The gut microbes found in the caecum and colon play a crucial role in the digestion of food for the host by helping to digest foods that cannot be broken down by stomach and intestine enzymes. Additionally, they play an important role in the host immune defenses along the intestine, including a mucus barrier, help prevent potentially harmful bacteria from causing damage to tissues. Furthermore, the microbiota assists in the production of vitamins B and K. A healthy and balanced diet has been shown to maintain a stable and healthy gut microbiota and reduce the risk of various diseases [43]. The ingested foods are mainly digested in the stomach and small intestine but the indigestible food components and endogenous proteins secreted in the small intestine move towards the large intestine were fermentation and putrefaction take place with the help of microbes [44]. Therefore, gut microbes are recognized as a fundamental organ and an important factor in human physiology and nutrition [45, 46]. Gut microbes also enhance metabolic capabilities and protect their host against pathogens [46, 47]. The metabolic actions of microbiota are ultimately modulated by dietary proteins from plant and animal sources. This has been proven in many studies that observed protein sources and amounts as well as the way they affect the intestinal microbial balance [48].

The beneficial effect of gut microbiota on host

The gut bacteria do not only benefit the host by acting as a defense system, but also help to maintain the normal functions in the gut. Gut bacteria benefit the host by producing vitamins, metabolizing xenobiotic substances, regulating gut motility, transforming bile acid and steroids, activating, and absorbing minerals, and destroying toxins such as genotoxins and mutagens [42, 49]. High quantities of short-chain fatty acids (SCFA), such as acetic, butyric, and propionic acids in the proportion of 1:1:3 is produced in the proximal region of the colon. These SCFA act as energy sources for colonic mucosa, peripheral body tissues, and also for the metabolites of undigested complex carbohydrates. Collectively, these activities lead to the conservation of "lost" energy from the small intestine [50]. Bacteria like *Lactobacillus*, *Bifidobacterium*, and *Bacteroides* contribute to the synthesis of secondary bile acids, which are important components of lipid transport and turnover [51]. Vitamin B12 is synthesized by lactic acid bacteria, which cannot be synthesized by animals, plants, or fungi [52, 53]. *Bifidobacterium* also synthesizes important vitamins like K, B12, biotin, folate, and thiamine which are helpful for major metabolic process including DNA synthesis and repair [54]. Furthermore, gut microbiota have been shown to synthesize riboflavin, pantothenic acid, pyridoxine, and thiamine [55]. Numerous lipids with biological activity are produced by bacteria, including lipopolysaccharide (LPS), a component in the cell wall of gram-negative bacteria that can cause tissue inflammation [56]. Many enzymes produced by microbe's influence digestion and health. *Bacteroides thetaiotamicron* especially produces many enzymes that are helpful for the breakdown of complex carbohydrate [57]. Likewise, bacterial phytases facilitate the degradation of phytic acid present in grains in order to release minerals such as calcium, magnesium, and phosphate [58].

Gut bacteria and diseases

The interaction between bacteria and human cells is also important for the maintenance of human health [59]. The gut bacteria live in a commensal manner within the human body, but if the microbiome undergoes abnormal changes, the gut bacteria may potentially become harmful. Hence, many diseases in humans and animal models can be used by dysbiosis [60]. For example, *Clostridium difficile* can cause pseudomembranous colitis due to antibiotic treatments administered after surgery. Similarly, *Enterococcus faecalis*, *Escherichia coli*, *Enterococcus faecium*, and *Bacteroides fragilis* can cause intra-abdominal abscesses [61]. Due to these imbalances in gut bacteria, the intestine often produces symptoms like bloating, diarrhea, and abdominal pain. A large number of *Bifidobacteria* have a negative correlation with abdominal pain and the reduced number of Streptococcus, particularly *S. alactolyticus*, leads to diarrhea [62, 63]. They also play an important role in appetite control, immune function, behavioral perturbations, energy balance, and allergies [62]. Additionally, there are many other diseases related to gut bacteria such as inflammatory bowel diseases [43], obesity [64, 65], heart diseases [23], cancers [66, 67], and diabetes [68]. Therefore, although the exact mechanisms are unknown, an understanding of the human microbiota can be applied to a wide range of health effects in human development, nutrition, immunity, and physiology [69].

Effect of proteins on gut microbiota

The effect of dietary protein on gut bacteria was first described by Hentges *et al.* [70]. In a culture-based study, they found that, subjects consuming a meatless diet, had decreased counts of *Bifidobacterium adolescents* as compared to subjects that consumed high beef diets and had increased counts of *Bacteroides* and *Clostridia* [70]. However, upon the consumption of animal protein, the counts of bile tolerant anaerobes such as *Bacteroides*, *Alistipes*, and *Bilophila* were increased [71]. This study supported former research in which the Italian and rural African village children's microbiotas were compared by the researchers. It was found that in Italian children, there was a large increase of

Bacteroides and *Alistipes* in their microbiota upon the consumption of animal protein [72].

In most studies, protein consumption is positively associated with overall microbial diversity [73]. For example, the intake of a pea protein extract was previously reported to increase the microbes in the gut like *Bifidobacterium* and *Lactobacillus* and decrease pathogenic microbes like *Bacteroides fragilis* and *Clostridium perfringens* [74]. Additionally, the intestinal levels of SCFA, which act as anti-inflammatory agents and maintain the mucosal barrier, were increased by pea protein [75]. To perform bioactivity, the transformation of natural compounds like lignans by gut bacteria is essential. These natural lignans are present in a variety of foods like vegetables, fruits, and flaxseed. The metabolization of lignans in flaxseed to enterolactone and enterodiol by gut microbiota can protect against diseases like cardiovascular disease, breast cancer, prostate cancer, colon cancer, hyperlipidemia, osteoporosis and menopausal syndrome [76]. Gut bacteria are necessary for the production and bioavailability of these enterolignans. The two gut bacteria, *Peptostreptococcus* SECO-Mt75m3 and *Eggerthella lenta* SECO-Mt75m2 allow demethylation and dehydroxylation of secoisolariciresinol which is one of the most abundant dietary lignans [77].

According to several studies, the consumption of soy foods positively alters the composition of the gut microbiota population. Soy and soy foods provide nutrients and energy that support the growth of certain gut microbiota [78]. Increased consumption of soy milk by people in Asia and the United States is a good example of the plant-based protein diet [79]. The many valuable nutrients in soy milk are used by gut microbiota and cause shifts in bacterial numbers [80]. The effect of soy milk consumption on the gut microbiota was previously examined by Fernandez-Raudales and his colleagues. They primarily found that there was an increased amount of total gut bacterium in overweight and obese men. Additionally, the intake of soy milk changed the composition of bacteria by increasing the abundance of *Bacteroidetes* and *Proteobacteria* and reducing the populations and reducing the populations of *Bifidobacteria* and *Firmicutes* [81]. This shift causing an increase in *Bacteroidetes* and a decrease in *Firmicutes* ratio suggested that soy milk consumption reduces the risk of obesity and other metabolic syndromes [82]. Other evidence showed that soy protein from plants can bind to phytoestrogen compounds and induce lipid metabolism which lowers total cholesterol, low-density lipoprotein cholesterol, and triglyceride and also reduces insulin resistance, resulting in a better blood profile [83].

The proteins of algal extracts enhance growth and gut health by altering the gut microbiota population and increasing the digestibility and absorption of nutrients. Moreover, protein from seaweed alters the gut microbiota and modulates immune response, strengthening the gut barrier function [84]. Hutchins *et al.* [85] reported that the proteins in flaxseed diets significantly reduced the serum concentrations of 17β-oestradiol and oestrone sulfate and increased prolactin. Compared to plant-based diets, animal-based diets are high in fat which also affects the composition of microbes. Consequently, the mortality rate is lower in individuals that consume plant-derived proteins than in those who consume primarily animal-derived proteins (Fig. 1) [86]. Various studies on the effects of dietary proteins on diseases are depicted in Table 2.

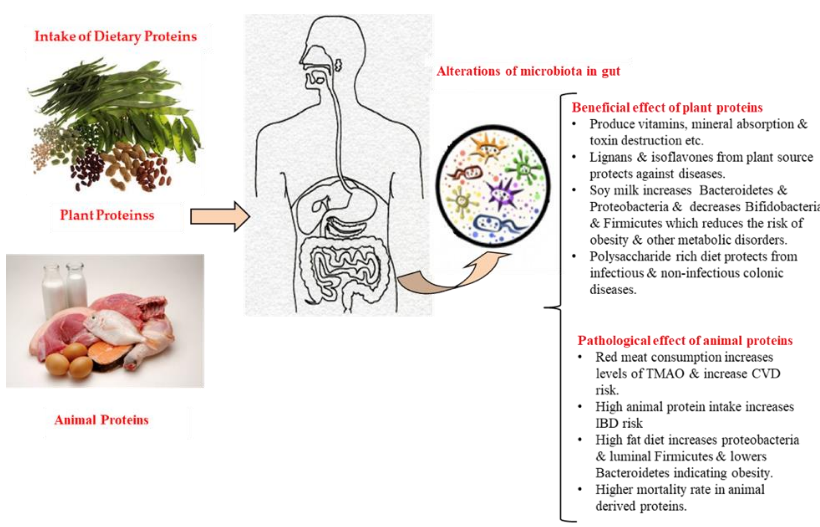

Figure 1. Beneficial and pathological effects of plant and animal proteins

Table 2. The different studies on the effects of dietary proteins on diseases

SI.no	Dietary Component Intake	Study Model	Duration	Main Finding	Study Cohort (References)
1.	Soy food	20 untreated patients with chronic glomerular diseases	8 weeks	Vegetarian soy diet could correct the hypercholesterolemia in chronic glomerular disease patients.	[87]
2.	Soy food	10 cohort studies, 12,888 cases among 452,916 participants	10 years	Decreased the risk of breast cancer.	[88]
3.	Plant protein	A cohort study of 70,696 Japanese adults aged 45 to 74 years	18 years	A high intake of plant protein was related to lower total mortality. Reduces the risk of cancer and cardiovascular disease-related mortality.	[89]
4.	Animal protein (Red meat)	37,698 men from the Health Professionals Follow-up Study and 83,644 women from the Nurses' Health Study who were free of cardiovascular disease (CVD) and cancer	Up to 22 years for men and 28 years for women	Red meat consumption is associated with an increased risk of CVD, and cancer mortality.	[90]
5.	Unprocessed red and processed meats	100 g/day - 9 cohort studies, 447,333 individuals and 28,206 events. 50g/day – 8 cohort studies, 372,391 participants and 26,234 events		Unprocessed red and processed meats increased the risk of type 2 diabetes.	[91]
6.	Fresh red meat and processed meats	8 cohort studies, 19,912 cases among 691,383 participants		Increased risk of breast cancer.	[88]
7.	Animal protein	NHANES study, 6,381 adults	18 years	Increased death rate by 75% and cancer death rate by 400%	[92]
8.	Animal protein	6,381 participants aged 50-65 years		High protein intake displayed an increased in IGF-I levels, a 75% increase in overall mortality and a 4-fold increase in cancer and diabetes.	[93]
9.	Animal protein	2,641 Finnish men, aged 42-60 years	5 years	A higher ration of an animal to plant protein diet and higher meat intake were associated with increased mortality risk.	[94]
10.	Animal and plant protein	Nurses health study 85,013 women and 46,329 men and health professionals Follow-up study	32 years	Animal protein intake was positive with mortality whereas plant protein was inversely.	[95]
11.	Plant and animal proteins	Adventist health study 281,337 men and women	5 years	Plant proteins showed less cardiovascular mortality whereas animal proteins showed a high mortality rate.	[96]

12.	Plant and animal proteins	Kuopio ischaemic heart disease risk factor study, 2441 men, aged 42 to 60 years	5 years	In middle-aged men, higher protein intake was marginally associated with increased risk of heart failure.	[97]
13.	Animal protein	Health professional's follow-up study, 40,475	20 years	A low-carbohydrate diet high in animal protein and fat was positively associated with the risk of type 2 diabetes.	[98]
14.	Animal protein	36 studies, 1803 participants, 22 to 70 years	2 to 36 weeks	Substituting red meat with high-quality plant protein sources leads to more favorable changes in blood lipids and lipoproteins.	[5]
15.	Animal protein	43,396 Swedish women, aged 30-49 years	15.7 years	Low carbohydrate-high protein diets used regularly are associated with increased risk of cardiovascular disease.	[99]
16.	Animal proteins and plant proteins	112 randomized controlled trials	3 weeks	Plant protein in substitution of animal protein decreased low-density lipoprotein cholesterol.	[100]
17.	Animal protein and plant protein	A meta-analysis of randomized controlled trials	3 weeks	Replacing animal protein with plant protein control glycemic level in diabetes.	[101]
18.	Animal protein	196 patients, 177 who complied with the dietary advice	2-7 years	Animal protein as the main cause of heart disease.	[102]
19.	Plant protein	Among 1380 adults, 30 to 54 years of ages	12 years	Plant protein maintains muscle mass and function better than animal protein.	[103]
20.	Plant protein	Framingham third-generation study, 2986 men and women, aged 19-72 years	3 years	Consuming plant protein food can build muscles.	[104]
21.	Animal protein (Red meat)	37,035 men, aged 45 to 79 years with no history of Heart Failure, ischemic heart disease, or cancer	11.8 years	Processed red meat consumption, but not unprocessed red meat, is associated with an increased risk of heart failure.	[6]
22.	Plant Protein (Soy)	59 postmenopausal women, aged 44-65 years)	12 weeks	Greater improvement was observed in cardiovascular disease risk factors in postmenopausal women on incorporating 30 g of soy protein and 4 g of phytosterols per day.	[105]
23.	Plant protein (Soy)	Male Zucker Diabetic Fatty (ZDF/Lepr(fa)) rats	11 weeks	Soy protein with low or high isoflavone content may have therapeutic significance in reducing the severity of diabetes, and renal disease.	[106]
24.	Plant protein (Soy)	Male Sprague-Dawley rats (4-16 wk old) and yellow KK mice (6-10 wk old) were made obese by feeding high-fat diets containing 30% fat	4 weeks	Soy protein isolate and its hydrolysate are suitable protein sources in energy-restricted diets for the treatment of obesity.	[107]

25.	Plant protein (Soy)	Randomized crossover trial in 15 postmenopausal women with abdominal obesity	4 weeks	Partly replacing meat products with soy products could be important in preventing Metabolic Syndrome.	[108]
26.	Plant protein (Soy)	Obese Zucker rats	160 days	Renoprotection by Soy protein.	[109]
27.	Animal Protein (Dairy & meat)	52,062 women aged 35-50 years	12 years	Breast cancer risk for African-American women with dairy and meat intake.	[110]
28.	Animal Protein (Red meat)	44,231 women aged 33-52 years	13 years	Higher consumption of red meat during adolescence was associated with premenopausal breast cancer.	[111]

DIETARY PROTEIN AND HUMAN HEALTH

Dietary protein and cancer

As shown in recent epidemiological studies, the consumption of large quantities of animal protein increases the risk of cancer and diabetes [90, 112]. Heme iron, heterocyclic amines, and endogenous N-nitroso compounds initiate carcinogenesis by enabling lipid peroxidation of epithelial cells and facilitating DNA and cellular damage of the gastrointestinal tract, eventually lead to adenocarcinoma. Cross *et al.* [113] proved this in a cohort study that found a significant association between colorectal cancer and the intake of heme iron, nitrate from processed meat, and heterocyclic amines. Further, the study added that both red and processed meat intake was positively associated with colorectal cancer. Processed meat is also a predominant source of nitrite for human. In contrast to red meat, white meat is not associated with an elevated risk of colorectal cancer [113]. This has been confirmed recently by a large group of studies involving the Health Professional Follow-up Study, Nurse's Health Study, and the Multiethnic Cohort [114].

Dietary protein, diabetes, and cardiovascular disease

Grapes, cocoa, tea, grains, and berries are dietary polyphenols, which generally promote health and prevents diseases like cancer and cardiovascular diseases [115]. L-Carnitine from red meat produced by microbial metabolism forms the intermediate trimethylamine-N-oxide (TMAO) that could potentially increase atherosclerosis risk [116, 117]. The by-product of choline, trimethylamine (TMA), is found in liver, eggs, red meat, milk, poultry and fish may increase the risk of stroke and heart disease. This has been proven through the lifestyle of Western people, who consume highly processed omnivorous diets of poor nutritional quality. These diets have dense energy, which is, high in animal protein, total and saturated fats, and simple sugars but low in fruits, vegetables, and other plant-based foods. Thereby, this Western lifestyle diet is related to a high occurrence of chronic diseases such as colorectal cancer, type II diabetes, and cardiovascular diseases [118].

Dietary protein and obesity

In the gut, a high-fat diet alters the composition of bacteria by facilitating high levels of *Proteobacteria* and luminal *Firmicutes* and lower levels of *Bacteroidetes* [119]. This change in the levels of certain gut bacteria indicates a decrease in diversity and a potential linkage to obesity. The ratio of *Firmicutes* to *Bacteroides* is correlated to body weight and in people who are obese, there is a higher ratio between the two bacteria [120]. Moreover, gut bacteria could also affect obesity by promoting chronic inflammatory status [121]. The infection of *Clostridium difficile* has also been proven to potentially cause obesity [122].

Dietary protein and inflammatory bowel disease (IBD)

Several mechanisms prove that diet could influence the occurrence of IBD, which includes a change in the gut microbiota, direct dietary antigens, and altered the permeability of the gastro intestine [123]. Additionally, dietary components have an important relationship with the risk of IBD development. The intake of sugar and refined carbohydrates is the first dietary component that leads to the development of IBD [124]. Diet fatty acids and protein compositions have a reliable association with the development of IBD that has been observed in cohort and ecological studies [125]. High-fat diets also cause increased bowel permeability, a hallmark of Chron's disease, through the diet-induced changes in gut bacteria [126]. The consumption of saturated fat from milk alters bile acid compositions and allows the extensive growth of sulfate-reducing bacteria by producing large amounts of hydrogen sulfide, which causes mucosal damage. Sulphur amino acid, found mainly in meats, is the major source of hydrogen sulfide in the bowel and is produced by bacterial fermentation [127]. Hydrogen sulfide contributes to bowel inflammation by impairing the utilization of direct toxic effects and short-chain fatty acids [128]. Thus, from many studies, it has been observed that diet is strongly associated with the development of IBD. Additionally, Jowett *et al.* found that patients were more likely to have a relapse of ulcerative colitis when consuming more of eggs, red meat, and alcohol. Thus, red meat and processed meat have a stronger association with ulcerative colitis that is not seen with fish consumption [129]. The influence of diet on microbiota and host health is depicted in Table 3.

Table 3. Some examples of studies on the influence of diet on the microbiota and host health.

SI. No	Diet	Effect on microbiota	Effect on host	References
1.	Pea nut	Increased the *Bifidobacterium* communities, and reduced the *Enterobacteria* and *Clotridium perfringensa*	Inhibited the growth of enterohemorrhagic *Escherichia coli, Listeria monocytogenes,* and *Salmonella Typhimurium.*	[130]
2.	Soybean	Increased communities of *Escherichia* and *Propionibacterium*	Escherichia and Shigella, modulate salt and water metabolism without impairment of intestinal mucosa.	[131]
3.	Soy protein	Elevated levels of *Bifidobacteriaceae* and *Clostridales* spp.	Reduced total cholesterol, TG and VLDL levels. Higher expression of 3- hydroxy-3-methylglutaryl-CoA reductase (Hmgcr), lanosterol synthase (Lss), and farnesyl-diphosphophate farnesyltransferase 1 (Fdft1), and lower steroyl-CoA desaturase-1 (Scd1) expression.	[78]
4.	Seaweed	Increase the beneficial bacteria such as *Lactobacillus* spp. and *Bifidobacterium* and decreased the potentially pathogenic bacteria such as *Enterobacteria*	Altering gut microbiota and/or modulating immune function and thus strengthening the gut barrier function.	[84]
5.	High beef diet	The decrease in *Bifidobacterium adolescents* and increase in *Bacteroides* and *Clostridia*	Increases Trimethylamine N-oxide and decreases Short-chain fatty acids leads to Cardio-vascular & Inflammatory Bowel Diseases.	[70]
6.	Whey & Pea protein extract	Increase in *Bifidobacterium* & *Lactobacillus* and Decrease in *Bacteroides fragilis* & *Clostridium perfringens*	Increases Short-chain fatty acids which lead to an increase in the gut barrier, T-regulatory cells & decreases inflammation.	[74]
7.	Animal-based diet	The increase of bile tolerant anaerobes such as *Bacteroides*, *Alistipes* and *Bilophila*	Increases Trimethylamine N-oxide and leads to Cardio-vascular & Inflammatory Bowel Diseases.	[132]
8.	Soy milk	Increases *Bacteroidetes* and *Proteobacteria* and Decreases *Bifidobacteria* and *Firmicutes*	Reduces the risk of Obesity and other Metabolic syndromes.	[82]
9.	Low fruit, vegetables, and fish	Reduces microbial gene richness	Increases insulin resistance, fasting serum triglyceride and LDL cholesterol levels and inflammation.	[71]

DIETARY PROTEIN

This review provides an overview of recent research detailing the importance of the of the interaction between dietary proteins and gut bacteria and human health and diseases. Many diseases like obesity, diabetes, IBD, and cancer, are impacted by the imbalance of gut bacteria mainly by affecting the immune-regulatory activity. Thus, these diseases are due to diet-induced dysbiosis. There are also many studies undergone related to the beneficial effect of diets to the gut microbiota in the host. For example, plant-based diets minimize cardiovascular disease risk. Through the discussion of various studies, this review describes how plant proteins, rather than animal proteins, are beneficial the plant protein acts beneficial to the gut bacterial microbiota and prevent many serious diseases in humans.

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