Systematic Review of Beef Protein Effects on Gut Microbiota: Implications for Health

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ABSTRACT

The influence of diet on the gut microbiota is an emerging research area with significant impact on human health and disease. However, the effects of beef, the most consumed red meat in the United States, on gut microbial profile are not well studied. Following Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols, the objective of this systematic review was to conduct a rigorous and thorough review of the current scientific literature regarding the effects of beef protein and the resulting bioactivity of beef protein and amino acids on the gut microbiota, with the goal of identifying gaps in the literature and guiding future research priorities. Utilizing MEDLINE Complete, PubMed, ScienceDirect, Scopus, and Google Scholar databases, we conducted searches including terms and combinations of the following: animal protein, amino acid, beef, bioactive compounds, diet, health, microbiome, peptide, processed beef, and protein. We identified 131 articles, from which 15 were included in our review. The effects of beef on mouse and rat models were mostly consistent for the bacterial phylum level. Short-term (1–4-wk) beef intakes had little to no effect on microbial profiles in humans. Most studies utilized high beef feeding (240–380 g/d), and no study examined recommended amounts of protein [∼3.71 oz/d (105 g/d) meats, poultry, and eggs, or ∼26 oz/week (737 g/wk) from these food sources] according to US dietary guidelines. Additionally, the majority of animal and human studies with adverse findings examined the impact of beef in the context of a diet high in fat or sugar. In conclusion, an extensive gap exists in the literature regarding beef and the microbiota. More studies are necessary to elucidate the role of the microbiota following the consumption of beef, especially in interaction with other dietary compounds, and how beef preparation, processing, and cooking methods differentially influence the biological effects of beef on human health. *Adv Nutr* 2021;12:102–114.

Keywords: beef, beef protein, health, microbiota, processed meat, protein, red meat

Introduction

The United States is a leading nation in the consumption of red meat, with 2017 estimates indicating 49.5 kg (109 lb) per capita, which is expected to increase to 50.8 kg (112 lb) by 2027 (1). A recent NHANES evaluation of trends in meat consumption from 1999 to 2016 reported beef as the most abundantly consumed type of red meat in the United States (2). Given the increasing health concerns about red meat consumption (3), it is crucial to understand how the biological functions of the nutrients in red meat, particularly beef, vary and differentially impact health since the nutritional profile of meat varies by the type of meat, for

example, white or red meat, processed or unprocessed meat (see **Table 1** for defined terminology) (4).

Protein exerts nutritional, functional, and biological properties and plays an essential role in human health. A comprehensive assessment of dietary protein quality includes amino acid composition, digestibility, rate of protein digestion, and potential for generation of biologically active peptides (i.e., bioactive peptides) (5). Upon consumption, animal protein provides all 9 essential amino acids required by the human body. Distinctively, red meat is also a source of heme iron, which has higher bioavailability (i.e., meaning it is more absorbable) compared with nonheme iron found in plants (6), in addition to vitamins, especially B vitamins, and minerals, such as copper, manganese, zinc, and iron (7).

Moreover, recent research suggests that sources of dietary protein (animal compared with plant) and their associated nutrients can differently influence the gut microbiota (8–10), which is recognized as an important mediator between food and host (11) that can instigate or prevent chronic

TABLE 1 Relevant terms related to beef

Term	Definition
Meat	The flesh of an animal as food
Processed meat	Meat that has been preserved by methods other than freezing, such as salting, smoking, marinating, air-drying, or heating (e.g., ham, bacon, sausages, hamburgers, salami, corned beef, and tinned meat)
Red meat	All types of mammalian muscle meat, such as beef, veal, pork, and lamb (fresh, minced, and frozen)
Beef	The flesh of a cow, bull, or ox, used as food
Protein	Any of a class of nitrogenous organic compounds that consist of large molecules composed of ≥ 1 long chains of amino acids and are an essential part of all living organisms, especially as structural components of body tissues such as muscle
Peptide	A compound consisting of ≥ 2 amino acids linked in a chain
Amino acid	A simple organic compound containing both a carboxyl (–COOH) and an amino (–NH_2) group
Protein-derived bioactive compounds	Intermediates of proteolysis or amino acid sequences which exert a beneficial effect on body function and/or positively impact human health, beyond its known nutritional value

and metabolic diseases, including cancer and cardiovascular disease (12, 13). The human intestinal tract houses 10 trillion microorganisms, including bacteria, viruses, fungi, and protozoa. Of these, the intestinal bacterial profile, known as the "gut microbiota," is of significant interest, given its role in human disease (14, 15). Differentiation of the microbiota—or specific changes in particular microbes or groups of microbes—alters gut homeostasis. Gut dysbiosis is characterized by adverse disruptions in microbial profile (16), which increase systemic inflammation through leaks of inflammatory substances from the gut (such as bacterial LPSs). Inflammation further contributes to increased risk of metabolic and chronic diseases, such as obesity, diabetes, and cancer (14, 17).

There are 5 major bacterial phyla in the human digestive tract, including *Firmicutes*, *Bacteroidetes*, *Actinobacteria*, *Proteobacteria*, and *Verrucomicrobia*. *Firmicutes* (Gram-positive) and *Bacteroidetes* (Gram-negative) constitute the majority, making up ~65% of total bacteria (18). Resident microorganisms of the human gut vary among individuals based on several factors, including mode of birth, sex, age, health, body weight, diet, physical activity, and medicinal history, particularly the use of antibiotics (19). Changes in diet rapidly alter colonic microflora, indicating that diet can strongly influence microbiota, even more than host genetics (20, 21). Because these bacteria are primarily responsible for breaking down indigestible starches, several published studies have focused on the microbiota's response to dietary carbohydrate (22, 23). Additionally, human studies have also focused on the response of the microbiota to quantity and quality of dietary fat intake (24, 25). However, less is known regarding the microbiota's response to and digestion of protein.

Protein and the microbiota

Colonic microbes present considerable proteolytic power. Metabolic activity of the gut microbial community is perhaps even more efficacious than that which occurs in the small intestine under enzymatic control of the host (26, 27). In the gastrointestinal tract, proteins are first hydrolyzed by peptidases to polypeptides and further to sequences of amino acids—tripeptides, dipeptides, and single amino acids. Bacterial proteases can generate small peptides and single amino acids that can be fermented to produce SCFAs, including acetate, propionate, and *n*-butyrate, as well as derivatives of branched-chain amino acids, branched-chain fatty acids, which include isobutyrate, isovalerate, and 2-methylbutyrate (28, 29). The amino acids Arg, Asp, Gly, Phe, Pro, Ser, Thr, and Trp more likely undergo bacterial, rather than host, digestion (30). Although digestion and absorption of dietary protein is efficient in healthy humans, ~10% reaches the large intestine and is available for bacterial fermentation (31, 32). Early human fecal culture–based microbiology techniques identified *Bacteroides* and *Propionibacterium* as two dominant proteolytic genera (28). Other proposed important genera include *Bifidobacterium*, *Clostridium*, and *Streptococcus* (28, 33).

Many factors can influence the proportion of dietary protein that reaches and is digested by bacteria in the large intestine. However, protein modifications during cooking, as well as interactions with other dietary nutrients, can alter protein bioavailability (34). Additionally, microbial enzymes use different cleavage sites than digestive enzymes and thus produce different peptides with different biological activity (35).

Interestingly, recent studies indicate that bacterial presence in the human digestive tract might mediate the production of toxic compounds from proteins, such as the production of trimethylamine from L-carnitine via microbial metabolism (36). Thus, the interactions of colonic microflora and dietary protein have prompted significant interest in their implications for human health since the microbial profile is impacted by diet, and the activity of microbial enzymes impacts the production of protein-derived bioactive compounds.

Dietary protein from beef

Protein-derived bioactive compounds are usually low-molecular-weight peptides (<5 kDa), which are either intermediate products of proteolysis (protein degradation), or

amino acid sequences within the protein that, upon isolation, exert a beneficial effect on body function with potential positive impacts on human health, beyond any known nutritional value (37). There are 3 ways in which bioactive peptides can be generated: *1*) during digestion via digestive enzymes; *2*) during digestion via microbial enzymes; and *3*) during food processing or ripening using purified or microbial enzymes (38, 39). Both digestion site and responsible enzyme result in various peptides, thus altering the bioactivity (35). Processes that generate peptides, and limitations of and opportunities within these processes, have been extensively reviewed (40). Although protein requirements are well established—the RDA for protein is 0.8 g/kg body weight/d, with an intake of ≤2.5 g/kg body weight/d being acceptable (41)—there are no federal/medical recommended values for protein-derived bioactive compounds, and little information regarding requirements and relational health benefits.

Protein-derived peptides have various bioactive properties, including antihypertensive, mineral-binding, antimicrobial, immunomodulating, cell-modulating, anticarcinogenic, anti-inflammatory, and cholesterol-lowering properties (40, 42–45). Widely studied, the role of biologically active peptides from dietary protein sources, such as milk (46), fish (47), seaweed (43), and soybeans (48), in human health is established; however, that of bioactive compounds from protein-rich foods, including beef, is less known.

Muscle (meat)-derived bioactive peptides and amino acids include anserine (β-Ala-1-methyl-His), carnosine (β-Ala-His), L-carnitine (β-hydroxy-γ-trimethylaminobutyric acid), glutathione (γ-Glu-Cys-Gly), and taurine (49–51). Of these, the histidine-containing dipeptides, carnosine (β-Ala-His) and anserine (β-Ala-1-methyl-His), are the major dipeptides present in mammalian skeletal muscle (49). A limited number of studies exist on the presence of amino acids and peptides present in beef, and those that do present incomplete information and inconsistent findings. Only one study on beef (52) has sought to determine all (proteinogenic and nonproteinogenic) amino acids and small peptide content in beef, and reported glutamine to be the most abundant amino acid, followed by taurine, alanine, glutamate, and β-alanine (52). Postmortem protein degradation results in the production of polypeptide fragments, which can be further hydrolyzed via peptidyl peptidases and aminopeptidases to generate smaller peptides and individual amino acids (53). Concentrations of these bioactive dipeptides are lower in cooked beef meat compared with fresh muscle (54, 55); however, cooked beef is still a substantial source of carnosine and anserine (55).

It is critical to understand how individual strains of the gut microbiota respond, as well as how they interact with one another as functional groups when exposed to carbohydrate, fat, and protein, and how, in turn, these changes impact the production of their enzymatic products. Therefore, through this systematic review, we conducted a rigorous and thorough review of the current scientific literature regarding the effects of beef consumption on gut microbiota; beef was chosen because it is the most abundantly consumed red meat in the United States. We examined the bioactivity of beef proteins and amino acids on gut microbiota and identified gaps within the literature to guide future research priorities.

Methods

This systematic review referred and followed checklists (**Supplemental Table 1**) provided by the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) (56). The literature search identified animal and human studies published from database inception to July 31, 2019. We collected peer-reviewed, English-written articles from: *1*) MEDLINE Complete, *2*) PubMed, *3*) ScienceDirect, *4*) Scopus, and *5*) Google Scholar. Search terms included combinations of the following: animal protein, amino acid, beef, bioactives, diet, health, microbiome, peptide, processed beef, and protein. We retrieved and reviewed relevant articles, and from those we closely analyzed references to identify any missed articles. Articles containing a "red meat" descriptor, where the study specified the red meat was composed of beef as the primary protein source, were included in this systematic review (**Figure 1**). Articles that did not include beef as a food type were excluded. Three independent reviewers determined article eligibility.

Results

Overall, there has been a minimal number of studies that have examined the role of beef protein on the microbiota. Given our criteria, our search yielded a total of 15 eligible articles and included 10 animal and 5 human studies.

Beef protein and gut microbiota: animal studies

The effects of beef on mouse and rat models are consistent for bacterial phylum level (**Table 2**), with increases in the relative abundance of *Proteobacteria* (10, 57), and *Firmicutes* (10, 57, 58) and decreases in *Bacteroidetes* (10, 57). The lactic acid–producing genus, *Lactobacillus*, increased when just beef extract was fed (10, 58). Our literature search also indicates that beef feeding increases *Proteobacteria* both in mice and pig models (59). See **Table 3** for findings from pig studies. Beef consumption showed a mixed impact on some of the SCFA-producing bacterial genera. For example, beef increased the genera *Clostridium* (57, 60) and *Blautia* (58, 61), whereas *Bifidobacterium* (62) and *Akkermansia* (61, 62) decreased. All mouse and rat studies were conducted on males, emphasizing the need for further studies on female animal models.

Beef protein and gut microbiota: human studies

Of the 5 human studies that were relevant to our topic of beef protein and gut microbiota in humans, a considerable variation existed on the influence that beef has on the gut microbiota (**Table 4**); most likely this is a result of differences in objectives, study design, intervention duration, subject characteristics, beef portion, and diet composition. For example, subjects ranged from breastfed infants (63)
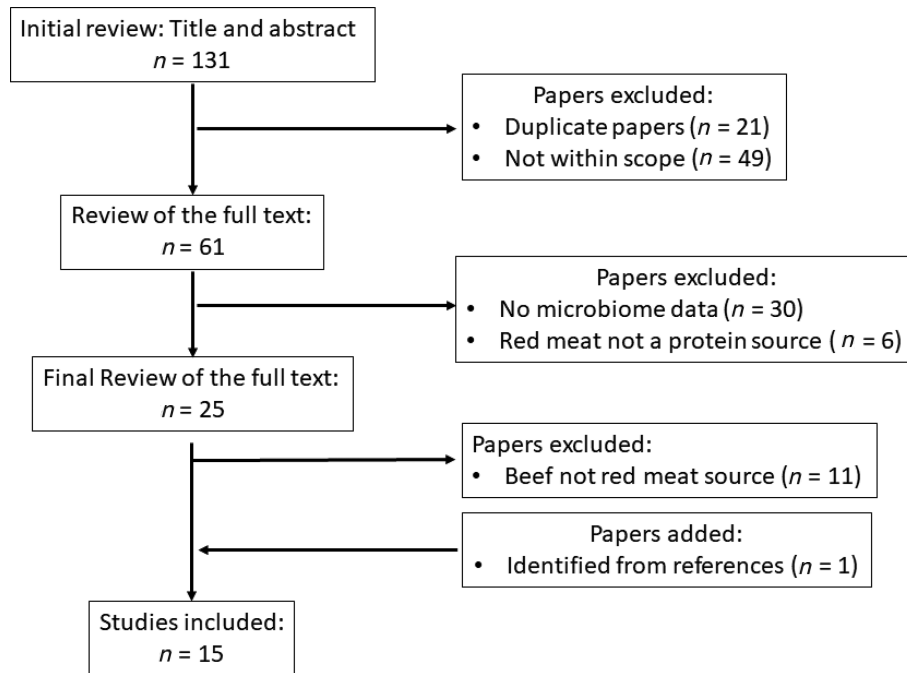
FIGURE 1 PRISMA flow diagram representing overview of literature selection process for inclusion in systematic review. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

to endurance athletes (64). Consistently, short-term (1–4-wk) beef intakes had little to no effect on microbial profile (65–67). Most studies utilized high beef feeding (240–380 g/d) (65–67), and no study examined recommended amounts of protein according to Dietary Guidelines for Americans (68).

Discussion

Animal meat is a complete source of dietary protein, composed of all essential amino acids, and is also a source of fatty acids, vitamins, and minerals (69). Furthermore, animal protein promotes satiety and enhances energy expenditure and fat loss compared with plant proteins (70). Observational studies have reported red meat consumption as a risk factor for cardiovascular disease and other metabolic diseases, such as type 2 diabetes mellitus, although recent studies indicate that this link might only exist with the consumption of processed red meat (3). Respective of the controversial health findings, the majority of studies included in this review examined the impact of excessive intakes of beef in the context of a diet high in fat or sugar. This type of diet, sometimes identified as the Western diet or standard American diet, is independently associated with increased chronic noncommunicable disease risk (71), and is often associated with a high intake of refined and processed foods, including processed meats and simple (added) sugars and fat and low intake of fruits, vegetables, and whole grains. Furthermore, a recent clinical investigation reported that ultraprocessed foods increase weight gain independent of energy intake (72), highlighting the need to better understand the association

of unprocessed and processed red meat with chronic disease risk (73, 74), particularly regarding the role of gut microbiota and related metabolites in mediating effects of lean beef or beef proteins.

In conjunction with a diet high in fat or sugar, beef protein can adversely affect health, microbial composition, and the gut barrier when compared with casein or white meat protein (61, 75), for example, by increasing numbers of the *Proteobacteria* (75), which are associated with dysbiosis (76). However, changes in bacterial composition in response to high-fat + beef and high-sucrose + beef feedings are comparable with those reported in Westernized diet feedings in animal studies, with increases in *Desulfovibrionaceae* and decreases in *Lactobacillaceae* (77, 78). Interestingly, high-fat diet–related decreases in *Bacteroidetes* and increases in both *Firmicutes* and *Proteobacteria* are independent of obesity (78), implying the influence of diet composition, particularly fat, in the microbial response. Moreover, there were no significant differences in serum indicators of health or microbial profile when various protein sources (beef, casein, soy) were consumed in conjunction with a low-fat diet (61).

Gram-negative bacteria, such as *Bacteroidetes*, produce LPS, (79, 80), an endotoxin that drives systemic inflammation and metabolic endotoxemia by upregulating proinflammatory cytokines if leaked into circulation from the intestine (81, 82). Few animal studies reported decreased relative abundance of *Bacteroidetes* in response to beef feeding compared with a nonpurified diet (57) or casein diet (10, 58). Additionally, LPS-binding protein, an indicator of gut barrier damage, was highest in the casein group when compared with

TABLE 2 Effects of beef feeding on the microbiota of male mice and rats[1]

Animal model	n	Beef diet	Other diet	Duration, d	Impact on microbial community		Reference
					Increased	**Decreased**	
C57BL/6 mice	40	Freshly prepared steamed beef	Nonpurified diet	56	↑*Firmicutes* (P) ↑*Oscillospira* (G) ↑*Clostridium* (G) ↑*Proteobacteria* (P) ↑*Escherichia* (G)	↓*Bacteroidetes* (P) ↓*Prevotella* (G)	57
C57BL/6 mice	60	LFB (12% kcal), and HFB (60% kcal)	Casein	84	Changes in LFB: *Verrucomicrobia* (P) ↑*Akkermansia* (G) *Deferribacteres* (P) ↑*Deferribacteraceae* (F) ↑*Mucispirillum* (G) *Proteobacteria* (P) ↑*Desulfovibrionaceae* (F) *Bacteroidetes*(P) ↑*Bacteroidaceae* (F) Changes in HFB: *Deferribacteres* (P) ↑*Mucispirillum* (G) *Proteobacteria* (P) ↑*Escherichia* (G) ↑*Shigella* (G) *Tenericutes* (P) ↑*Mollicutes* (C) *Firmicutes* (P) ↑*Blautia* (G) ↑*Romboutsia* (G) ↑*Oscillibacter* (G) *Bacteroidetes* (P) ↑*Odoribacter* (G)	Changes in HFB: *Verrucomicrobia* (P) *↓*Akkermansia* (G) *Firmicutes* (P) *↓*Anaerotruncus* (G) *↓*Butyricicoccus* (G) *↓*Lactobacillus* (G)	61

(Continued)

TABLE 2 (*Continued*)

Animal model	n	Beef diet	Other diet	Duration, d	Impact on microbial community		Reference
					Increased	**Decreased**	
Sprague Dawley rats	32	Proteins were extracted from beef muscle, cooked at 72°C, freeze-dried, and ground into powder	Casein	90	Fusobacteria (P) ↑Fusobacterium (G) ↑Bacteroidetes (P)	↓ Firmicutes (P)	83
Sprague Dawley rats	55	Proteins were extracted from beef muscle, cooked at 72°C, freeze-dried, and ground into powder	Casein	14	*↑Firmicutes (P) *↑Allobaculum (G) *↑Blautia (G) *↑Lactobacillus (G)	Bacteroidetes (P) *↓Bacteroides (G) Firmicutes (P) *↓Lachnospiraceae (F)	58
Sprague Dawley rats	66	Proteins were extracted from beef muscle, cooked at 72°C, freeze-dried, and ground into powder	Casein	90	↑Firmicutes (P) ↑Lactobacillus (G) ↑Proteobacteria (P)	Firmicutes (P) *↓Roseburia (G) ↓Bacteroidetes (P) *↓Alloprevotella (G)	10
SPF Wistar rats	60	Powdered beef: a lean cut of beef was chosen, minced, and dehydrated in a drying oven, with air circulating at 105°C, for 3–4 h. The dried meat was then ground to a fine "flour"	Casein	60	Firmicutes (P) *↑Clostridium (G) *↑Enterococcus spp. (G) Proteobacteria (P) *↑Enterobacteriaceae (F) Bacteroidetes (P) *↑Bacteroides (G)	Firmicutes (P) *↓Lactobacillus (G)	60
BALB/c mice	32	Cooked red meat at a concentration of 30 g/100 g diet, and cooked red meat at a concentration of 30 g/100 g diet mixed with high-amylose maize starch at a concentration of 10 g/100 g diet	Casein	12	↑Bacteroides—Prevotella group Proteobacteria (P) ↑Escherichia coli	Verrucomicrobia (P) ↓Akkermansia muciniphila Actinobacteria (P) ↓Bifidobacterium spp. Bacteroidetes (P) ↓Parabacteroides distasonis Firmicutes (P) ↓Clostridium leptum ↓Faecalibacterium prausnitzii ↓Ruminococcus gnavus ↓Enterococcus spp. (G)	62

[1]C, class; F, family; G, genus; HFB, high-fat beef; LFB, low-fat beef; O, order; P, phylum. Arrows indicate changes reported: ↑, increased; ↓, decreased. Taxa (phyla) without arrows are listed for clarification. *Significant change, $P < 0.05$. Arrows without * indicate changes based on relative abundance.

other low-fat groups ([61]). Therefore, high-fat diets could be of greater concern than dietary protein sources for adversely impacting microbial profile.

In animal studies, beef feeding increased the relative abundance of *Firmicutes* ([10], [57], [58]), while decreasing *Bacteroidetes* ([10], [57]). In other words, red meat can increase the *Firmicutes*/*Bacteroidetes* ratio, which is often associated with increased BMI in human subjects ([84], [85]). Related findings were variable in the few human studies we identified in our literature search, with contradictory changes in the relative abundance of *Firmicutes* being reported ([63], [64]). Additionally, bacterial cultures following high-beef feeding (380 g/d) in humans indicated significant increases in *Bacteroides* ([65]), a genus of the *Bacteroidetes* phylum. According to the 2015–2020 Dietary Guidelines for Americans, 26 oz/wk (737 g/wk), or ∼3.71 oz/d (105 g/d), from protein foods, including meats, poultry, and eggs, is recommended. Assuming that 1 oz (28.35 g) of meat contains ∼7 g protein, this equates to ∼26 g protein/d from this food type ([68]); however, protein recommendations can vary according to need, and thus more protein could be consumed from this food group to meet upper protein recommendations (2.5 g/kg/d) based on body weight, for example ([41]). Gaps between protein recommendations and amounts used in human studies denote a need for evaluating the impact of protein quality and quantity on human microbiota, especially in populations with elevated protein intakes, such as athletes ([86]).

Food processing, preparation, and storage affect the nutritional, functional, and biological properties and digestibility of protein. In vitro studies of human fecal batch cultures indicate that meat type and cooking method both impact microbial profile ([87]). Additionally, adverse findings associated with excessive beef intake include those related directly to cooking at high temperatures, which can result in the production of polycyclic aromatic hydrocarbons and heterocyclic amines ([88]), *N*-nitroso compounds generated as microbial byproducts, or the presence of the nonhuman sialic acid *N*-glycolylneuraminic acid ([89]).

Moreover, mechanisms linking beef and the development of chronic noncommunicable diseases are not fully understood but could be related to micronutrients because iron and zinc have reportedly influenced microbial profile ([63]). For example, several studies have examined the effect of heme iron on health and microbial composition; however, these cannot be translated directly to beef feeding ([90]). Additionally, even though iron content can be standardized when comparing protein diets, animal and plant proteins comprise different types of iron (heme and nonheme, respectively), which can differentially impact microbial profile. Accordingly, heme studies and animal protein studies have conflicting results—elevated heme intake results in decreased *Lactobacillus* and increased *Proteobacteria* ([91]), whereas proteins extracted from beef have the opposite effect on *Lactobacillus* ([10], [58]). *Lactobacillus* is considered a key player in host energy metabolism ([92], [93]) and in reducing inflammation by positively shifting the gut microbial profile and protecting the gut barrier ([82], [94], [95]). These findings

TABLE 3 Effects of beef feeding on the microbiota of pigs[1]

Animal model	n (sex)	Beef	Other diet	Duration, wk	Impact on microbial community		Reference
					Increase	Decrease	
Pigs (German Landrace × Large White × Piétrain)	45 (F)	Cooked lean beef	Lupin protein isolate as source of a plant protein and casein	4	↑*Proteobacteria* (P)	↓*Actinobacteria* (P)	59
Pigs (Large White)	20 (M)	Beef steak (trimmed of fat, cooked, minced, and dried)	Arabinoxylan + beef	4	*Firmicutes* (P) ↑*Ruminococcus** (G) ↑*Clostridium** (G)	*Bacteroidetes* (P) ↓*Prevotella ruminicola** ↓*Prevotella disiens* *Firmicutes* (P) ↓*Faecalibacterium** (G)	96

[1]G, genus; P, phylum. Arrows indicate changes reported based on relative abundance: ↑, increased; ↓, decreased. *Significant change, P < 0.05. Taxon (phylum) listed without arrow for clarification.

TABLE 4 Effects of beef feeding on the microbiota of humans[1]

n (M/F)	Participants' age	Beef	Other diet	Duration	Impact on microbial community		Reference
					Increase	**Decrease**	
23 (17/6)	62.4 y	HRM (300 g/d), and HRM + HAMSB	Crossover design	4 wk/diet	HRM: NC HAMSB: *Firmicutes* (P) *↑*Ruminococcus bromii* *↑*Clostridium coccoides* group *↑*Clostridium leptum* group *↑*Lactobacillus* spp. *Bacteroidetes* (P) *↑*Parabacteroides distasonis*	HRM: NC HAMSB: *Proteobacteria* (P) *↓*Escherichia coli* *Firmicutes* (P) *↓*Ruminococcus gnavus* *↓*Ruminococcus torques*	66
27 (18/9)	40–85 y	PRM (240 g/ d), and RM (240 g)	No meat	1 wk	PRM: NC RM: NC	PRM: *Actinobacteria* (P) ↓*Bifidobacterium*(G) RM: NC	67
45 (N/A)	5 mo	Pureed red meat (71 g/ d)	Fortified cereal	20 wk	↑*Firmicutes* (P) *↑*Clostridium* group XIVa	↓*Proteobacteria* (P) ↓*Enterobacteriaceae* (F)	63
			Iron-fortified cereal	20 wk	*↑*Actinobacteria* (P)	*↓*Bacteroidetes* (P)	
10 (10/0)	N/A	High red meat (380 g)	No meat	4 wk/diet	*Firmicutes* (P) *↑*Bacilli* (C) *Actinobacteria* (P) *↑*Bifidobacterium adolescentis* *Bacteroidetes* (P) *↑*Bacteroides* (G) ↑*Bacteroides fragilis*	—	65
18 (18/0)	18–45 y	Beef hydrolysate (10 g) + whey isolate (10 g)	Carbohydrate	10 wk	↑*Bacteroidetes* (P) ↑*Bacteroides* (G)	*Firmicutes* (P) *↓*Bacilli* (C) *↓*Lactobacillales*	64

(Continued)

TABLE 4 (Continued)

n (M/F)	Participants' age	Beef	Other diet	Duration	Impact on microbial community		
					Increase	**Decrease**	**Reference**
						Actinobacteria (P) * ↓*Bifidobacterium longum* *Proteobacteria* (P) ↓*Citrobacter* (G) * ↓*Synergistetes* (P) * ↓*Synergistia* (C) * ↓*Synergistales* (O) *Firmicutes* (P) * ↓*Blautia* (G) * ↓*Coprococcus* (G) * ↓*Lachnospiraceae* (F) * ↓*Roseburia* (G)	

¹C, class; F, family; G, genus; HAMSB, high-lean red meat + butyrylated high-amylose maize starch; HRM, high-lean red meat; NC, no changes between baseline and following 4 wk of HRM; O, order; P, phylum; PRM, processed red meat; RM, red meat. Arrows indicate reported changes: ↑, increased; ↓, decreased. Taxa (phyla) without arrows are listed for clarification. *Significant change, $P < 0.05$. Arrows without * indicate changes based on relative abundance.

emphasize the impact of individual components of beef (i.e., heme compared with proteins extracted from beef) compared with beef as a whole on microbial profiles. Animal studies indicate significant decreases in *Lactobacillus* with high-fat beef feeding compared with casein (61), and beef feeding compared with chicken (75). A systematic review of adverse compounds associated with red meat suggests that better designed and controlled studies that use relevant concentrations of meat or meat-derived compounds in conjunction with diets representative of human diets are needed (97). Furthermore, approaches to prevent the toxicity associated with red meat consumption have been explored, for example, by increasing calcium in the diet, altering meat processing, or adding vitamin E (98). As these studies evolve, future microbiome and microbiota studies need to include the effects of these combinations, processing methods, and additives in regard to beef consumption.

Future Perspectives

More studies are necessary to elucidate the role of the gut microbiota following the consumption of beef, especially in interaction with other food compounds, particularly fat and carbohydrate (**Figure 2**). Studies are needed in both animals and humans to understand how different beef preparation, processing, and cooking methods differentially influence the biological effects of beef. Further, animal protein sources vary in composition, for example, by fatty acid profile, which is largely influenced by the diet of the animals (99) and is an important consideration for studies comparing microbial changes and chronic disease risk in response to diet (100). These diets must be standardized in fatty acid profile and micronutrients, for example. Moreover, several techniques have been utilized to understand microbial digestion of dietary protein and the resulting bioactive compounds; however, there is a need to develop more cost-effective and appropriate techniques because there are many factors that influence this process, including the presence of other macro- and micronutrients (40).

Additionally, microbiome-related metabolomics studies are needed to determine the impact of beef consumption on changes in gut microbiota and how these correlate with host physiology and health. Moreover, how these diets affect metabolism in a tissue-specific manner is not well studied in animal models. Further mechanistic studies investigating the role of beef-associated bioactive compounds, in the context of various diets, are needed. For example, L-carnitine has been shown to ameliorate the negative influence of high-fat diets on the lipid profile in rats (101) but has also been shown to increase the production of toxic byproducts (36). However, the metabolism of these protein-related compounds largely depends on the colonic microbiota composition and its metabolic influence; therefore, paired analyses of protein-derived bioactive compounds and microbially related metabolites should be considered.

SCFAs are the end-products of carbohydrate and protein microbial digestion in the large intestine, which can
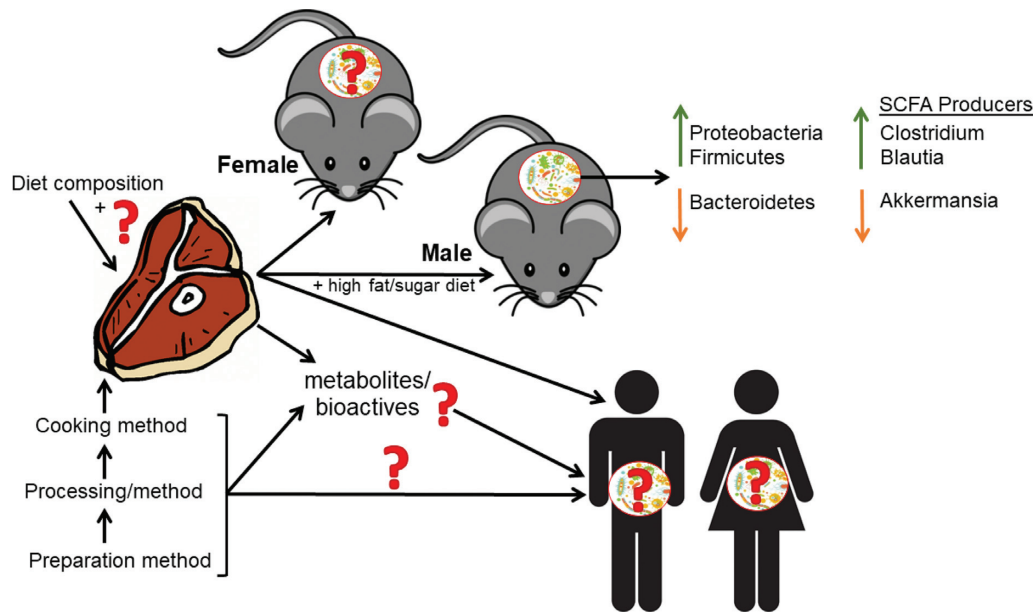
FIGURE 2 Extensive gaps exist in the literature regarding beef, its related bioactive compounds, and effects on gut microbiota. Various preparations, processing and cooking methods, and temperatures are utilized in the examined literature, which likely impact the bioactivity of beef. Research subjects varied in age and models used from rodents to human subjects. The effects of beef on the male mice and rats were mostly consistent, indicating increased *Proteobacteria* and *Firmicutes* and decreased *Bacteroidetes*. Findings regarding effects on SCFA-producing bacterial genera were discrepant, with increases in *Clostridium* and *Blautia* and decreases in *Akkermansia*. Short-term (1–4-wk) beef intakes had little to no effect on microbial profiles in humans. Most studies with adverse findings (animal and human studies) examined the impact of red meat or excessive intakes of red meat in the context of a diet high in fat or sugar.

positively impact health (102). Production of SCFAs varies by microbiota profile—bacteria produce different SCFAs based on substrate preference—and also by the undigested substrate that enters into the large intestine (103–105). To our knowledge, only 2 animal studies (by the same research group) have compared different protein extracts from different sources on SCFA production in conjunction with changes in microbial composition (58, 83). Each reported higher SCFA production following consumption of soy protein compared with protein extracted from chicken and beef (58, 83); however, this could be due to the limited bioavailability of soy compared with meat protein (70). Several animal studies have demonstrated that resistant starch, in addition to red meat, decreased the risk of colon cancer (106–108). A similar human study by the same group reported increased SCFA production and changes in microbial profile following a high-beef (300 g/d) + butyrylated high-amylose maize starch diet for 4 wk (66). Interestingly, pureed beef as a complementary food in otherwise breastfed infants increased fecal SCFA-producing bacteria (63), which could have implications in the healthy development of the infant microbiota, nutrient metabolism, and immune system development (109). Future studies are needed to investigate the long-term combined effects of starch and beef proteins in recommended amounts on microbial composition and respective SCFA production, and, further, to investigate the impact of this combination in overweight individuals or in the context of a high-fat/high-sucrose diet.

Conclusions

In conclusion, when consumed at higher than recommended levels as part of a diet high in sugar or fat, beef has adverse consequences for the gut microbiota. Human studies indicate minimal changes in the gut microbial profile in response to short-term (1–4-wk) beef feeding. Future research is needed to: *1*) elucidate changes in the microbiota in response to the consumption of beef, itself, in recommended and excessive amounts according to dietary guidelines, and in combination with other nutrients; *2*) conduct microbiome-related metabolomics studies to understand how changes in microbiota correlate with host physiology; *3*) investigate the role of beef-derived bioactive compounds in the context of various diets; *4*) determine if other nutrients, such as complex carbohydrates, can ameliorate some negative effects of increased beef consumption as part of high-fat and/or high-sucrose diets; *5*) identify alterations in SCFA production with beef consumption; and *6*) develop more cost-effective and appropriate techniques to understand microbial digestion of dietary protein, including food types such as beef.

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