Significance of African Diets in Biotherapeutic Modulation of the Gut Microbiome

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ABSTRACT: Diet plays an essential role in human development and growth, contributing to health and well-being. The socio-economic values, cultural perspectives, and dietary formulation in sub-Saharan Africa can influence gut health and disease prevention. The vast microbial ecosystems in the human gut frequently interrelate to maintain a healthy, well-coordinated cellular and humoral immune signalling to prevent metabolic dysfunction, pathogen dominance, and induction of systemic diseases. The diverse indigenous diets could differentially act as biotherapeutics to modulate microbial abundance and population characteristics. Such modulation could prevent stunted growth, malnutrition, induction of bowel diseases, attenuated immune responses, and mortality, particularly among infants. Understanding the associations between specific indigenous African diets and the predictability of the dynamics of gut bacteria genera promises potential biotherapeutics towards improving the prevention, control, and treatment of microbiome-associated diseases such as cancer, inflammatory bowel disease, obesity, type 2 diabetes, and cardiovascular disease. The dietary influence of many African diets (especially grain-base such as millet, maize, brown rice, sorghum, soya, and tapioca) promotes gut lining integrity, immune tolerance towards the microbiota, and its associated immune and inflammatory responses. A fibre-rich diet is a promising biotherapeutic candidate that could effectively modulate inflammatory mediators' expression associated with immune cell migration, lymphoid tissue maturation, and signalling pathways. It could also modulate the stimulation of cytokines and chemokines involved in ensuring balance for long-term microbiome programming. The interplay between host and gut microbial digestion is complex; microbes using and competing for dietary and endogenous proteins are often attributable to variances in the comparative abundances of *Enterobacteriaceae* taxa. Many auto-inducers could initiate the process of quorum sensing and mammalian epinephrine host cell signalling system. It could also downregulate inflammatory signals with microbiota tumour taxa that could trigger colorectal cancer initiation, metabolic type 2 diabetes, and inflammatory bowel diseases. The exploitation of essential biotherapeutic molecules derived from fibre-rich indigenous diet promises food substances for the downregulation of inflammatory signalling that could be harmful to gut microbiota ecological balance and improved immune response modulation.

KEYWORDS: Microbiota, therapeutic, immune response, endotoxemia, inflammation, host

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Introduction

Complex microbial communities, called the gut microbiota, inhabit the human gut and they play many vital roles in the body. The microbiota support resistance to pathogens, influencing the immune system.[1,2] They take part in digestion and metabolism[3]; they control epithelial cell proliferation and differentiation[4] and modify insulin resistance.[5-7] Factors that contribute to gut microbiota development include host genetics, diet, age,[8,9] mode of birth,[10,11] antibiotics,[12-14] geographical location, maternal lifestyle (urban or rural), and foetal swallowing amniotic fluid.[15-17] However, diet is a leading factor that affects the gut system's microbial ecology as it dictates health and disease conditions. Understanding the influential contribution of diets due to socio-economic value, diverse cultural perspective, and population dietary formulation would help improve a healthy gut system and prevent diseases. Imbalance dietary combinations usually resulted in microbiome-mediated poor growth, malnutrition, occasional induction of bowel diseases, and occasional death, particularly among children. Poor dieting contributes to dwindling immune responses and the induction of several gastrointestinal disorders, accounting for more than 80% death rate in developing countries.[11,18]

The human gut ecology constitutes a vast microbial ecosystem that frequently interrelates to maintain a healthy gut system, balance immune response with well-coordinated cellular and humoral immune signalling to prevent metabolic dysfunction, pathogens dominance, and induction of systemic diseases.[19] Over the years, indigenous diets have been poorly used as biotherapeutic agents for prevention, treatment, and prophylaxis, particularly in developing countries.[20] The human gut microbiota comprises several bacteria, fungi, and viruses, and protozoa with a collection of diverse genomic signatures that influence varying metabolic and biochemical activities. This gut microbiota is usually shaped by some dietary composition

(usually fermented food and beverages).[20,21] The most abundant bacteria population in the gut belongs to *Firmicutes*, *Bacteroides*, *Proteobacteria*, *Fusobacteria*, *Verrucomicrobia*, *Cyanobacteria*, *Actinobacteria*, with *Firmicutes* and *Bacteroides* communities colonizing various parts of the human lumen, and influence the gut pH, digestive enzymes, mucus content, and metabolic capacity.[22] Among several ethnic groups (mainly from Ghana, Nigeria, Benin, Burkina Faso, Uganda, Kenya, Ethiopia, and South Africa) with diverse indigenous diets, the microbial abundance and population characteristics are usually determined by a combination of their indigenous diets. They could act as health-promoting compounds with potential probiotic activity.[23] Components of these diets influence the gut microbiome population pattern at various stages of growth from birth to adulthood, which sometimes gives rise to inhibition of metabolic disease because of the negative influence of intolerance to the immune system.[24,25]

Modulation of the gut microbiome with biotherapeutic substances developed from prebiotics- and probiotics-rich indigenous foods is a novel strategy for preventing gut colitis, colorectal cancer (CRC), and induction of diabetes, particularly among the adult age group,[26] with less or no adverse effect. Immunomodulatory effects of certain biotherapeutics (prebiotics or probiotics) are major innovations for maintaining a healthy gut, suppressing gut mucosa inflammation, and enhancing colon immune cell activities,[27] and differential activation of B cells, downregulation of interleukin functionality, inflammatory responses, and natural killer cell signalling.[28,29] In addition to being advantageous, the immunomodulatory effect of prebiotics and probiotics changes the genetic modification and inhibits the synthesis of aberrant protein that could shift the pro-inflammatory to an anti-inflammatory pattern, which in turn could facilitate induction or inflammation of degenerative mediators for CRC polyposis.[30,31]

Modulation of the gut microbial population enhances the host's physiological processes. This occurs by favouring the release of specific factors (such as microRNAs) and nonspecific factors (eg, antimicrobial peptides [AMPs], mucus, and immunoglobulin A), which facilitates the stabilization of the niche colonization, improvement of metabolic and nutritional homeostasis, cellular and humoral immunity, and prevention of degenerative mucosal diseases.[21] This article discusses the potential of indigenous diets as possible biotherapeutics to improve human well-being and immune responses and to advance knowledge on the influence of diet on the human gut microbiome community and its implications for the immune system and disease control through pedagogical review and analysis. Understanding the associations between certain diets and the predictability of the gut bacteria genera dynamics promises potential biotherapeutics towards improving prevention, control, and treatment of microbiome-associated diseases such as cancer, inflammatory bowel disease (IBD), obesity, type 2 diabetes, and cardiovascular disease. We have evaluated the knowledge gap in the current understanding of indigenous diet components' impact and utilization for structural transformation and improvement of the gut microbiome assemblage for enhanced health conditions.

Microbe-Host Cell Interaction

Notably, the immune system determines, to no small degree, the composition of the microbiota.[21] Therefore, there is a constant interaction between microbial antigens, their metabolites, and cells in the gut. Despite the classical immune perspectives, the relationship between gut microbes and cells of the immune system has elucidated novel functions. For instance, specific microbial genes actively contribute to energy metabolism modulation and glucose and lipid balance.[21,32,33] Studies using animal models showed an increased level of metabolic endotoxemia in diet-induced diabetes and obesity. Metabolic endotoxemia, a condition of circulating lipopolysaccharides (LPS), has also been confirmed in humans.[34-36] Other pathogen-associated molecular patterns (PAMPs), apart from LPS, such as peptidoglycans or flagellin, also trigger the modulation of similar metabolic pathways.[37,38]

The gut microbiota is crucial in nutrient uptake, drug metabolism, antimicrobial defence, immunoregulation, gut barrier integrity maintenance, and the gastrointestinal tract's structure.[39] However, a shift in the normal gut flora, referred to as commensals, can confer resistance to or encourage pathogenic bacteria.[40,41] The imbalance between the healthy gut flora and pathogens is what triggers the shift in the gut microbiome. Inflammation triggered by unusual immune responses affects gut microbiota balance negatively, thereby leading to intestinal diseases.[41,42] During antibiotic therapy, antibiotics generate selective pressure, thereby promoting the population of pathogenic bacteria. Pathogenic bacteria survive in the gut by using carbon and nitrogen sources of gut commensals as nutrients and control signals to enhance their increase and virulence.[43] The mechanisms by which gut bacteria resist pathogen establishment include direct killing, improvement of immune responses, and the struggle for limited nutrients.[44]

Understanding the interactions between host gut microbiota and pathogens provides systems for manipulating the microbiota against infectious diseases.

Host-Gut Microbiota Interaction With Pathogens

Microbes found in the human gut play vital roles in host metabolism.[21] The mammalian intestine accommodates a heterogeneous and dynamic microbes community, including bacteria, fungi, and viruses.[45] This composition of the microbial populations co-evolved with the host to develop a beneficial symbiotic relationship.[46] Studies indicate that the gut microbiota takes part in the immune system's maturation and plays a crucial role in host defence against invading pathogens.[47] Gut microbiota helps in the repair of damaged intestinal mucosal barrier.[48,49] Studies using germ-free mice have offered insight

into the intestinal microbiota[50,51] and its relevance to host health.[52,53] Recent studies show that over a thousand different gut microbiota species belonging to the phyla Actinobacteria, Bacteroidetes, Firmicutes, Proteobacteria, and a few others, aid host defence against pathogenic microbes.[38,44]

Impact of Dietary Habits on Microbiome Taxon Diversity

The human gut contains lots of microorganisms, which include bacteria, yeast, single-cell eukaryotes, viruses, and small parasitic worms. Some commonly found genera of gut bacteria are *Lactobacillus*, *Escherichia coli*, *Clostridium*, *Bacteroides*, and so on.[54] There is variation in the composition of microorganisms in the human gut in different individuals. Factors associated with the disease, especially in humans, are the imbalance in the gut microbial population. The role of microbiota in maintaining health is significant. However, gut microbes produce many bioactive compounds that can influence health, some of which may be beneficial or toxic. Some beneficial microorganisms help to keep detrimental or harmful bacteria at bay by competing for nutrients and sites of colonization.[55] Due to disturbance resulting from prolonged use of antibiotics, some diets could hinder interactions, making the body system vulnerable to disease. Microbial diversity in the human gut tends to associate with the spectrum of microbial enzymatic capacity needed to lower the quality of nutrients, especially those complex carbohydrates consumed by humans.[56] Distal gut microbiota contributes to host health through the biosynthesis of vitamins, essential amino acids, and generation of critical metabolic by-products from nutritional components, left undigested by the small intestine.[57]

The composition of food and several changes observed in the gut microbiota may result from what we take in as food, ie, eating habits and attitude.[58] The impact of diet on gut microbiota diversity relies on the abundance or lack of the 3 main dietary components: fats, carbohydrates, and proteins. This dietary source serves as energy for the proliferation of microorganisms in the gut. However, most differences in gut microbiota appear to be limited to the phylum and genus levels rather than species.[58] Carbohydrates are possibly the most studied dietary component, existing in 2 different types: digestible and non-digestible. Enzymes can degrade polysaccharides into starch and sugars such as glucose, fructose, lactose, and sucrose. *Bifidobacteria* are prominent due to high glucose, fructose, and sucrose in date fruits with reduced *Bacteroides*.[59] Microbiota-accessible carbohydrates (MACs) are a good source of dietary fibre that gives the host energy and carbon source.[60] Fats are 1 of the 3 main macronutrients, along with carbohydrates and proteins present in meat, chicken, groundnuts or cashew nuts, milk, cheese, butter and margarine, oils, pork, fish, grain products, and so on. A high-fat diet leads to decreased *Eubacterium rectale* and *Blautiacoccoides* (Firmicutes phylum) and *Bacteroides* spp. from the Bacteroidetes phylum.[61]

Recent evidence demonstrates that the human gut microbiota in the small and large intestine also plays a role in host dietary protein breakdown. The interplay between host and gut microbial digestion is complex, with microbes using and even competing for dietary and endogenous proteins. The metabolites produced by the intestinal bacteria resulting from amino acid fermentation can affect host cell protein uptake and the breakdown and affect host cell makeup.[62] Vegetables harboured diverse bacterial communities dominated by the phyla Actinobacteria, Bacteroidetes, Firmicutes, and Proteobacteria, but their composition was significantly different for each vegetable species. These differences were often attributable to variances in the comparative abundances of *Enterobacteriaceae* taxa.[63]

The Adverse Effect of Pathogen Cellular Signalling Pathways on the Gut Microbiome and Immune Responses

In the host gut system, initiation of pathogen-host interaction usually cascades from recognizing conserved microbial components known as the PAMPs through the host pattern recognition receptors (PRRs).[64] This molecular pattern that serves as the host's first line of defence critically determines the immune response's outcome by sensing PRRs present at the cell surface or intracellularly in the most innate immune cellular component.[65] Following the signal, the transduction of PRRs initiates a complex cascade of cellular immune reactions, leading to an early host response that contributes to pathogen recognition and elimination. How specific dietary formulations modulate cell signalling, and activation of another cellular immune complex for the subversion of pathogens remains unclear as it affects the gut ecology. Understanding host defence components at the molecular and cellular levels as it affects the innate immune receptors, autophagy, and other organelles, as well as signalling cascades of immune repertoire, could pave the way for novel identification of innovative anti-infective dietary therapies.

Dietary Influence on Gut Microbiome and Immune System

The consumption of foods containing chemicals such as pesticides, plastics, and food additives with a significant level of toxicity affects the gut microbiota.[66,67] The host's food requirement increases proportionally with the substrate for gut microbiota due to incorporating the microbiome community's necessitated food budget. Suboptimal nutrition provision for the microbiota is associated with dysbiosis, dysfunction of the microbiota, endotoxemia, and, ultimately, chronic inflammatory reactions.[68] These diseases have been linked to chronic, non-communicable, lifestyle-associated diseases such as obesity, type 2 diabetes, and liver cirrhosis.[69] The gut microbiome is dominated by enterotypes belonging mainly to the 2 taxa *Bacteroidetes* and *Firmicutes*.[70] An imbalance in the relative proportions of the 2

taxa may be associated with outcomes such as obesity,[15,71] which contributes to the distribution of enterotypes in the gut. For instance, a diet primarily made up of plant-derived carbohydrates has contributed to a gut microbiota predominated by *Prevotella*. In contrast, animal protein and saturated fat-rich diets are associated with a gut microbiota dominated by *Bacteroides*.[72] Three interconnected systems modulate dietary responses: the quality and quantity of the diet, which includes the nutritional composition and the caloric content of consumed food; the microbiota, which consists of the network of bacterial strains present within the host; and the host physiology and metabolism, which includes the digestive mechanisms of the host in addition to the host immune response.[73-75]

High intake of dietary fat has been associated with an increase in pro-inflammatory cytokine levels[76,77] and an increase in gut permeability, ultimately increasing susceptibility to Gram-negative bacterial infections, especially invasive *E coli* infections.[78] Although considered safe for consumption, some artificial sweeteners have been linked to the development of metabolic or inflammatory disorders by induction of dysbiosis in the gut. A prime example includes the association between saccharin consumption and the development of liver inflammation in mice.[79] Equally, the association between sucralose maltodextrin and disrupted lipid metabolism[80] and intestinal inflammation, especially in Crohn disease, is strongly influenced by IBD dietary choices.[81] On the contrary, many African diets, especially those derived from grains such as millet, maize, brown rice, sorghum, soya, and tapioca, benefit the microbiota. They also promote gut health as they are healthy, gluten-free foods and are especially helpful for individuals with gluten sensitivity.[79] The intestinal microbiota helps maintain the intestinal barrier, usually by priming the intestinal immune defences while simultaneously promoting immune tolerance towards the microbiota.[80] Thus, probiotic-rich and whole-grain diets (such as a few local African diets), due to their capacity to maintain the microbiota, contribute to preventing intestinal permeability and its associated immune and inflammatory responses.

Breast-feeding is also an essential factor in influencing the immune response directly through neonatal contact with microbiota in breast milk and indirectly through milk oligosaccharides, immunoglobulins (IgA), and antimicrobial components, all of which influence growth and metabolism.[81] The infant formula lacks these components, which leaves formula-fed infants predisposed to a variety of childhood illnesses. Infants placed on formula could be hospitalized with respiratory, gastrointestinal, and urinary tract infections than exclusively breast-fed infants.[82] Exclusive breast-feeding is associated with reduced diarrhoea-related dysbiosis of the gut and increased gut microbiota diversity, among other good outcomes.[83] The gut microbiota of breast-fed infants also differs from those of infants fed with pumped breast milk due to the exposure of pumped breast milk to opportunistic environmental bacteria such as the Pseudomonadaceae and *Stenotrophomonas*.[84] Human milk oligosaccharides, found in breast milk, modulate inflammatory mediators' expression associated with immune cell migration, lymphoid tissue maturation signalling pathways, and the array of cytokines and chemokines involved in ensuring a balance between types 1 and 2 T helper cells.[85] The microbiome constitution is shaped within the first 3 years of life,[86] the period that has been described as a 'window of opportunity' for long-term microbiome programming.[87] This process only serves to highlight the importance of breast-feeding to infant gut microbiome and immune development.

However, it is noteworthy that the application of agrochemicals and non-caloric artificial sweeteners may result in residues of heavy metals, pesticides, polycyclic aromatic hydrocarbons, dioxins, polychlorinated biphenyls, and so on in foodstuff and breast milk. A recent study posits that these xenobiotics may be significantly counterproductive to nutritional impacts on the gut microbiome. Therefore, it is essential to properly screen the sources of the diets before administration for optimal results.[88] Changes in gut microbiota seem to make individuals susceptible to type 1 diabetes, as observed in the United States and other geographically different Asian and African countries.[89] Investigations are still underway towards this relatively recent drive towards establishing causation. Arguably, the most successful of the approaches developed from such studies is faecal microbiota transplantation. This approach entails the horizontal transfer of intestinal microbiota from individuals cured of a disease using functional foods to diseased individuals not treated with functional foods. It is an excellent example of applying the classic Koch's postulates.[90]

Modulation of Gut Immune Responses by Indigenous Dietary Constituents

Mounting evidence suggests that gut microbiota plays a pivotal role in immune system maturation and function and mediates host defence against pathogens.[91,92] The regulatory T cell population is decimated in the gut of germ-free and antibiotic-dosed mice. Nevertheless, following recolonization with eubiosis-enhancing species such as *Bacteroides fragilis*, both population and function are restored.[91] Mechanisms by which gut microbiota enhances host immune response include (1) stimulation of Paneth cells in the host's small intestine to synthesize AMPs like (pro) defensins, cathelicidins, and C-type lectins, which regulate the growth of pathogens. Certain bacterial species and bacterial metabolites such as muramyl dipeptide, lipid A, lipopolysaccharide, and lipoteichoic acid are now known to elicit AMP synthesis; (2) maintenance of intestinal epithelium integrity via activation of genes that influence proliferation and fortification; (3) amplification of interleukins (IL-10, IL-17, and IL-22) expression to destroy attacking pathogens; (4) activation of inflammasomes through the initiation of pyroptosis, as well as the generation of the pro-inflammatory cytokines IL-18

and IL-1β; (5) IgA secretion; and (6) development of T helper cells, and elicitation of regulatory T (Treg) cells.[91,93]

Since the turn of the 20th century, the world has witnessed a shift in dietary patterns owing to urbanization and rising incomes, with an increasing number of people consuming refined foods, processed grains and sugars, fats, and animal-derived foods.[94] Furthermore, dietary constituents that can alter microbiota composition and their metabolic activities will influence inflammation, immune function, and disease development.[46,95] The indigenous African diet is characterized by vegetables, wild fruits, lean meats, legumes, and staple starches[96] with high fibre[97] and phytochemical profiles.[98] Phytochemicals, lauric acid, retinoids, tocotrienols, and carotenoids have been identified in oil palm, and yam contains dioscorin, biotin, thiocynate, potassium, and lipoic acid.[99] It has been established that West Africans, due to the adoption of western diets, are predisposed to metabolic syndrome among other diseases.[99] Despite a lack of information on the structure and mechanism of action, yam (*Dioscorea*) is touted as a promising source for developing functional foods that can modulate gut microbiota and prevent dysbiosis. Another component of yam, biotin (Vitamin B_7), is crucial to the proliferation and maintenance of gut microbiota and is thought to initiate immunometabolism. Biotin exerts anti-inflammatory effects by shutting off the activation of NF-κB – a prime signalling molecule for the generation of many pro-inflammatory cytokines (like tumour necrosis factor-α, IL-8, IL-6, and IL-1).[100]

Carotenoids are 1 of the bioactive components in palm oil. Albeit the metabolism of dietary carotenoids in the gut and their influence on the microbiome remains elusive, there are indications that carotenoids in the form of β-carotene may enhance gut immune homeostasis by directly modulating the production of IgA, consequently arresting the progression of dysbiosis.[51] Retinoids like retinoic acid (Vitamin A) perform a crucial function in modulating intestinal immune response.[101] Primarily, retinoic acid functions to trigger IgA generation in B cells and isotype switching.[102]

The molecular structures of dietary fibres are pivotal for the modulation of gut microbiota. Thus, deciphering the various dietary fibres' structural properties in indigenous vegetables could provide insights into their influence on gut microbiota structure and function.[103] Vegetables are rich sources of dietary phytochemicals, mainly phenols, and flavonoids.[104] Flavonoids provide defence against diseases as they possess antioxidative, immunomodulatory, anti-inflammatory properties, and gut microbiota.[105,106] Neutrophils are vital elements of innate immunity critical to sustaining gut microbiota balance.[106] Reduced recruitment of neutrophils can result in the inability of a cell to fight off invading microorganisms.[107] For instance, Vitamin D is reported to modulate both adaptive and innate immune responses, thus enhancing the elimination of invading pathogenic bacteria, fungi, and viruses. In contrast, Vitamin E is reported to strengthen T-cell-mediated functions.[46]

Detrimental Effects of the Gut Microbiome in Inducing Colitis

Modification in genomic, functional, and taxonomic features of the microbiota could bring swift and occasionally long-lasting impact. A recent report submits that about 6 to 8 million cases of IBD globally, in 2017, with the total years lived with disability (YLD) almost doubling in many regions between 1990 (0.56 million cases) and 2017 (1.02 million cases), thus posing a substantial economic and social burden on governments and health systems in the coming years.[108] In the lumen, both *Salmonella typhimurium* and *Clostridium difficile* catabolize sialic acid as a carbon source for their growth.[109] Increased availability of these free sugars in the intestinal lumen is made possible by the presence of saccharolytic *Bacteroides thetaiotaomicron*, on which *C difficile* and *S typhimurium* rely.[110]

By the preceding, exploiting these molecules derived from the microbiota as both signals and nutrients remains critical for the hosts' pathogenic bacterial infection. Although such organisms have developed many strategies of circumventing the resistance to colonization given by the microbiota, and in other situations even employ its help, the microbiota offers repulsion and thus creates intense competition for resources. The colonic microbiome's detrimental impacts are tied along with antibiotics,[111] which erodes an overlying microbial community and elicits hydrolysing actions on mucosal glycans. Currently, probiotics and prebiotics are being employed to treat these diseases and have shown encouraging outcomes. Therefore, as this review provides a current understanding of gut bacteria's detrimental roles in inducing colitis, a particular focus on 'human gut microbiomics' would offer more precise knowledge of the relationship between gut microbiota and diets, human health, and disease manifestation. This knowledge is expected to deliver perspectives and frontiers for personalized gut microbiota bacteriotherapy and management.

Indigenous Diet as a Biotherapeutic Source for Improving Microbiota

Several dietary compositions in sub-Saharan Africa primarily contain carbohydrates and fats, affecting the metabolism and key microbiota profile among people from different cultures background.[112] Their gut microbiota is a critical element in developing and preventing specific diseases peculiar among other ethno-geographical cross sections. And this has a premise on the provision of suitable dietary biotherapeutics. The implications of many indigenous diets in health and illness proffer potential limitations to its modification as biotherapeutics for treatment, prevention, and restoration of a healthy gut. A combination of some indigenous diets, usually vegetables, fibres, and protein, improves the gut microbiota's homeostasis, making it maintain various functional requirements for maintaining human health and preventing certain autoimmune, allergic diseases. Interaction of specific intestinal bacteria populations could trigger high infectivity of pathogens, leading to

Table 1. Gut microbiota influence by modulation of the African diets.

PHYLA	GENUS	SELECT FOOD SOURCE(S)	COUNTRY	REFERENCE(S)
Actinobacteria	*Bifidobacterium*	Vegetables, millet, maize, brown rice, sorghum, soya, and tapioca	Ethnic groups from Ghana, Nigeria, Benin, Burkina Faso, Uganda, Kenya, Ethiopia, and South Africa	Cheng et al[38], Statovci et al[44], Hiel et al[58], Sivakumar et al[104]
Bacteroidetes	*Prevotella* *Bacteroides*			Groussin et al,[22] Hiel et al,[58] Mobeen et al[70]
Firmicutes	*Clostridium* *Eubacterium* *Oscillibacter* *Butyricicoccus* *Sporobacter* *Bacilli* *Erysipelotrichia* *Roseburia spp*			Groussin et al[22], Cheng et al[38], Statovci et al[44], Hiel et al[58], Mobeen et al[70]
Proteobacteria	*Succinivibrio* *Shigella* *Escherichia* *Clostridia spp* *Ruminococcus* *Lactobacillus* *Enterococcus*			Groussin et al[22], Statovci et al[44], Guindo et al[54], Hiel et al[58], Sivakumar et al[104]
Verrucomicrobia	*Methylacidimicrobium* Methylacidiphilales Spartobacteria Verrucomicrobiae			Groussin et al[22]

disease development in susceptible hosts. Therefore, the application of indigenous biotherapeutics, such as prebiotics, probiotics, and functional food, would favour health-promoting microbial populations, which can be exploited for biotherapeutics. Fibre-rich foods that are essentially consumed in Africa influence the composition of the gut microbiota, serving as a key potential therapeutic indigenous diet in various ethnic groups enhancing gut microbial diversity, composition, and stability (Table 1).

Enhancement of the Indigenous Diet on Microbiota and Immune Interaction in CRC

Colorectal cancer is 1 of the leading global causes of death with an estimated medical care cost of more than $14 billion.[113] In the intestinal epithelium, a synergistic mutation in tumour suppressor genes, proto-oncogenes, and DNA repair genes trigger carcinogenesis.[114] Most mutations occur in the pathways linked to transforming growth factor β (TGF-β) signalling, Wnt-β-catenin signalling, DNA mismatch repair, tyrosine kinase receptors, and genes associated with apoptosis and regulatory agents of the cell cycle.[114] Asides from genetic alterations, a microbiota-predominated tumour microenvironment may contribute significantly to CRC initiation, promotion, and progression, which may culminate in an attendant metastatic condition.[115] Dietary intake and the intestinal microbiota are leading carcinogenic factors in the luminal enteric microenvironment.

Some strains of *E coli* transmitted via food products produce the genotoxin named colibactin, which is capable of inducing DNA double-strand breaks in intestinal epithelial cells leading to mitotic and chromosomal aberrations.[116,117] These alterations increase the likelihood of gene mutations and cancerous growth initiation.

Indigenous antineoplastic diets notably play vital roles by either promoting or inhibiting tumorigenesis and CRC pathogenesis.[118,119] In vitro experiments have shown that butyrate, a short-chain fatty acid and a by-product of microbial fermentation of indigestible complex carbohydrates such as fibre, initiates growth arrest and apoptosis of colonic epithelial cells.[97] These dietary fibres consist of complex carbohydrates mainly found in vegetables, legumes, and fruits. Their fibrous structure characterizes their indigestibility to humans. As such, they contribute no calories to the human diet. Gut microbiota contributes to the host's health through the biosynthesis of vitamins, essential amino acids, and critical metabolic by-products from undigested dietary components in the small intestine. Such by-products include short-chain fatty acids such as butyrate, propionate, and acetate that act as vital energy sources for intestinal epithelial cells and hence may fortify the mucosal barrier.[118] Studies on germ-free mice suggest that the microbiota directly promotes local intestinal immunity by influencing toll-like receptor (TLR) expression, antigen-presenting cells, differentiated T cells, and lymphoid follicles. Microbiota may also foster systemic immunity through increased splenic CD4+ T cells and systemic antibody expression.[65]

In sub-Saharan Africa, particularly Nigeria, indigenous dietary fibre sources include nuts, whole grains, beans, fibrous

vegetables, and dense fruits such as cashew, watermelon, pineapples, and apples. Suboptimal provision of nutrition for the microbiota is associated with dysbiosis, dysfunction of the microbiota, and endotoxemia, which may progress into chronic inflammatory reactions, all of which are, in turn, linked to chronic, non-communicable, lifestyle-associated diseases such as obesity, type 2 diabetes, and liver cirrhosis.[113]

The gut microbiome is dominated by enterotypes belonging mainly to the 2 taxa *Bacteriodetes* and *Firmicutes*.[66] An imbalance in the relative proportions of these taxa may be associated with outcomes such as obesity.[119] Diet contributes to the distribution of enterotypes in the gut. For instance, a diet primarily made up of plant-derived carbohydrates has contributed to a gut microbiota predominated by *Prevotella*. In contrast, animal protein and saturated fat-rich diets are associated with a gut microbiota dominated by *Bacteroides*.[64] High intake of dietary fat has been associated with an increase in pro-inflammatory cytokine levels[120,121] and an increase in gut permeability, ultimately increasing susceptibility to Gram-negative bacterial infections, especially invasive *E coli* infections.[19]

Ultimately, while there is a consensus on the existence of a correlation between gut microbiota dysbiosis and (for instance) IBD, a cause-and-effect relationship has often appeared challenging to establish, especially as chronic inflammation (through the changes it exerts on the oxidative and metabolic environment of the gut) is an underlying cause of dysbiosis. Dysbiosis is probably both a consequence and driver of chronic inflammation.[122] Investigations are still underway on the relatively recent drive towards establishing the causation. Arguably, the most successful of the approaches developed from such studies is faecal microbiota transplantation.

Conclusions

The potential contribution of nutrition to a healthy gut is expected to enhance microbiota growth, metabolic activities, and interrelationship at the lumen ecological niche and synergistically suppress dysbiosis, mucosal dysfunction, and endotoxemia that induce chronic inflammatory reactions associated with chronic and non-communicable (obesity, type 2 diabetes, and liver cirrhosis). Enriched plant-derived carbohydrate diets modulate systemic responses, host physiology, caloric and protein metabolism, and host immune response. Many African diets, especially those based on grains such as millet, maize, brown rice, sorghum, soya, and tapioca, are useful biotherapeutics and are essential components of a healthy diet, gluten-free and are very useful for individuals with gluten sensitivity. Several traditional food fermentation approaches in sub-Saharan Africa increase digestion and absorption along the gastrointestinal tract and prime the intestinal immune defences, promoting immune tolerance and associated immune and inflammatory responses. There is a need for more approaches for using indigenous diets in sub-Saharan African as a functional food for biotherapeutic agents as a source of treatment of endogenous diseases. The high content of fibre polysaccharides in many African diets affects the microbiota stability, digestibility influence, and healthy mucosal layers of the colon, preventing pathogenic bacteria and expanding opportunistic pathogens. The exploitation of essential biotherapeutic molecules derived from the fibre-enriched diet could help downregulate inflammatory signalling that could be harmful to gut microbiota ecological balance and offers repulsion to gut pathogenic microbial taxa to successfully compete for nutrients with commensal species that are essential for colon absorption capacity.

Exploiting several indigenous dietary components as biotherapeutic and anti-quorum sensing would further enhance gut health, consequently preventing metabolic and infectious diseases through improved immune response modulation. Understanding the influence of these diets would avoid the excessive use of antibiotics. It would also increase gut microbiota ecology in preventing immune deficiency diseases such as CRC, IBD, and dysbiosis, which are becoming a significant threat to human livelihood.

Author Contributions

O.O. Obembe conceived the idea about the topic, mobilised other authors to write different aspects of the manuscript, reviewed and edited the various drafts till the final version was produced.

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