Review Article

Modulation of gut microbiota with Ayurveda diet and lifestyle: A review on its possible way to treat type 2 diabetes

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Abstract

Background: The prevalence of type 2 diabetes (T2D) has increased substantially in the past few decades throughout the world. In India, the epidemic of diabetes continues to increase irrespective of area, status, and age. Despite various scientific societies involved in the treatment of diabetes, still, the burden of diabetes keeps growing. **Aims:** The aim of this work is to explore the Ayurvedic concept of a personalized diet to modulate the gut microbiota for the treatment of T2D. **Material and methods:** A thorough study of literature from online scientific databases including Web of Science, PubMed, Scopus, and Google Scholar as well as from classical texts of Ayurveda was done. A careful compilation was done to extract the valuable output of the personalized diet to modulate the gut microbiota. **Results:** There are various diets used to control blood glucose levels, and their effects are also being studied on the transcriptome or epigenome despite 99.9% genomic similarity among human beings. However, microbiomes have only 10% similarity. Ayurvedic diet is given on the basis of *Prakriti* (body constitution), therefore, it is also called personalized diet. **Conclusion:** The diets prescribed for T2D in Ayurveda are high in fibers, polyphenols, and complex carbohydrates which enrich butyrate-producing bacteria and decrease lipopolysaccharide-producing bacteria. Hence, there is a need to have a personalized diet to manage the glucose level by enriching beneficial gut microbiota. The approach of a personalized diet associated with gut microbiota can be helpful in maintaining blood sugar in T2D patients.

Keywords: Ayurvedic diet, gut microbiota, personalized diet, *Prakriti*, type 2 diabetes

Introduction

Type 2 diabetes (T2D) is a metabolic disorder mainly characterized by increased blood glucose level due to reduced insulin level, insulin resistance, or impaired beta-cell function, i.e., delayed or inadequate insulin release.[1] According to the World Health Organization,[2] the major risk factors of T2D include genetic, metabolic, ethnicity, family history, previous gestational diabetes combined with older age, obesity, unhealthy diet, physical inactivity, and smoking. As per the report of the International Diabetes Federation,[3] an estimation of 425 million people worldwide are diabetic sufferers, in which there were over 72 million cases only reported in India in 2017.

Much emerging evidence indicates that the risk of developing T2D may involve a particular environmental factor, specifically the collection of microorganisms that inhabit the intestine and can get influenced by diet.[4] The human intestine harbors millions of different microorganisms such as bacteria, viruses, fungi, and archaea to form an ecosystem that remains with the human throughout life.[5] This ecosystem or gut microbiome contributes to metabolic and immune functions, which results to affect most of the physiological functions.[6] Gut microbiome is passed from mother to new born, hence, it acts as a natural factor that interacts with host genetics to shape phenotype.[7] The composition of the gut microbiome can be modulated with

Access this article online

Quick Response Code:

Website: www.ayujournal.org

DOI: 10.4103/ayu.AYU_7_20

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How to cite this article: Chauhan A, Semwal DK, Semwal RB, Joshi SK, Adhana RK, Goswami MS. Modulation of gut microbiota with Ayurveda diet and lifestyle: A review on its possible way to treat type 2 diabetes. AYU 2022;43:35-44.

Submitted: 14-Jan-2020 **Revised:** 06-Jul-2021
Accepted: 17-Apr-2023 **Published:** 02-Aug-2023

dietary habits,[8] while its physiology and gene expression can be affected by xenobiotics.[9]

The earlier studies suggested that certain bacteria are associated with certain *Prakriti* (physical-psychological constitution of an individual also referred to as genotype) in healthy individuals which suggests that these gut bacteria may be *Prakriti* specific and useful for an individual's health.[10] According to Ayurveda, *Prakriti* arises due to a unique combination of the status of three *Doshas* (biological factors) and is decided at the time of conception.[11] On the other hand, the gut microbiota arises later and its composition depends on the transfer of microbiota from the mother, environmental factors, and food habits. These bacteria seem to be responsible to respond differently to similar kinds of food; therefore, the blood glucose of an individual varies with food.[12] Ayurveda emphasizes preventive and promotive aspects of health rather than curative. It laid the concepts of daily/seasonal regimens and moral/social conduct for a healthy life. In addition, Ayurveda suggests a certain healthy diet and lifestyle for individuals based on their *Prakriti*.[13] However, in today's busy life, the suggested healthy diet and lifestyle are very difficult to follow; as a result, there is a rise in lifestyle disorders of which T2D is the most threatening one. Therefore, each person needs a personalized diet and lifestyle to resume a healthy life.

Generally, insulin or oral hypoglycemic agents are prescribed for T2D patients if diet and exercise alone fail to lower the glycemic level. The drugs for T2D only control the glucose level but neither cure nor stop the further progress of the disease. Besides, conventional antidiabetic drugs are either expensive or often associated with adverse effects. In recent times, a lot of studies have come up involving microbiota-based interventions in humans which emphasize that altered gut microbiota may directly modulate host metabolism in humans. However, it will be essential to determine which particular diet is suitable for beneficial gut microbiota to enrich their population. This approach may be helpful in preventing and treating obesity and T2D. The approach can be further correlated to an *in vivo* study by Lee and Ko,[14] which confirmed that metformin influences the gut microbiota and their metabolic pathways.

Material and methods

A detailed survey of literature from online scientific databases including Web of Science, PubMed, Scopus, and Google Scholar as well as from classical texts of Ayurveda and other relevant books was conducted. Selected keywords such as gut microbiota, diabetes, Ayurveda, personalized diet, and microbiomes were searched from the online databases to collect the relevant literature. A careful compilation and a critical analysis were done to extract the valuable output of the personalized diet to modulate the gut microbiota.

Results and Discussion

Gut microbiota in human

Microbiota is the community of commensal; symbiotic and pathogenic microorganisms present in a specific environment. During the last decade, many studies have been conducted to know the precise composition of human microbiota in various geographical locations by assessing several samples from the skin, mouth, and gut.[15,16] Among them, the most interesting part is the gastrointestinal tract or gut, where microbial colonization occurs at different efficiency from the oral cavity to the rectum, depending on different environmental conditions. Particularly, dietary carbohydrates that transit through the gut are able to influence the composition and stability of the gut microbiota and disturb the balance between beneficial versus harmful intestinal bacteria which may result in a condition of dysbiosis. In such conditions, there occurs an overgrowth of harmful bacteria that could negatively affect the important functions of the microbiota, such as immunity and gut function of the host.[17,18] On the basis of molecular analyses, the two main bacterial phyla that reside in the gut are *Bacteroidetes* and *Firmicutes*. The *Bacteroidetes*, a phylum of Gram-negative bacteria, includes the genus *Bacteroides*. The bacteria of this genus are able to use a vast range of substrates and majorly produce propionate. On the other hand, bacterial species from *Firmicutes* are able to produce butyrate from indigestible polysaccharides.[19] Besides these, other phyla such as *Actinobacteria* (includes *Bifidobacterium* spp.), *Proteobacteria* (includes *Escherichia coli*), and *Verrucomicrobia* (includes *Akkermansia muciniphila*) are also important and usually present in smaller numbers in the healthy gut microbiota.

A diet, containing high-fat and high calories, alters the gut microbiota which further leads to obesity and its complications such as insulin resistance, hyperlipidemia, and atherosclerosis.[20] The studies proved that a disturbing ratio of *Firmicutes* and *Bacteroidetes* in gut microbiota is directly associated with obesity and T2D.[21] It has been found that probiotics such as *Bifidobacterium* spp. and *Pediococcus pentosaceus* are decreased in obesity, systemic inflammation, and metabolic disorders whereas pro-inflammatory bacteria such as Desulfovibrionaceae are increased in humans. In addition, other species such as *Enterobacter cloacae*, *A. muciniphila*, *Clostridium bolteae* and *Desulfovibrio* are also associated with obesity and T2D.[22]

Role of gut microbiota in the prevention and treatment of type 2 diabetes

Over the past few decades, the prevalence of T2D is rapidly increased throughout the world, mainly due to rapid environmental changes that have had a negative impact on risk factors of diabetes, such as dietary habits and a sedentary lifestyle. The composition of gut microbiota is affected by genetic and environmental factors such as diet and physical exercise. In the case of adults, the composition of gut microbiota is considered to be stable whereas this composition is unstable in children due to several factors including geographical conditions, delivery mode, breastfeeding, and antibiotics used by the mother.[23] However, biological functions that are regulated by the gut microbiota and their composition are dependent on adjustable factors such as diet

and drugs. Thus, new evidence is emerging for the use of the modifiable capacity of the gut microbiota for the prevention and treatment of T2D.[24]

Patients with T2D usually have an increased number of opportunistic pathogens, such as *Bacteroides caccae*, *Clostridium hathewayi*, *Clostridium ramosum*, *Clostridium symbiosum*, *Eggerthella lenta,* and *E. coli*, and the decreased number of butyrate-producing bacteria.[25] Such patients have different gut microbiota composition as compared to healthy individuals which can be seen at the phylum level.[26] The composition of these gut microbiota is different during the development of diabetes, e.g., *Verrucomicrobia* is found as a potential marker of T2D due to its lower abundance in T2D patients.[27] Interestingly, metformin, the most widely used drug for T2MD, shows a glucose-lowering effect through gut microbiota by increasing the population of butyrate-producing bacteria. It has also been found that the population of *Lactobacillus* species increases with the treatment of metformin.[28] Similarly, individuals treated with metformin were also observed to have an increased abundance of *E. coli* in the gut. The study also proved that gut microbiota can play an important role in insulin resistance in patients.[29] Among many other bacteria, *A. muciniphila* is one of the microbes that decrease in individuals with prediabetes and newly diagnosed T2D, which seems to have the potential of a biomarker for glucose intolerance.[27] Similarly, *Bifidobacterium* is found more frequently in healthy people and decreases with the progress of T2D,[30] while its high abundance is associated with a healthier metabolic status with greater improvements in glucose homeostasis and body composition after energy restriction.[31] Recent research also found that the gut microbiota of T2D patients consists of Gram-negative bacteria predominantly.[32]

Mechanisms via gut microbiota to develop type 2 diabetes

The human gut microbiota comprises diverse communities which provide remarkable enzymatic capability and hence play a fundamental role in manipulating host physiology. There are mainly five bacteria: phyla, *Firmicutes*, *Bacteroidetes*, *Actinobacteria*, *Proteobacteria*, and *Verrucomicrobia*, which are dominant components of the human gut microbiota.[33] It is established that 90% of the bacterial population consists of Gram-negative anaerobes which include *Bacteroides*, *Eubacterium*, *Bifidobacterium*, and *Fusobacterium*.[34] These gut microbiota are vital for carbohydrate fermentation and nutrient absorption,[35] protection from pathogenic bacteria,[36] and regulation of metabolic disorders such as T2D.[37]

Metabolic endotoxemia/lipopolysaccharide/toll-like receptor 4/cluster of differentiation 14 system

Earlier studies have reported that high-fat diet-induced structural changes in the intestine further lead to increased intestinal permeability, and favor the translocation of plasma lipopolysaccharide (LPS) to the bloodstream.[38] A many-fold increase in LPS concentrations in serum, also known as metabolic endotoxemia, further activates toll-like receptor (TLR) 4-mediated inflammatory activation and leads to low-grade inflammation and T2D. Food enriched with oligofructose increases bifidobacteria content, which reduces the inflammatory tone by reducing endotoxemia and pro-inflammatory cytokines.[39,40] LPS in combination with a cluster of differentiation 14 (CD14) serves as a ligand for TLR4. Hence, the LPS/CD14/TLR4 system seems to set the threshold for a diet having high fat-induced insulin resistance and the onset of diabetes and obesity. [Figure 1]

Mucosa permeability system

The intestinal mucosa has a vital role in the absorption of vital nutrients and avoidance of the firm adhesion of bacteria to the epithelial cells, thus preventing bacterial translocation, and hence, regulation of barrier functions. LPS binding of LPS-protein complexes to TLR4 activates the cellular nuclear factor-kappa B (NF-κB) signaling pathway which leads to the production of various pro-inflammatory cytokines and chemokines 4. Elevated serum LPS activity levels have been linked with a number of unfavorable changes in human health. In diabetes and in obese subjects, high LPS levels have been shown to be negatively correlated with insulin sensitivity.[41] The integrity of mucosa is ensured through intercellular tight junctions, mucus secretion, antimicrobial peptide secretion from paneth cells, and immunoglobulin secretions from resident immune cells. Although, it has been found that a diet with high fats significantly increases intestinal permeability via reduced expression of epithelial tight junction proteins, including zonulin and occluding which allow endotoxin to pass and lead to inflammation. It is already demonstrated that prebiotic-treated mice exhibited lower plasma LPS and cytokines decreased hepatic expression of inflammation, and were associated with lower intestinal permeability and improved tight junction integrity.[42] [Figure 1]

Intestinal alkaline phosphatase system

Intestinal alkaline phosphatase (IAP) has a key role in intestinal homeostasis. It regulates lipid absorption across the apical membrane of enterocytes. It also controls bacterial endotoxin-induced inflammation by dephosphorylation and detoxifying intestinal LPS, and hence acts as a host defense factor against LPS. The dietary fats and gut microbiota negatively influence the expression of this enzyme.[43] Earlier studies confirmed that consumption of a high-fat diet is associated with changes in the gut microbiota and also increased level of LPS. Thus, excess chylomicron formation during high-fat feeding facilitates endotoxin translocation by reducing IAP activity and inducing intestinal inflammation that is present in obesity and insulin-resistant states.[44] The studies also showed that gut microbiota may promote metabolic inflammation through TLR signaling upon challenge with a saturated lipid-rich diet.[45]

The dietary fats lead to paracellular leakage of LPS across the intestinal epithelium which reaches circulation and initiates activation of TLR2 and TLR4 and LPS receptor CD14, leading to increased activation of inflammatory pathways. It is further

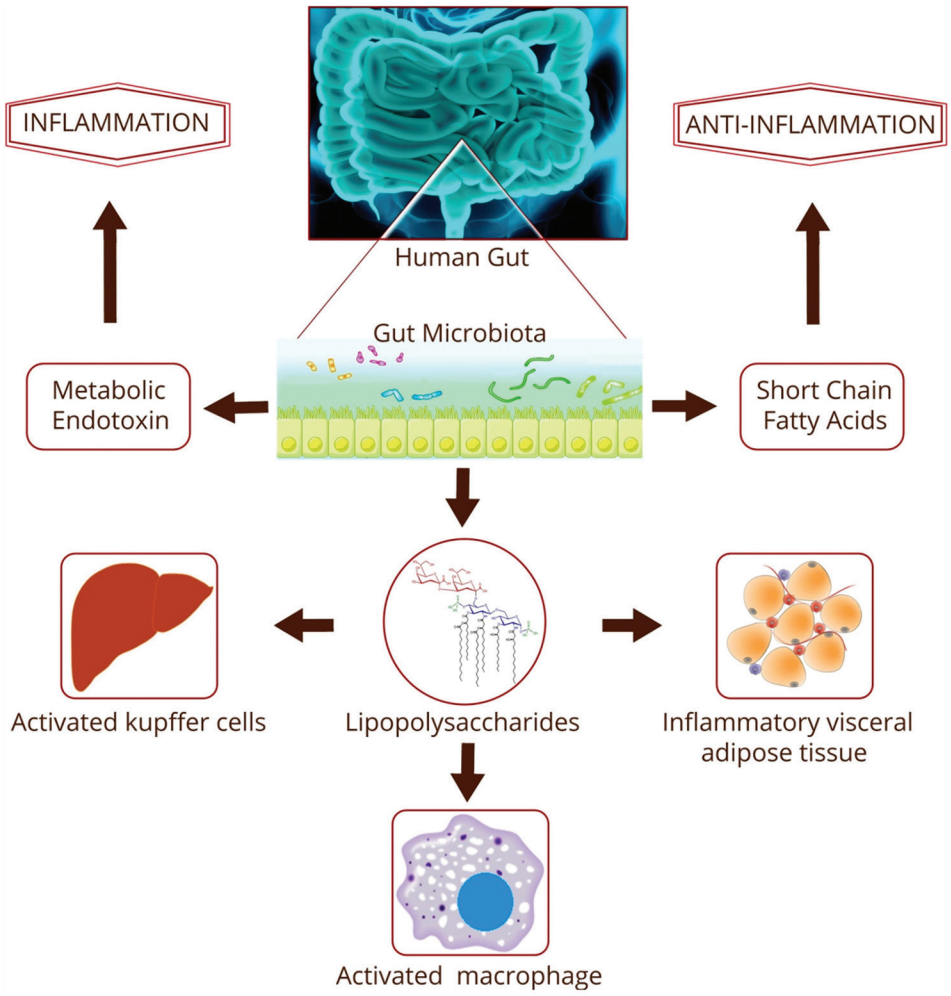

Figure 1: Possible pathways to cause insulin resistance via gut microbiota. (1) Inflammation in visceral adipose tissue and activation of kupffer cells and macrophage due to LPSs can cause insulin resistance. (2) SCFAs normalize intestinal permeability, which helps in maintaining insulin sensitivity. LPSs: Lipopolysaccharides, SCFAs: Short-chain fatty acids

impaired insulin signaling through decreased phosphorylation of the insulin receptors, insulin receptor substrate (IRS), and protein kinase B (Akt). In addition, it increased the inhibitory serine phosphorylation of IRS-1 which results in insulin resistance.[46] Now, it is clear that chylomicrons promote intestinal LPS absorption. Therefore, the high-fat diet facilitates endotoxin translocation by reducing IAP activities, which further induces intestinal inflammation that leads to insulin resistance [Figure 1]

Energy storage system

Energy metabolism is strongly regulated by host gut microbiota as the microbiota modulates energy balance. In support of this, it has been reported that microbiota transplantation from an obese donor mouse to a lean recipient results in a significant increase in body fat over 2 weeks, without differences in dietary intake. The results from this study further revealed that gut microbiota is an additional contributing factor to the pathophysiology of obesity.[47] The energy has a tendency to remain in equilibrium between intake and expenditure. Therefore, this hypothesis is called a storage effect hypothesis, as obesity-associated gut microbiota has an increased capacity for energy harvest from the diet. This hypothesis is based on the fermentation of dietary polysaccharides by bacteria, as it is evident that dietary nondigestible polysaccharides by a human are fermented into SCFAs including acetates, propionates, and butyrates, and other subproducts in the cecum and colon which is perhaps due to the presence of anaerobic bacteria.[48]

These SCFAs are known to regulate intestinal immune homeostasis and serve as an energy source for colonic epithelial cells. These are also absorbed from the gut and can have potent effects on energy expenditure and insulin sensitivity in peripheral metabolic tissues through different G protein-coupled receptors, such as GPR41 and GPR43.[49] Certain facultative and anaerobic bacteria in the large bowel produce secondary bile acids from the pool of bile salts secreted into the intestine. A small fraction of these bacterially derived bile acids are absorbed into the bloodstream and can modulate hepatic or systemic lipid and glucose metabolism

through nuclear or G protein-coupled receptors, such as FXR or TGR5, respectively.[50]

The host response for the diet is dependent on the relative proportion of SCFA and subsequent liver clearance, where they induce *de novo* hepatic lipogenesis and other processes, while only a small subset enters into the systemic circulation.[51] A clinical study by Schwiertz *et al*. correlated the composition of gut microbiota and proportions of SCFA with obesity.[52] In this study, the obese mice showed an increased propionate level in comparison to the lean mice with an altered phyla ratio of *Bacteroides* to *Firmicutes* as well as an increased proportion of *Bacteroidetes*. SCFAs produced by the microbiota in the cecum and the colon can be found in the hepatic, portal, and peripheral blood. These SCFAs affect lipid, glucose, and cholesterol metabolism in various tissues. These are transported from the intestinal lumen into the blood compartment of the host and taken up by organs where they act as substrates or signal molecules.[53]

Similarly, other study observations demonstrate that gut microbiota stimulates monosaccharides absorption from the gut lumen and hence enhances intestine absorption capacity.[44] Gut microbiota coordinates with increased hepatic lipogenesis by promoting the storage of calories from the diet as fat, through suppression of fasting-induced adipose factor, resulting in increased lipoprotein lipase activity in adipocytes. Moreover, the gut microbiota has been also found an active player in fatty acid oxidation through β-oxidation. The level of carnitine palmitoyl transferase and acetyl-CoA is found high in the presence of dietary fats.[48] [Figure 1]

Therapeutic approaches for the treatment of type 2 diabetes through gut microbiota

Probiotic approach

Probiotics are live microorganisms administered in sufficient amounts to give a health benefit to the host such as humans.[54] *Lactobacillus* genera such as *L. plantarum* 299 v, *Lactobacillus acidophilus* NCFM, and *L. gasseri* SBT2055 strain are majorly used because of beneficial effects on glucose metabolism.[55-57] The effect may appear to be discordant, as some *Lactobacillus* species have been shown to be increased in T2D. So far, increasing level of *Lactobacillus* species in T2D has never been demonstrated strong causative agent for the disease. Therefore, it is imperative to investigate other beneficial bacteria that are decreased in patients with diabetes.

Antibiotics

Antibiotics inhibit the growth of microorganisms. The administration of these antimicrobial agents is another viable option to modulate gut microbiota. In this regard, the study suggests that norfloxacin and ampicillin in ob/ob mice modulate gut microbiota which improves glucose tolerance of mice by altering the genes involved in inflammation and metabolism, by changing the hormonal, inflammatory, and metabolic status.[58] However, the approach also seems to be nonspecific because together with harmful bacteria, many beneficial bacteria are also killed during treatment. Moreover, drug resistance is another serious problem due to the regular use of antibiotics.

Bariatric surgery

Bariatric surgery has become a promising treatment that not only reduces weight but also improves or resolves T2D in obese patients.[59] It gives the opportunity to study the gut microbiota profile and its association and beneficial metabolic/inflammatory effects during weight loss and resolution of T2D. In addition, the complete characterization of T2D remission determinants and unraveling the effect of surgery on T2D-associated disorders are other shortcomings of bariatric surgery.

Gut microbiota transfer

The process of transferring gut microbiota samples from a healthy individual to a diabetic one is able to increase the levels of butyrate-producing bacteria and insulin sensitivity in insulin-resistant recipients.[60] Therefore, it is suggested that the transfer of the microbiota from fecal content might be developed as a therapeutic strategy to enhance insulin sensitivity in humans. However, this type of strategy to control diabetes in humans is currently a proof-of-concept rather than a potential therapy.

Nonbacterial colonizers of the gut

In addition to the classical probiotic, e.g., bacteria, several other types of living gut organisms might contribute to the therapeutic purpose for treating hyperglycemia. However, current knowledge on fungi, archaea, and helminths and their association with host glycemia and their contribution to health and disease remain in its infancy.[61] Therefore, this approach needs to explore further.

Nutrition in the management of glycemia-related dysbiosis

Nutrition plays a vital role in the management of T2D. Indeed, some nutrients are able to decrease the postprandial (PP) glucose response while some nutrients are also found to increase the response of PP glucose. It is reported that around 80% of T2D cases are preventable by just adopting a healthy diet and increasing physical activity.[62] Diet is a major factor in metabolic disorders because it helps to shape the gut microbiota. There are various studies to claim that the gut microbiota responds rapidly to large changes in diet, and even in many cases, the composition and function of the gut microbiota shift within 1–2 days.[14,63] These rapid dynamics and long-term dietary habits are still critical in determining the gut composition of an individual,[64] and further, the effectiveness of a specific diet largely relies on the initial composition of the gut microbiota.[65] It has been shown that the traditional rural population has diverse gut microbiota as compared to Western populations because of their different diet (fiber and fat content).[66] A study on 800 people revealed that the gut microbiome in an individual can make food healthy for one person whereas unhealthy for

another.[12] Hence, personalized diets can be recommended to T2D patients.

Personalized treatment in Ayurveda

All human beings are almost identical, but only 10% similarity is found in the gut microbiota from one person to another.[67] Various related agencies are doing efforts to guide people to manage the disease and lead healthy life. Still, generalized dietary and lifestyle guidelines for a particular disease are being formulated and prescribed for decades. However, the pandemic rise in metabolic diseases keeps on increasing. Now, it has become quite clear that the one-fit-for-all diet approach does not work, as there is a significant variation in the individual to individual in response to diet and lifestyle interventions. Technological advancement has cleared the source of this variation due to the genome and microbiome contributing to the unique dietary responses of an individual. However, variations in individuals' genomes influence the bioavailability and metabolism of nutrients, whereas microbes' functional potential, metabolite production, and metabolism modulation are influenced by inter-individual gut microbiota composition. Therefore, quantification and incorporation of these factors into a personalized nutrition approach may enable practitioners to wisely include individuals' nutritional recommendations for metabolic disorders.[68]

Ayurveda is the most comprehensive, holistic, and personalized health-care system based on scientific principles. Every person has a unique *Prakriti* and one can be considered healthy if the *Prakriti*-based *Doshas* (physiological entities) remain balanced. However, the imbalance in *Doshas* leads to diseases in an individual. Hence, the ayurvedic physician detects the extent of imbalance meant in *Doshas* and brings them back to normal by using drugs, diet, or changes in lifestyle and environment.[69] *Prakriti* is a result of the relative proportion of three *Doshas,* i.e., *Vata*, *Pitta,* and *Kapha*, which are genetically determined and influenced by the environment during development, especially maternal diet and lifestyle, and the age of the transmitting parents. Ethnicity, familial characteristics, and place of origin are also suggested to influence the development of *Prakriti*. The persons with different *Prakriti* have different body structures, mental makeup, even tolerance to various types of food and environment, and susceptibility to various diseases. In addition, the effect of various diets, lifestyles, environments, and treatments is different on the different *Prakriti*. Therefore, the theory of *Prakriti* provides a different paradigm for medical practitioners to understand the disease and make this system deliver personalized medicine for everyone. Even by knowing newborns, *Prakriti* can lead to inculcation and adoption of lifestyles to prevent chronic diseases and improve a healthy high-quality life.

Personalized diet and lifestyle in Ayurveda to manage glycaemia

Ayurveda emphasizes preventive and promotive aspects of health rather than curative. Dietetic and lifestyle are very much important for a healthy life, even in the present scenario, but hardly anyone appropriately follows them. As a result, there is a tremendous rise in lifestyle disorders as pandemics, T2D being the most menacing among them.[62] Ayurveda has also emphasized more on the importance of diet and lifestyle. Lifestyle modification and intervention based on the fundamental concept of *Tridosha* and *Prakriti* are helpful to maintain health. Selection of a preventive and curative regimen is principally based on a phenotypic assessment of a person which includes *Prakriti*. Distinct properties and functions have been attributed to each *Dosha*. For instance, *Vata* is responsible for the shape, cell division, signaling, movement, excretion of wastes, and cognition. *Vata* also regulates the activities of *Kapha* and *Pitta*. *Kapha* is responsible for the growth and maintenance of the structure, storage, and stability. *Pitta* is primarily responsible for metabolism, thermoregulation, energy homeostasis, pigmentation, vision, and host surveillance. Therefore, diversity in appearance in a population is because of a variety of relative proportions of *Doshas* resulting in seven possible constitutional types, namely *Vata*, *Pitta*, *Kapha*, *Vata-Pitta*, *Pitta-Kapha*, *Vata-Kapha,* and *Vata-Pitta-Kapha*.[70] According to Ayurveda, diet and lifestyle include the mode of food preparation, raw materials, food combinations, food timings, timings of work and rest, types of work, modes of entertainment and recreation, surrounding environment, and *Yoga*.

Ayurveda gives utmost importance to the maintenance of *Pathya Ahara* (wholesome diet). Further, it is stated that if a person practices a wholesome diet and activities suitable to all *Dhatus* (tissues), then he will never suffer from T2D.[71] As per Ayurveda, proper diet and lifestyle for the patient include multifactors like avoiding T2D-causing risk factors including a fatty diet and sedentary lifestyle. Diet for obese diabetic patients should be *Apatarpanaguna* (property of depleting and cleansing) and heavy for digestion whereas, for lean diabetic patients, a diet should be *Santarpanaguna* (property of nourishing and enriching) and light for digestion. In addition, lean diabetic patients' diets should not increase fat. The diet should be proper as per *Prakriti* (constitution), *Karana* (processing), *Samyoga* (combination) *Rashi* (quantity), *Desha* (place), *Kala* (time), *Upayogasamstha* (intake of food), and *Upayokta* (morality of individual who takes it). Further, the diet should be taken as per *Ritu* (seasons), in accordance with *Prakriti* and *Dosha*.

According to Ayurveda, personalized and wholesome diets[72] for different seasons are given in Table 1, which can be recommended for T2D patients also.

Pathyaahara (wholesome diet) for type 2 diabetes

As per Ayurveda, a diet rich in fiber and complex carbohydrates, and poor in fat components is most suitable for T2D patients. This kind of diet provides substrates for the gut microbial metabolism because bacteria are specialized in the fermentation of different substrates. A complex diet provides a range of factors for microbial growth and inhibition for specific phylotypes.[73] These allow a wide range of microbiota

Table 1: Personalized and wholesome diets for different seasons

Season (*Ritu*)	Status of *Dosha*	Wholesome diet
Winter (*Shishira*)	In this season, digestion becomes more powerful and the level of *Vata* is increased. Therefore, a specified diet, exercise, and massage are recommended to reduce *Vata*	Rice, wheat, sesame, milk and its products, fats, edible oil, flour products, green vegetables, ginger, garlic, myrobalan, and long pepper
Spring (*Vasantha*)	Increased *Kapha* is liquefied by the heat of the sun, which causes reduced digestive activity. Therefore, easy digestive food and vigorous physical exercise are recommended during this season	Rice, wheat, maize, barley, green gram, red gram, lentil, honey, khadir, cocograss, ginger, turmeric, tulsi, and neem
Summer (*Grishma*)	Due to sun and dryness, *Kapha* decreases and *Vata* increases which results in dehydration, exhaustion, lack of energy, and lethargicity. Hence, maintaining *Kapha* and *Vata*, there should be a selection of plenty of liquids and cool place to reside	Rice, green gram, mango, watermelon, fruit juices, coconut water, buttermilk, curd with pepper, meat soups, jaggery, and fennel
Rainy (*Varsha*)	The digestive activities weaken further and get vitiated by *Vata* due to lack of sunshine. Therefore, easy digestive food and less physical exertion should be adopted during the rainy season	Seasoned barley, rice, wheat, meat soups, vegetable soups, long pepper, chavak, zinger, and rock salt
Autumn (*Sharad*)	The dry and hot atmosphere aggravates *Pitta* due to sudden exposure to sunlight after the rain and cool atmosphere. Therefore, easy digestive food and bath with warm water should be adopted	Common cereals, pulses, green gram, the flesh of animals such as goat, chicken and rabbit, pointed gourd, fenugreek, Indian gooseberry, and dates
Late autumn (*Hemanta*)	Likewise cold and dewy season, during the winter season, the digestion becomes more powerful and the level of *Vata* is increased. Therefore, a specified diet, exercise, and dry massage are recommended to reduce *Vata*	Rice, wheat, sesame, milk and its products, fats, edible oil, flour products, green vegetables, ginger, garlic, myrobalan, and long pepper

to grow and ensure diversity in the gut. Furthermore, the end products of these bacterial metabolisms, especially vitamins and SCFAs, are vital for human health. Generally, complex carbohydrates such as cereals, whole grains, and vegetables are recommended for at least 50% of diabetic diet whereas simple sugars such as table sugar, honey, candy, jam, cakes, and pastries are contraindicated. It is evident that vegetable and fruit fibers delay sugar digestion and absorption, which improves insulin sensitivity and glucose utilization, and hence, reduces the risk of diabetes. Spices, the food adjuncts, are not only flavoring, coloring, and preservative agents, but these also have beneficial physiological effects including some antidiabetic effects like short-term blood glucose lowering and long-term glucose tolerance improving effects. Normally, a typical conventional approach would recommend a diet that comprises 60%–65% carbohydrate, 25%–35% fat, and 10%–20% protein, with limited or no alcohol consumption.[74] If the Ayurvedic diet is taken into eating routine, it needs to (a) intake six *Rasas* or tastes (sweet, salty, sour, bitter, pungent, and astringent); (b) eat mindfully and with concentration; (c) eat slowly by chewing; (d) eat before food get cold; (e) eat the proper quantity of food; and (f) eat only when your previous meal has been digested. The patients with T2D having *Vata Prakriti* should be given 3–4 meals per day whereas the patients having *Pitta* and *Kapha Prakriti* should be given 3 and 2 meals per day, respectively, after a certain interval.[75]

Pathya Vihara (wholesome routine) for type 2 diabetes

For preventing T2D, it has been recommended that walking 100 *Yojan* in 100 days, i.e., 1 *Yojan* per day (1 *Yojan* is 7.5 km). Exercise is also important as it has been found that lack of exercise is one of the main factors for bad glycemic control in chronic cases. The risk of getting diabetes can be reduced by regular exercise and maintaining an ideal body weight. Here, it is also worth noting that obese patients with T2D are advised to do exercise, horse riding, wrestling, and vigorous walking while the lean diabetic patient does not need, as they need to protect their strength as obese and lean patients have different etiology and lifestyle intervention.[71,76] Waking up, sleeping, and eating time is also important and should be decided for healthy living. Day napping and short night sleep are reported as potential risk factors for diabetes.[77] It is evident that physical exercise has also been linked to an increase in gut biodiversity.[78] Therefore, all lifestyles or activities help in the management of glucose in the blood.

It has been also seen that lifestyle intervention can reduce or delay >60% risk factor in 3 years in high risk of impaired glucose tolerance in patients with T2D. These include intense lifestyle modification with the aim of losing more than 7% of weight and 2.30 h physical activity per week. It emphasized diet habits by including fiber in food and physical exercise can help to reduce blood glucose levels.[79]

Role of Ayurvedic diet in the management of type 2 diabetes through modulation of gut microbiota

An ayurvedic diet is enriched with fiber, polyphenols, and complex carbohydrates which may manage glucose levels by following approaches.

- Ayurvedic diet maintains the intestinal mucous membranes by introducing prebiotic soluble fiber to create the best possible environment for beneficial gut microbiota to flourish
- Introduce probiotics that remove harmful, nonfunctional gut microbiota and allow to beneficial, permanent residents to propagate
- Allow boosting permanent resident microbiota to complete the process of achieving flourishing microbiota diversity
- Allow maintaining the composition of the beneficial microbiota, probiotics, and small amounts of fermented foods.

A generalized diet is thought to be fit for all, but this is not the case. As, every person responds differently to the same food.

Moreover, in the case of patients with T2D, it is not affordable that glucose level goes high after consuming certain food which is generally considered to have a low glycemic index in another person that is mainly because of different *Prakriti* and gut microbiota. The Ayurvedic diet is a personalized diet decided on the basis of the *Prakriti* of the person. It is considered a perfect diet and enriches beneficial bacteria in the gut which lower the glucose level in the blood. A recent study by Shondelmyer *et al*.[80] also found that the ancient Thali diet is useful in maintaining healthy gut microbiota and also found to improve immunity. Therefore, it is possible that the Ayurvedic diet (wholesome diet) along with a wholesome lifestyle can enrich the beneficial bacteria in the gut and lower the blood glucose level in T2D. [Figure 2]

Despite many ways to control T2D, the prevalence of the disease has increased substantially in the past few decades throughout the world. Various earlier studies concluded that there is a certain composition of microbiota found in every human that is responsible for human health. Alteration in this composition causes various metabolic disorders including T2D. Now, it has been confirmed that gut microbiota plays a key role in the development of T2D. The study found even the composition of gut microbiota in the early stage is different from the fully developed stage of T2D. *Verrucomicrobia*, a microbiota, is considered a potential marker of T2D as it has a lower abundance in diabetic patients.[27]

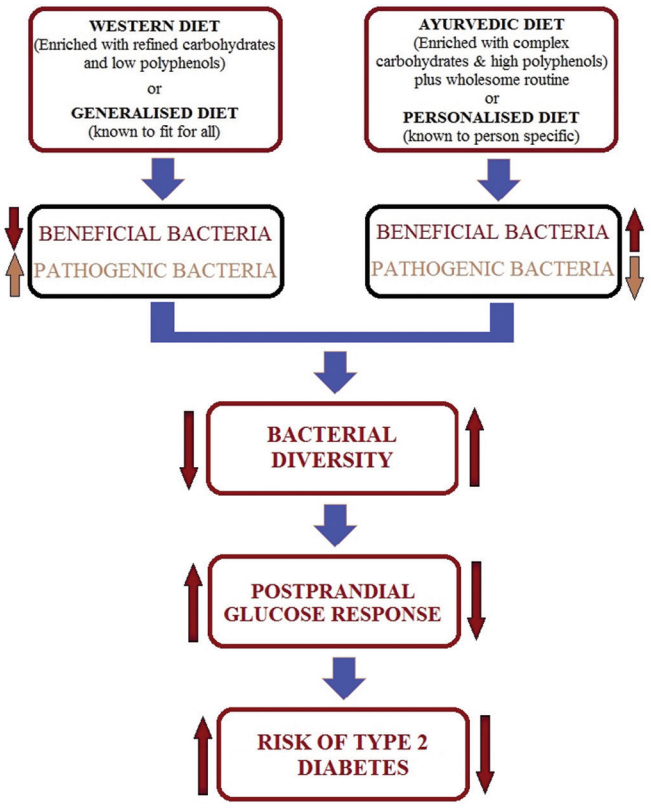

Figure 2: A schematic diagram showing the effect of Western and Ayurvedic diet on the risk of T2D. Upward arrow (↑) showing increase and downward arrow (↓) showing decrease. T2D: Type 2 diabetes

In T2D, diet plays a significant role in the therapeutic strategy to maintain the sugar level of a diabetic patient and prevent micro- and macrovascular complications. Various diets such as Western pattern diet and Mediterranean diets are in use for the management of blood glucose levels, but these all are generalized diets and not person specific. On the other hand, an Ayurveda diet is recommended on the basis of an individual's body constitution, time, season, and processing. This diet is rich in fiber which flourishes the beneficial microbiota in the gut.[80] Even, meta-analysis studies showed that when total dietary fiber was separated into cereal, fruit, and vegetable fiber groups, only a cereal fiber-rich diet significantly reduced the incidence of developing T2D as compared to participants who intake the lowest fiber in the diet.[81-84]

The beneficial bacteria proliferate and reduce the glucose level in the blood,[85] while other bacterial species increase the level of glucose in the bloodstream.[25]

Similarly, lifestyle or routine is evident to manage the glucose level. Dietary and lifestyle plans should be made in accordance with the day-to-day requirement of an individual. Hence, by knowing the constitution of gut microbiota, the level of glucose-lowering and glucose-increasing gut microbiota can be increased and decreased, respectively. This approach can not only be practiced in T2D but also in all metabolic disorders. Here, it is important to mention that the concepts of Ayurveda are not India specific, but they can apply to all populations in the world.

Conclusion

There are many ways, through which gut microbiota cause T2D. Similarly, several techniques are being used to treat the disease. So far, no cure is available for diabetes, but the disease can go into remission. In T2D, diet and physical exercise play a significant role in the therapeutic strategy to maintain the sugar level of a diabetic patient and prevent micro- and macrovascular complications. The Ayurveda diet is a personalized diet and rich in fiber which flourishes the beneficial microbiota in the gut. The beneficial bacteria proliferate and reduce the glucose level in the blood. Likewise, lifestyle or routine is evident to manage the glucose level. Dietary and lifestyle plans should be made in accordance with the requirement of an individual, hence called personalized. The present review concludes that the diet of a diabetic patient can be decided by assessing the gut microbiota and the microbiota can be modulated by modifying the diet to manage T2D.

Acknowledgments

The authors are thankful to the National Medicinal Plants Board, Ministry of AYUSH.

Financial support and sponsorship

This study was financially supported by the Government of India (Grant No. Z.18017/187/CSS/R and D/UK-01/2017-18-NMPB-IV A).

Conflicts of interest

There are no conflicts of interest.

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